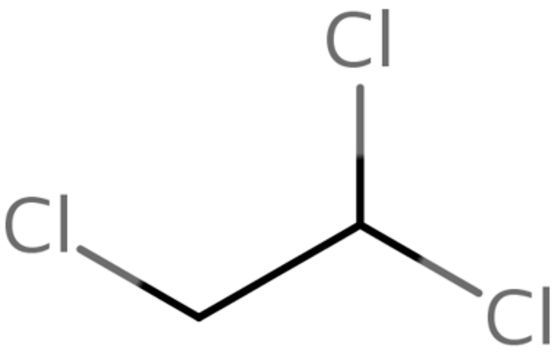
United States
Environmental Protection Agency

May 2026
Office of Chemical Safety and
Pollution Prevention

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

Systematic Review Support Document for the Draft Risk Evaluation

CASRN: 79-00-5



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 1,1,2-Trichloroethane* 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 1,1,2-Trichloroethane*.

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:	Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical:	1,1,2-Trichloroethane
Exposure Type:	Parent compound
HERO ID:	11164566
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 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite-Neat

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion setup is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). An infinite dose of 1,1,2-trichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or 1,2-dichloroethane) was applied to human skin (at least 5 replicates; surface area of 0.64 cm2). Volume applied (125 – 640 uL) was necessary to achieve the desired application rate of 100 uL/cm2. Human skin samples were dermatomed; samples contained epidermis and some dermis. The thickness of skin samples ranged from 200 to 400 um, the exact thickness was not reported. The skin was exposed to test substance under occluded conditions (PTFE screw lid) for 24 hours. The receptor solution (water fortified with 6% polyethoxyoleate 20 oleyl ether). OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. The flow rate of receptor fluid was 1.5 mL/hour. It was not specified whether the receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (volume not reported) were collected at 10 minutes, 30 minutes, 1 hour, 2 hours, and every 2 hours hence forth for 24 hours (16 samples) post-application and analyzed for radioactivity. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice background was considered to be below the limit of accurate determination.” A steady state was reached.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. The percentage of recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. Coefficients of variation (CV) values were not reported but could be determined based on the SD relative to the mean.

Domain 3: Exposure Characterization

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite-Neat

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of the test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however, the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The study did not use the same volume across all samples (ranging from 64ul – 640ul) however this was done in order to maintain a constant application rate and not expected to substantially impact results. The skin surface area of 0.64 cm2 was consistent across groups. However, the skin thickness was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and was 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 test substance was performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels”.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness skin samples were obtained from 15 female (race not reported) donors ranging in age from 31-70 years old, following elective surgery. The samples were stored frozen at -20 degrees C +/-10 degrees C. Prior to use, the skin samples were thawed, wiped to remove residual fat and blood, re-hydrated in purified water, and dermatomed using a mini-dermatome. The thickness ranged from 200 to 400 uM. The skin contained epidermis and some dermis. These methods were in agreement with OECD guidelines which state split thickness (dermatomed) skin is preferred. 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 5-10 replicates/dose.
Domain 5: Outcome Assessment				

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite-Neat

Domain	Metric		Rating	Comments
	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 and maximum absorption rate. An application rate of 100 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2 for infinite exposures.
	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 to allow for steady state portion of absorption profile to be obtained. Methods for determination of radioactivity are reported. “Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination.” Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post-exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial time point were included in the analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin has a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. A supposed equipment failure resulted in anonymously low TEWL measurements at 24 hours in the 10% 1,1,2-TCE group. An additional 4 samples were tested; results (Kp determinations) were comparable across all 10 samples. One replicate in the Neat group had a 24-hr TEWL value (27.9) above the criteria cut-off. There is no indication that this sample was excluded.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. The test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite-Neat

Domain	Metric		Rating	Comments
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported. Mathematical calculations used to determine Kp are reported and were appropriate. The Kp was based on the steady-state part of the absorption curve. CV values were not reported for Kp/flux measurements and maximum absorption rate, however the study provided sufficient data to independently calculate them.Calculated CV for Kp and maximum flux for the neat group are >50% for neat, but sufficient data are available for EPA to calculate an alternate value. Calculated CV for Kp and/or maximum flux for all other dose groups were >25% and <50%.
	Metric 20:	Data interpretation	Medium	The Kp and mean maximum absorption rate were derived from an appropriate exposure condition (infinite dose). The author state that "data indicates that true sink conditions were not maintained for some replicates. . . due to the volatility of the test item". Despite this, they do conclude that sufficient data were obtained to calculate Kp over the steady state portion of the absorption profile. Recovery was not reported but this determination is not relevant for infinite dose applications.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 50% in 1,2-DCE

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion setup is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). An infinite dose of 1,1,2-trichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or 1,2-dichloroethane) was applied to human skin (at least 5 replicates; surface area of 0.64 cm2). Volume applied (125 – 640 uL) was necessary to achieve the desired application rate of 100 uL/cm2. Human skin samples were dermatomed; samples contained epidermis and some dermis. The thickness of skin samples ranged from 200 to 400 um, the exact thickness was not reported. The skin was exposed to test substance under occluded conditions (PTFE screw lid) for 24 hours. The receptor solution (water fortified with 6% polyethoxyoleate 20 oleyl ether). OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. The flow rate of receptor fluid was 1.5 mL/hour. It was not specified whether the receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (volume not reported) were collected at 10 minutes, 30 minutes, 1 hour, 2 hours, and every 2 hours hence forth for 24 hours (16 samples) post-application and analyzed for radioactivity. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice background was considered to be below the limit of accurate determination.” A steady state was reached.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. The percentage of recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. Coefficients of variation (CV) values were not reported but could be determined based on the SD relative to the mean.

Domain 3: Exposure Characterization

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Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 50% in 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of the test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however, the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The study did not use the same volume across all samples (ranging from 64ul – 640ul) however this was done in order to maintain a constant application rate and not expected to substantially impact results. The skin surface area of 0.64 cm2 was consistent across groups. However, the skin thickness was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and was 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 test substance was performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels”.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full-thickness skin samples were obtained from 15 female (race not reported) donors ranging in age from 31-70 years old, following elective surgery. The samples were stored frozen at -20 degrees C +/-10 degrees C. Prior to use, the skin samples were thawed, wiped to remove residual fat and blood, re-hydrated in purified water, and dermatomed using a mini-dermatome. The thickness ranged from 200 to 400 uM. The skin contained epidermis and some dermis. These methods were in agreement with OECD guidelines which state split thickness (dermatomed) skin is preferred. 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 5-10 replicates/dose.
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Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 50% in 1,2-DCE

Domain	Metric		Rating	Comments
	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 and maximum absorption rate. An application rate of 100 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2 for infinite exposures.
	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 to allow for steady state portion of absorption profile to be obtained. Methods for determination of radioactivity are reported. "Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination." Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post-exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial time point were included in the analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin has a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. A supposed equipment failure resulted in anonymously low TEWL measurements at 24 hours in the 10% 1,1,2-TCE group. An additional 4 samples were tested; results (Kp determinations) were comparable across all 10 samples. One replicate in the Neat group had a 24-hr TEWL value (27.9) above the criteria cut-off. There is no indication that this sample was excluded.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. The test substance was demonstrated to be soluble in the receptor fluid.
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Unique ID: Infinite- 50% in 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported. Mathematical calculations used to determine Kp are reported and were appropriate. The Kp was based on the steady-state part of the absorption curve. CV values were not reported for Kp/flux measurements and maximum absorption rate, however the study provided sufficient data to independently calculate them.Calculated CV for Kp and maximum flux for the neat group are >50% for neat, but sufficient data are available for EPA to calculate an alternate value. Calculated CV for Kp and/or maximum flux for all other dose groups were >25% and <50%.
	Metric 20:	Data interpretation	Medium	The Kp and mean maximum absorption rate were derived from an appropriate exposure condition (infinite dose). The author state that "data indicates that true sink conditions were not maintained for some replicates. . . due to the volatility of the test item". Despite this, they do conclude that sufficient data were obtained to calculate Kp over the steady state portion of the absorption profile. Recovery was not reported but this determination is not relevant for infinite dose applications.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

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Exposure Type: Parent compound
HERO ID: 11164566
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 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
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	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Unique ID: Infinite- 50% in IPM

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set-up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). An infinite dose of 1,1,2-trichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or 1,2-dichloroethane) was applied to human skin (at least 5 replicates; surface area of 0.64 cm2). Volume applied (125 – 640 uL) was necessary to achieve the desired application rate of 100 uL/cm2. Human skin samples were dermatomed; samples contained epidermis and some dermis. The thickness of skin samples ranged from 200 to 400 um, the exact thickness was not reported. The skin was exposed to test substance under occluded conditions (PTFE screw lid) for 24 hours. The receptor solution (water fortified with 6% polyethoxyoleate 20 oleyl ether). OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. The flow rate of receptor fluid was 1.5 mL/hour. It was not specified whether the receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (volume not reported) were collected at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours henceforth for 24 hours (16 samples) post-application and analyzed for radioactivity. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice background was considered to be below the limit of accurate determination.” A steady state was reached.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. The percentage of recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. Coefficients of variation (CV) values were not reported but could be determined based on the SD relative to the mean.

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 50% in IPM

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The study did not use the same volume across all samples (ranged from 64ul – 640ul) however this was done in order to maintain a constant application rate and not expected to substantially impact results. The skin surface area of 0.64 cm2 was consistent across groups. However, the skin thickness was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and was 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 test substance was performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels”.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full thickness skin samples were obtained from 15 female (race not reported) donors ranging in age from 31-70 years old, following elective surgery. The samples were stored frozen at -20 degrees C +/-10 degrees C. Prior to use, the skin samples were thawed, wiped to remove residual fat and blood, re-hydrated in purified water, and dermatomed using a mini-dermatome. The thickness ranged from 200 to 400 uM. The skin contained epidermis and some dermis. These methods were in agreement with OECD guidelines which state split thickness (dermatomed) skin is preferred. 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 5-10 replicates/dose.
Domain 5: Outcome Assessment				

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 50% in IPM

Domain	Metric		Rating	Comments
	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 and maximum absorption rate. An application rate of 100 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2 for infinite exposures.
	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 to allow for steady state portion of absorption profile to be obtained. Methods for determination of radioactivity are reported. "Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination." Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial timepoint. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. A supposed equipment failure resulted in anonymously low TEWL measurements at 24 hours in the 10% 1,1,2-TCE group. An additional 4 samples were tested; results (Kp determinations) were comparable across all 10 samples. One replicate in the Neat group had a 24-hr TEWL value (27.9) above the criteria cut-off. There is no indication that this sample was excluded.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. The test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 50% in IPM

Domain	Metric		Rating	Comments
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported. Mathematical calculations used to determine Kp are reported and were appropriate. The Kp was based on the steady-state part of the absorption curve. CV values were not reported for Kp/flux measurements and maximum absorption rate, however the study provided sufficient data to independently calculate them.Calculated CV for Kp and maximum flux for the neat group are >50% for neat, but sufficient data are available for EPA to calculate an alternate value. Calculated CV for Kp and/or maximum flux for all other dose groups were >25% and <50%.
	Metric 20:	Data interpretation	High	The Kp and mean maximum absorption rate were derived from an appropriate exposure condition (infinite dose). Recovery was not reported but this determination is not relevant for infinite dose applications.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
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 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 10% in IPM

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set-up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). An infinite dose of 1,1,2-trichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or 1,2-dichloroethane) was applied to human skin (at least 5 replicates; surface area of 0.64 cm2). Volume applied (125 – 640 uL) was necessary to achieve the desired application rate of 100 uL/cm2. Human skin samples were dermatomed; samples contained epidermis and some dermis. The thickness of skin samples ranged from 200 to 400 um, the exact thickness was not reported. The skin was exposed to test substance under occluded conditions (PTFE screw lid) for 24 hours. The receptor solution (water fortified with 6% polyethoxyoleate 20 oleyl ether). OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. The flow rate of receptor fluid was 1.5 mL/hour. It was not specified whether the receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (volume not reported) were collected at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours henceforth for 24 hours (16 samples) post-application and analyzed for radioactivity. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice background was considered to be below the limit of accurate determination.” A steady state was reached.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. The percentage of recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. Coefficients of variation (CV) values were not reported but could be determined based on the SD relative to the mean.

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 10% in IPM

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The study did not use the same volume across all samples (ranged from 64ul – 640ul) however this was done in order to maintain a constant application rate and not expected to substantially impact results. The skin surface area of 0.64 cm2 was consistent across groups. However, the skin thickness was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and was 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 test substance was performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels”.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full thickness skin samples were obtained from 15 female (race not reported) donors ranging in age from 31-70 years old, following elective surgery. The samples were stored frozen at -20 degrees C +/-10 degrees C. Prior to use, the skin samples were thawed, wiped to remove residual fat and blood, re-hydrated in purified water, and dermatomed using a mini-dermatome. The thickness ranged from 200 to 400 uM. The skin contained epidermis and some dermis. These methods were in agreement with OECD guidelines which state split thickness (dermatomed) skin is preferred. 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 5-10 replicates/dose.
Domain 5: Outcome Assessment				

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 10% in IPM

Domain	Metric		Rating	Comments
	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 and maximum absorption rate. An application rate of 100 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2 for infinite exposures.
	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 to allow for steady state portion of absorption profile to be obtained. Methods for determination of radioactivity are reported. “Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination.” Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial timepoint. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. A supposed equipment failure resulted in anonymously low TEWL measurements at 24 hours in the 10% 1,1,2-TCE group. An additional 4 samples were tested; results (Kp determinations) were comparable across all 10 samples. One replicate in the Neat group had a 24-hr TEWL value (27.9) above the criteria cut-off. There is no indication that this sample was excluded.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. The test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 10% in IPM

Domain	Metric		Rating	Comments
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported. Mathematical calculations used to determine Kp are reported and were appropriate. The Kp was based on the steady-state part of the absorption curve. CV values were not reported for Kp/flux measurements and maximum absorption rate, however the study provided sufficient data to independently calculate them.Calculated CV for Kp and maximum flux for the neat group are >50% for neat, but sufficient data are available for EPA to calculate an alternate value. Calculated CV for Kp and/or maximum flux for all other dose groups were >25% and <50%.
	Metric 20:	Data interpretation	High	The Kp and mean maximum absorption rate were derived from an appropriate exposure condition (infinite dose). Recovery was not reported but this determination is not relevant for infinite dose applications.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation:	Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical:	1,1,2-Trichloroethane
Exposure Type:	Parent compound
HERO ID:	11164566
Unique ID:	Infinite- 10% in 1,2-DCE

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 10% in 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set-up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). An infinite dose of 1,1,2-trichloroethane (neat, 50%, or 10% dissolved in either isopropyl myristate or 1,2-dichloroethane) was applied to human skin (at least 5 replicates; surface area of 0.64 cm2). Volume applied (125 – 640 uL) was necessary to achieve the desired application rate of 100 uL/cm2. Human skin samples were dermatomed; samples contained epidermis and some dermis. The thickness of skin samples ranged from 200 to 400 um, the exact thickness was not reported. The skin was exposed to test substance under occluded conditions (PTFE screw lid) for 24 hours. The receptor solution (water fortified with 6% polyethoxyoleate 20 oleyl ether). OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. The flow rate of receptor fluid was 1.5 mL/hour. It was not specified whether the receptor fluid was continuously stirred as per OECD 428 guidelines. Receptor fluid samples (volume not reported) were collected at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours henceforth for 24 hours (16 samples) post-application and analyzed for radioactivity. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice background was considered to be below the limit of accurate determination.” A steady state was reached.
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. The percentage of recovered test substance was not reported. However, recovery determination is not generally relevant for studies only determining a Kp. Coefficients of variation (CV) values were not reported but could be determined based on the SD relative to the mean.

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 10% in 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The study did not use the same volume across all samples (ranged from 64ul – 640ul) however this was done in order to maintain a constant application rate and not expected to substantially impact results. The skin surface area of 0.64 cm2 was consistent across groups. However, the skin thickness was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/cm2. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	Exposure duration (24-hours) was reported and was 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 test substance was performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels”.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full thickness skin samples were obtained from 15 female (race not reported) donors ranging in age from 31-70 years old, following elective surgery. The samples were stored frozen at -20 degrees C +/-10 degrees C. Prior to use, the skin samples were thawed, wiped to remove residual fat and blood, re-hydrated in purified water, and dermatomed using a mini-dermatome. The thickness ranged from 200 to 400 uM. The skin contained epidermis and some dermis. These methods were in agreement with OECD guidelines which state split thickness (dermatomed) skin is preferred. 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 5-10 replicates/dose.
Domain 5: Outcome Assessment				

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 10% in 1,2-DCE

Domain	Metric		Rating	Comments
	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 and maximum absorption rate. An application rate of 100 uL/cm2 was used, which is in agreement with OECD guideline of using >100 uL/cm2 for infinite exposures.
	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 to allow for steady state portion of absorption profile to be obtained. Methods for determination of radioactivity are reported. “Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination.” Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial timepoint. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. A supposed equipment failure resulted in anonymously low TEWL measurements at 24 hours in the 10% 1,1,2-TCE group. An additional 4 samples were tested; results (Kp determinations) were comparable across all 10 samples. One replicate in the Neat group had a 24-hr TEWL value (27.9) above the criteria cut-off. There is no indication that this sample was excluded.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. The test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Infinite- 10% in 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 19:	Data analysis	Low	Means and standard deviations were calculated and reported. Mathematical calculations used to determine Kp are reported and were appropriate. The Kp was based on the steady-state part of the absorption curve. CV values were not reported for Kp/flux measurements and maximum absorption rate, however the study provided sufficient data to independently calculate them.Calculated CV for Kp and maximum flux for the neat group are >50% for neat, but sufficient data are available for EPA to calculate an alternate value. Calculated CV for Kp and/or maximum flux for all other dose groups were >25% and <50%.
	Metric 20:	Data interpretation	High	The Kp and mean maximum absorption rate were derived from an appropriate exposure condition (infinite dose). Recovery was not reported but this determination is not relevant for infinite dose applications.
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
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 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-Neat

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). Finite doses of 1,2-dichloroethane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or 1,2-dichloroethane was applied to human skin (at least 4 replicates; surface area of 0.64 cm2). Test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). This is in agreement with OECD guidelines. The cells were semi occluded by charcoal filter in the neck of the donor cell. Thickness of skin sample ranged from 200 to 400 um, exact thickness was not reported. The receptor solution was water fortified with 6% polyethoxyoleate 20 oleyl ether. OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. Flow rate of receptor fluid was 1.5 mL/hour. After 8 hours skin was washed. ”The surface of the membrane was rinsed three times (3 x 0.5 mL) with a mild solution of Dove™ soap in water (ca. 1%). The skin surface was swabbed twice with cotton buds soaked with the liquid soap solution. Finally, the membrane was rinsed with a small volume (0.5 mL) of water and a further cotton bud used to swab the surface of the membrane until dry”. Charcoal filters were collected at 8 and 24-hours post-dosing. Receptor fluid samples (volume not reported) were collected for one hour pre-dose and post-dose at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours hence forth for 24 hours (16 samples) and analyzed for radioactivity. After 24 hours, skin was tap-stripped up to 5 times. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice the background level was considered to be below the limit of accurate determination.”
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. Coefficients of variation (CV) values were reported. Further discussion of the CVs is provided in Metric 19. The percent recovery was 96.72% (neat), 100.03% (50% in IPM), 95.33% (10% in IPM), 105.43% (1% in IPM), 93.54% (50% in 1,2-DCE), 95.70 (10% in 1,2-DCE), and 92.25% (1% in 1,2-DCE).

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-Neat

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The application rate (10 uL/cm3) 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 was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/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. 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 were performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by the authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels.”
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The study used a single batch of radiolabeled 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post-exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial time point were included in the analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin has a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. One replicate in the 10% IPM group did not meet the specified criteria and was excluded. All other samples and replicates meet the requirements at the initial measurement time. 1-2 out of 6 replicates total in the 50% IPM, 10% IPM, and 1% IPM groups had 24-hour TEWL values above the specified criteria. There is no indication that these samples were excluded.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-Neat

Domain	Metric		Rating	Comments
	Metric 13:	Number/Replicates per group	Medium	There were no major reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. Minor deviations (e.g., temporary power outage) were noted and were considered to have no impact on the outcomes or integrity of the study.
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 which is appropriate for finite conditions. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.
	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. Methods for determination of radioactivity are reported. “Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination.” Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at both time points were included in analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were major reported differences among the study replicates that were unrelated to exposure. For the 50% IPM and 1% IPM groups a power outage occurred for 5-10 minutes which caused the pump to stop flowing; no receptor fluid was lost. The authors considered this glitch to no impact on the outcomes or integrity of the study. The test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	High	All statistical methods were described and were appropriate. Absorption estimates were based on appropriate measurements. More than half of the CV values within an individual scenario were <25%.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-Neat

Domain	Metric		Rating	Comments
	Metric 20:	Data interpretation	High	Absorption estimates were calculated appropriately. Measurements included dislodgeable doses from two skin washes, tape stripping, unexposed skin, total unabsorbed, exposed skin, receptor fluid, and receptor chamber fluid. Recovery of the applied test substance was adequate given its volatility (>92%).
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% IPM

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). Finite doses of 1,2-dichloroethane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or 1,2-dichloroethane was applied to human skin (at least 4 replicates; surface area of 0.64 cm2). Test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). This is in agreement with OECD guidelines. The cells were semi occluded by charcoal filter in the neck of the donor cell. Thickness of skin sample ranged from 200 to 400 um, exact thickness was not reported. The receptor solution was water fortified with 6% polyethoxyoleate 20 oleyl ether. OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. Flow rate of receptor fluid was 1.5 mL/hour. After 8 hours skin was washed. ”The surface of the membrane was rinsed three times (3 x 0.5 mL) with a mild solution of Dove™ soap in water (ca. 1%). The skin surface was swabbed twice with cotton buds soaked with the liquid soap solution. Finally, the membrane was rinsed with a small volume (0.5 mL) of water and a further cotton bud used to swab the surface of the membrane until dry”. Charcoal filters were collected at 8 and 24-hours post-dosing. Receptor fluid samples (volume not reported) were collected for one hour pre-dose and post-dose at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours hence forth for 24 hours (16 samples) and analyzed for radioactivity. After 24 hours, skin was tap-stripped up to 5 times. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice the background level was considered to be below the limit of accurate determination.”
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. Coefficients of variation (CV) values were reported. Further discussion of the CVs is provided in Metric 19. The percent recovery was 96.72% (neat), 100.03% (50% in IPM), 95.33% (10% in IPM), 105.43% (1% in IPM), 93.54% (50% in 1,2-DCE), 95.70 (10% in 1,2-DCE), and 92.25% (1% in 1,2-DCE).

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% IPM

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The application rate (10 uL/cm3) 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 was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/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. 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 were performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by the authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels.”
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The study used a single batch of radiolabeled 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post-exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial time point were included in the analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin has a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. One replicate in the 10% IPM group did not meet the specified criteria and was excluded. All other samples and replicates meet the requirements at the initial measurement time. 1-2 out of 6 replicates total in the 50% IPM, 10% IPM, and 1% IPM groups had 24-hour TEWL values above the specified criteria. There is no indication that these samples were excluded.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% IPM

Domain	Metric		Rating	Comments
	Metric 13:	Number/Replicates per group	Medium	There were no major reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. Minor deviations (e.g., temporary power outage) were noted and were considered to have no impact on the outcomes or integrity of the study.
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 which is appropriate for finite conditions. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.
	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. Methods for determination of radioactivity are reported. “Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination.” Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at both time points were included in analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were major reported differences among the study replicates that were unrelated to exposure. For the 50% IPM and 1% IPM groups a power outage occurred for 5-10 minutes which caused the pump to stop flowing; no receptor fluid was lost. The authors considered this glitch to no impact on the outcomes or integrity of the study. The test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	High	All statistical methods were described and were appropriate. Absorption estimates were based on appropriate measurements. More than half of the CV values within an individual scenario were <25%.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% IPM

Domain	Metric		Rating	Comments
	Metric 20:	Data interpretation	High	Absorption estimates were calculated appropriately. Measurements included dislodgeable doses from two skin washes, tape stripping, unexposed skin, total unabsorbed, exposed skin, receptor fluid, and receptor chamber fluid. Recovery of the applied test substance was adequate given its volatility (>92%).
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% IPM

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). Finite doses of 1,2-dichloroethane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or 1,2-dichloroethane was applied to human skin (at least 4 replicates; surface area of 0.64 cm2). Test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). This is in agreement with OECD guidelines. The cells were semi occluded by charcoal filter in the neck of the donor cell. Thickness of skin sample ranged from 200 to 400 um, exact thickness was not reported. The receptor solution was water fortified with 6% polyethoxyoleate 20 oleyl ether. OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. Flow rate of receptor fluid was 1.5 mL/hour. After 8 hours skin was washed. ”The surface of the membrane was rinsed three times (3 x 0.5 mL) with a mild solution of Dove™ soap in water (ca. 1%). The skin surface was swabbed twice with cotton buds soaked with the liquid soap solution. Finally, the membrane was rinsed with a small volume (0.5 mL) of water and a further cotton bud used to swab the surface of the membrane until dry”. Charcoal filters were collected at 8 and 24-hours post-dosing. Receptor fluid samples (volume not reported) were collected for one hour pre-dose and post-dose at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours hence forth for 24 hours (16 samples) and analyzed for radioactivity. After 24 hours, skin was tap-stripped up to 5 times. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice the background level was considered to be below the limit of accurate determination.”
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. Coefficients of variation (CV) values were reported. Further discussion of the CVs is provided in Metric 19. The percent recovery was 96.72% (neat), 100.03% (50% in IPM), 95.33% (10% in IPM), 105.43% (1% in IPM), 93.54% (50% in 1,2-DCE), 95.70 (10% in 1,2-DCE), and 92.25% (1% in 1,2-DCE).

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% IPM

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The application rate (10 uL/cm3) 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 was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/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. 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 were performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by the authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels.”
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The study used a single batch of radiolabeled 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post-exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial time point were included in the analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin has a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. One replicate in the 10% IPM group did not meet the specified criteria and was excluded. All other samples and replicates meet the requirements at the initial measurement time. 1-2 out of 6 replicates total in the 50% IPM, 10% IPM, and 1% IPM groups had 24-hour TEWL values above the specified criteria. There is no indication that these samples were excluded.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% IPM

Domain	Metric		Rating	Comments
	Metric 13:	Number/Replicates per group	Medium	There were no major reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. Minor deviations (e.g., temporary power outage) were noted and were considered to have no impact on the outcomes or integrity of the study.
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 which is appropriate for finite conditions. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.
	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. Methods for determination of radioactivity are reported. “Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination.” Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at both time points were included in analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were major reported differences among the study replicates that were unrelated to exposure. For the 50% IPM and 1% IPM groups a power outage occurred for 5-10 minutes which caused the pump to stop flowing; no receptor fluid was lost. The authors considered this glitch to no impact on the outcomes or integrity of the study. The test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	High	All statistical methods were described and were appropriate. Absorption estimates were based on appropriate measurements. More than half of the CV values within an individual scenario were <25%.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% IPM

Domain	Metric		Rating	Comments
	Metric 20:	Data interpretation	High	Absorption estimates were calculated appropriately. Measurements included dislodgeable doses from two skin washes, tape stripping, unexposed skin, total unabsorbed, exposed skin, receptor fluid, and receptor chamber fluid. Recovery of the applied test substance was adequate given its volatility (>92%).
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% 1,2-DCE

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). Finite doses of 1,2-dichloroethane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or 1,2-dichloroethane was applied to human skin (at least 4 replicates; surface area of 0.64 cm2). Test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). This is in agreement with OECD guidelines. The cells were semi occluded by charcoal filter in the neck of the donor cell. Thickness of skin sample ranged from 200 to 400 um, exact thickness was not reported. The receptor solution was water fortified with 6% polyethoxyoleate 20 oleyl ether. OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. Flow rate of receptor fluid was 1.5 mL/hour. After 8 hours skin was washed. ”The surface of the membrane was rinsed three times (3 x 0.5 mL) with a mild solution of Dove™ soap in water (ca. 1%). The skin surface was swabbed twice with cotton buds soaked with the liquid soap solution. Finally, the membrane was rinsed with a small volume (0.5 mL) of water and a further cotton bud used to swab the surface of the membrane until dry”. Charcoal filters were collected at 8 and 24-hours post-dosing. Receptor fluid samples (volume not reported) were collected for one hour pre-dose and post-dose at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours hence forth for 24 hours (16 samples) and analyzed for radioactivity. After 24 hours, skin was tap-stripped up to 5 times. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice the background level was considered to be below the limit of accurate determination.”
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. Coefficients of variation (CV) values were reported. Further discussion of the CVs is provided in Metric 19. The percent recovery was 96.72% (neat), 100.03% (50% in IPM), 95.33% (10% in IPM), 105.43% (1% in IPM), 93.54% (50% in 1,2-DCE), 95.70 (10% in 1,2-DCE), and 92.25% (1% in 1,2-DCE).

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The application rate (10 uL/cm3) 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 was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/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. 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 were performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by the authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels.”
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The study used a single batch of radiolabeled 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post-exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial time point were included in the analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin has a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. One replicate in the 10% IPM group did not meet the specified criteria and was excluded. All other samples and replicates meet the requirements at the initial measurement time. 1-2 out of 6 replicates total in the 50% IPM, 10% IPM, and 1% IPM groups had 24-hour TEWL values above the specified criteria. There is no indication that these samples were excluded.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 13:	Number/Replicates per group	Medium	There were no major reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. Minor deviations (e.g., temporary power outage) were noted and were considered to have no impact on the outcomes or integrity of the study.
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 which is appropriate for finite conditions. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.
	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. Methods for determination of radioactivity are reported. “Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination.” Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at both time points were included in analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were major reported differences among the study replicates that were unrelated to exposure. For the 50% IPM and 1% IPM groups a power outage occurred for 5-10 minutes which caused the pump to stop flowing; no receptor fluid was lost. The authors considered this glitch to no impact on the outcomes or integrity of the study. The test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	High	All statistical methods were described and were appropriate. Absorption estimates were based on appropriate measurements. More than half of the CV values within an individual scenario were <25%.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 20:	Data interpretation	High	Absorption estimates were calculated appropriately. Measurements included dislodgeable doses from two skin washes, tape stripping, unexposed skin, total unabsorbed, exposed skin, receptor fluid, and receptor chamber fluid. Recovery of the applied test substance was adequate given its volatility (>92%).
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% 1,2-DCE

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). Finite doses of 1,2-dichloroethane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or 1,2-dichloroethane was applied to human skin (at least 4 replicates; surface area of 0.64 cm2). Test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). This is in agreement with OECD guidelines. The cells were semi occluded by charcoal filter in the neck of the donor cell. Thickness of skin sample ranged from 200 to 400 um, exact thickness was not reported. The receptor solution was water fortified with 6% polyethoxyoleate 20 oleyl ether. OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. Flow rate of receptor fluid was 1.5 mL/hour. After 8 hours skin was washed. ”The surface of the membrane was rinsed three times (3 x 0.5 mL) with a mild solution of Dove™ soap in water (ca. 1%). The skin surface was swabbed twice with cotton buds soaked with the liquid soap solution. Finally, the membrane was rinsed with a small volume (0.5 mL) of water and a further cotton bud used to swab the surface of the membrane until dry”. Charcoal filters were collected at 8 and 24-hours post-dosing. Receptor fluid samples (volume not reported) were collected for one hour pre-dose and post-dose at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours hence forth for 24 hours (16 samples) and analyzed for radioactivity. After 24 hours, skin was tap-stripped up to 5 times. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice the background level was considered to be below the limit of accurate determination.”
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. Coefficients of variation (CV) values were reported. Further discussion of the CVs is provided in Metric 19. The percent recovery was 96.72% (neat), 100.03% (50% in IPM), 95.33% (10% in IPM), 105.43% (1% in IPM), 93.54% (50% in 1,2-DCE), 95.70 (10% in 1,2-DCE), and 92.25% (1% in 1,2-DCE).

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The application rate (10 uL/cm3) 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 was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/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. 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 were performed in two different vehicles (isopropyl myristate or 1,2-dichlorethane). Justification for dose selection is provided by the authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels.”
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The study used a single batch of radiolabeled 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post-exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial time point were included in the analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin has a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. One replicate in the 10% IPM group did not meet the specified criteria and was excluded. All other samples and replicates meet the requirements at the initial measurement time. 1-2 out of 6 replicates total in the 50% IPM, 10% IPM, and 1% IPM groups had 24-hour TEWL values above the specified criteria. There is no indication that these samples were excluded.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 13:	Number/Replicates per group	Medium	There were no major reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. Minor deviations (e.g., temporary power outage) were noted and were considered to have no impact on the outcomes or integrity of the study.
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 which is appropriate for finite conditions. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.
	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. Methods for determination of radioactivity are reported. “Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination.” Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at both time points were included in analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were major reported differences among the study replicates that were unrelated to exposure. For the 50% IPM and 1% IPM groups a power outage occurred for 5-10 minutes which caused the pump to stop flowing; no receptor fluid was lost. The authors considered this glitch to no impact on the outcomes or integrity of the study. The test substance was demonstrated to be soluble in the receptor fluid.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	High	All statistical methods were described and were appropriate. Absorption estimates were based on appropriate measurements. More than half of the CV values within an individual scenario were <25%.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-10% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 20:	Data interpretation	High	Absorption estimates were calculated appropriately. Measurements included dislodgeable doses from two skin washes, tape stripping, unexposed skin, total unabsorbed, exposed skin, receptor fluid, and receptor chamber fluid. Recovery of the applied test substance was adequate given its volatility (>92%).
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% IPM

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). Finite doses of 1,2-dichloroethane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or 1,2-dichloroethane was applied to human skin (at least 4 replicates; surface area of 0.64 cm2). Test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). This is in agreement with OECD guidelines. The cells were semi occluded by charcoal filter in the neck of the donor cell. Thickness of skin sample ranged from 200 to 400 um, exact thickness was not reported. The receptor solution was water fortified with 6% polyethoxyoleate 20 oleyl ether. OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. Flow rate of receptor fluid was 1.5 mL/hour. After 8 hours skin was washed. ”The surface of the membrane was rinsed three times (3 x 0.5 mL) with a mild solution of Dove™ soap in water (ca. 1%). The skin surface was swabbed twice with cotton buds soaked with the liquid soap solution. Finally, the membrane was rinsed with a small volume (0.5 mL) of water and a further cotton bud used to swab the surface of the membrane until dry”. Charcoal filters were collected at 8 and 24-hours post-dosing. Receptor fluid samples (volume not reported) were collected for one hour pre-dose and post-dose at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours hence forth for 24 hours (16 samples) and analyzed for radioactivity. After 24 hours, skin was tap-stripped up to 5 times. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice the background level was considered to be below the limit of accurate determination.”
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. Coefficients of variation (CV) values were reported. Further discussion of the CVs is provided in Metric 19. The percent recovery was 96.72% (neat), 100.03% (50% in IPM), 95.33% (10% in IPM), 105.43% (1% in IPM), 93.54% (50% in 1,2-DCE), 95.70 (10% in 1,2-DCE), and 92.25% (1% in 1,2-DCE).

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% IPM

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The application rate (10 uL/cm3) 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 was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/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. 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 or 1,2-dichlorethane). Justification for dose selection is provided by authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels”.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full thickness skin samples were obtained from 15 female (race not reported) donors ranging in age from 31-70 years old, following elective surgery. The samples were stored frozen at -20 degrees C +/-10 degrees C. Prior to use, the skin samples were thawed, wiped to remove residual fat and blood, re-hydrated in purified water, and dermatomed using a mini-dermatome. The thickness ranged from 200 to 400 uM. The skin contained epidermis and some dermis. These methods were in agreement with OECD guidelines which state split thickness (dermatomed) skin is preferred. Membrane integrity was determined by measuring trans epidermal 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 4-6 replicates/dose.
Domain 5: Outcome Assessment				

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% IPM

Domain	Metric		Rating	Comments
	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 which is appropriate for finite conditions. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.
	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. Methods for determination of radioactivity are reported. "Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination." Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial time point were included in the analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. One replicate in the 10% IPM group did not meet the specified criteria and was excluded. All other samples and replicates meet the requirements at the initial measurement time. 1-2 out of 6 replicates total in the 50% IPM, 10% IPM, and 1% IPM groups had 24-hour TEWL values above the specified criteria. There is no indication that these samples were excluded.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no major reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. Minor deviations (e.g., temporary power outage) were noted and were considered to have no impact on the outcomes or integrity of the study.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	All statistical methods were described and were appropriate. Absorption estimates were based on appropriate measurements. Either half or more than half of the CV values within an individual scenario were >50%; however, standard deviations were provided which will allow for EPA to calculate an alternate upper end value to account for variability in the results.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-50% IPM

Domain	Metric		Rating	Comments
	Metric 20:	Data interpretation	High	Absorption estimates were calculated appropriately. Measurements included dislodgeable doses from two skin washes, tape stripping, unexposed skin, total unabsorbed, exposed skin, receptor fluid, and receptor chamber fluid. Recovery of the applied test substance was adequate given its volatility (>92%).
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% 1,2-DCE

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	Test substances were identified as non-radiolabeled 1,1,2-trichloroethane and radiolabeled [14C]-1,1,2-trichloroethane, CAS number:79-00-5. The structure was reported for the radiolabeled substance noting the location of the radiolabel within the structure.
	Metric 2:	Test substance source	High	The non-radiolabeled, 1,2-dichloroethane was sourced from Sigma-Aldrich; the radiolabeled 1,2-dichloroethane was sourced from Moravek Inc. The study included certificates of analyses that included lot/batch numbers and HPLC outputs.
	Metric 3:	Test substance purity	Medium	The radiochemical purity of the radiolabeled test substance was reported to be 100% by GC-MS. The purity of the non-radiolabeled substance was ≥98%. Impurities were not reported. Radiochemical purities of prepared solution were determined by study authors using HPLC prior to application; all were ≥95.2%, impurities were not reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	High	Testosterone (non-labelled and radiolabeled) was used as a reference compound in accordance with OECD 28 guidelines. Data are fully reported for testosterone studies. 1 mg/ml was administered to the skin (0.012 mg/cm2); n=4. Study authors report mean mass balance of 93.40% (CV = 1.13), total absorbed dose (receptor fluids and receptor camber) 9.98% (CV=50.9), and maximum absorption rats as 0.337 ug/cm2/hr (CV=81.99) "The absorption profiles and distribution of radioactivity obtained from this experiment showed the expected trends and the data was comparable with results obtained in the multi-center comparison study conducted by Van de Sandt et al, 2004."

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 5:	Assay procedures	Medium	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 flow through diffusion set up is sufficiently reported including a schematic drawing. The study does not report if there was an equilibration period after the skin was placed into the chamber (guidelines recommend a 30-minute equilibrium period). Finite doses of 1,2-dichloroethane (neat, 50%, 10%, and 1% dissolved in either isopropyl myristate or 1,2-dichloroethane was applied to human skin (at least 4 replicates; surface area of 0.64 cm2). Test substance was applied to the skin at an application rate of approximately 10 uL/cm2 (6.4 uL dose). This is in agreement with OECD guidelines. The cells were semi occluded by charcoal filter in the neck of the donor cell. Thickness of skin sample ranged from 200 to 400 um, exact thickness was not reported. The receptor solution was water fortified with 6% polyethoxyoleate 20 oleyl ether. OECD 156 guidelines recommend <6% polyoxyethelene (20) oleyl ether in water for lipophilic compounds. The solubility of 1,1,2-trichloroethane was tested in the receptor fluid prior to the study and determined dissolution of 1,1,2-trichloroethane was not rate-limiting. The skin membranes were maintained at 32 degrees C; humidity ranged from 30-70%. Flow rate of receptor fluid was 1.5 mL/hour. After 8 hours skin was washed. ”The surface of the membrane was rinsed three times (3 x 0.5 mL) with a mild solution of Dove™ soap in water (ca. 1%). The skin surface was swabbed twice with cotton buds soaked with the liquid soap solution. Finally, the membrane was rinsed with a small volume (0.5 mL) of water and a further cotton bud used to swab the surface of the membrane until dry”. Charcoal filters were collected at 8 and 24-hours post-dosing. Receptor fluid samples (volume not reported) were collected for one hour pre-dose and post-dose at 10 minutes, 30 minutes, 1 hour, 2 hours and every 2 hours hence forth for 24 hours (16 samples) and analyzed for radioactivity. After 24 hours, skin was tap-stripped up to 5 times. Radioactivity was measured using a liquid scintillation counter. “Radioactivity in gross amounts less than twice the background level was considered to be below the limit of accurate determination.”
	Metric 6:	Standards for tests	Medium	The integrity of the skin was determined by stable trans epidermal water loss (TEWL) prior to dose application and at the end of the experiment. A TWEL of $\leq$ 13 gm-2h-1 was considered acceptable. This is a slight deviation from guidelines which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. Skin that did not meet criteria were allowed to dry and TEWL was remeasured. Skins that failed to meet the criteria were not included in analysis. TEWL readings were reported. Coefficients of variation (CV) values were reported. Further discussion of the CVs is provided in Metric 19. The percent recovery was 96.72% (neat), 100.03% (50% in IPM), 95.33% (10% in IPM), 105.43% (1% in IPM), 93.54% (50% in 1,2-DCE), 95.70 (10% in 1,2-DCE), and 92.25% (1% in 1,2-DCE).

Domain 3: Exposure Characterization

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of test substance was partially reported. The volume of radiolabeled, non-radiolabeled and diluent used for each dose solution was reported. Dilutions were magnetically stirred if deemed necessary by study authors (criteria not reported). The activity and homogeneity of the diluted doses were assessed from the top, middle, and bottom of the solution. All doses were considered homogenous (data not shown). Storage conditions of stock radiolabeled and non-radiolabeled 1,2-dichloroethane were reported. It is unclear how far in advance the dilutions were made, however the study does state that quality control aliquots were taken throughout the dosing procedure. The solubility of the test substance in the receptor fluid was determined to be 24.9 mg/ml. This was deemed appropriate; solubility in receptor solution was considered not to be rate-limiting.
	Metric 8:	Consistency of exposure administration	Low	The application rate (10 uL/cm3) 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 was reported as a range (200 to 400 uM). It is unclear if the variation in thicknesses was consistent across groups, and this may have contributed to some of the endpoint variations (and subsequently high CVs) observed.
	Metric 9:	Reporting of concentrations	High	The applied dose is reported as dpm, mg, and mg/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. 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 or 1,2-dichlorethane). Justification for dose selection is provided by authors. The study authors state the doses were “selected to be representative of potential in-life exposure levels”.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	The test model and descriptive information were reported. Samples of full thickness skin samples were obtained from 15 female (race not reported) donors ranging in age from 31-70 years old, following elective surgery. The samples were stored frozen at -20 degrees C +/-10 degrees C. Prior to use, the skin samples were thawed, wiped to remove residual fat and blood, re-hydrated in purified water, and dermatomed using a mini-dermatome. The thickness ranged from 200 to 400 uM. The skin contained epidermis and some dermis. These methods were in agreement with OECD guidelines which state split thickness (dermatomed) skin is preferred. Membrane integrity was determined by measuring trans epidermal 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 4-6 replicates/dose.
Domain 5: Outcome Assessment				

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% 1,2-DCE

Domain	Metric		Rating	Comments
	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 which is appropriate for finite conditions. Measurement techniques and timing were reported and appropriate. A finite dose was used to determine absorption.
	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. Methods for determination of radioactivity are reported. "Radioactivity in gross amounts of less than twice the background level was considered to be below the limit of accurate determination." Scintillation counts were not shown. 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 1,1,2-trichloroethane. Human abdominal skin was obtained from 15 female donors, ranging in age from 31 to 70 years old. The large age range may influence results. The split-thickness was reported as a range (200-400 um). This variation in skin thickness may result in inconsistencies between samples. Skin integrity was confirmed by TEWL both pre and post exposure. Only skin meeting inclusion criteria ($\leq$ 13 grams/m2/hour) at the initial time point were included in the analysis. This is a slight deviation from OECD 428 and 156 which suggested viable skin have a TEWL reading of less than 10 grams/m2/hour. All TEWL measurements are reported. One replicate in the 10% IPM group did not meet the specified criteria and was excluded. All other samples and replicates meet the requirements at the initial measurement time. 1-2 out of 6 replicates total in the 50% IPM, 10% IPM, and 1% IPM groups had 24-hour TEWL values above the specified criteria. There is no indication that these samples were excluded.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	There were no major reported differences among the study replicates that were unrelated to exposure. Various deviations and errors were clearly reported and experiments were repeated or additional replicates were added as appropriate. Minor deviations (e.g., temporary power outage) were noted and were considered to have no impact on the outcomes or integrity of the study.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	All statistical methods were described and were appropriate. Absorption estimates were based on appropriate measurements. Either half or more than half of the CV values within an individual scenario were >50%; however, standard deviations were provided which will allow for EPA to calculate an alternate upper end value to account for variability in the results.

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Study Citation: Labcorp Early Development, (2023). 1,1,2-Trichloroethane: Rates of penetration through human skin using a flow through in vitro system (Amended final report 1).
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 11164566
Unique ID: Finite-1% 1,2-DCE

Domain	Metric		Rating	Comments
	Metric 20:	Data interpretation	High	Absorption estimates were calculated appropriately. Measurements included dislodgeable doses from two skin washes, tape stripping, unexposed skin, total unabsorbed, exposed skin, receptor fluid, and receptor chamber fluid. Recovery of the applied test substance was adequate given its volatility (>92%).
	Metric 21:	Reporting of data	High	Data for all relevant endpoints were reported quantitatively as means ± SD. Individual replicate data were provided.

Overall Quality Determination High

Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Neat 1,1,2-trichloroethane

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure were provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substance was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups.
	Metric 5:	Standards for Tests	Uninformative	No criteria were stated in the study. The study did not measure recovery or report CV values, and insufficient information is provided to conduct an independent analysis. Therefore, the study does not meet the basic standard for an in vivo dermal absorption study.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Medium	Preparation and storage details were not provided; however, the test substance was applied neat, so limited preparation was required, and the lack of details is unlikely to have a significant impact on the study results.
	Metric 7:	Consistency of exposure administration	Low	Limited details were provided. The study referenced two other publications for methodological details (Jakobson et al., 1977 HERO ID 5465271, and Bowmann et al., 1989 – Not in HERO). The first reference was reviewed; it also had minimal details and cites yet another reference (Wahlberg, 1976; HERO ID 74541), which was reviewed. Bowman et al. 1989 is not available for review. One reference (HERO ID 74541) indicated that the exposure area (3.1 cm2) was ~0.7% of the total body area of the guinea pigs (370 to 378 g in that reference); OECD Guidelines suggest 5-10% of an animal's body surface is ideal. Based on the lack of information, the consistency of application cannot be assessed.
	Metric 8:	Reporting of concentrations	Low	The skin exposure area was 3.1 cm^2. The study did not report the doses or concentrations applied. Two of the references cited for methods (HERO IDs 5465271 and 781351) applied 1.0 mL of pure (e.g., neat) test substance to the skin depots. It is unclear whether the same volume was used in the current study, resulting in substantial ambiguity about the exposure dose.
	Metric 9:	Exposure duration	High	Based on the figures provided, animals were exposed for up to 360 minutes (6 hours). This duration is appropriate and consistent with current OECD guidelines.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Neat 1,1,2-trichloroethane

Domain	Metric		Rating	Comments
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested the neat test substance as well as groups of emulsions containing three concentrations of the COI with surfactants, Triton X-100 and SDS. The authors stated that these compounds are typical additives added to vehicles in topical drug formulations.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	Guinea pigs were used; no further descriptive information was reported in the main study. One of the studies cited for methods (HERO ID 5465271) indicated that the animals were obtained from a commercial source, that both sexes were used, and animals weighed between 600 and 800g. The other study cited for methods HERO ID 781351) reported using female outbred albino and pigmented guinea pigs weighing 500-700g. It is clear what the characteristics of the test animals were that were used in THIS study.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Low	The number of animals per group was not reported in the study methods. Based on figures provided in the study, data were reported for 3 animals per experiment and at least two experiments were included. The neat COI was used as the "control" comparator in different experiments for other test formulations, but it is unclear whether the conditions were the same across experiments, precluding the ability to combine data for the 6 animals used. OECD guidelines recommend at least 4 animals per test preparation.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Insufficient details were provided. Given the lack of details, it is unclear whether an infinite or finite exposure scenario was used; however, if the same volume was used as reported in the cited methods papers (1mL), with a skin surface area of 3.1 cm2 this would be an infinite exposure scenario, the applicate rate would be 0.31 mL/cm2 (310 uL/cm2). It was not specified whether the sites were occluded. The only compartment analyzed was blood, and details of blood sampling were reported and also described in a referenced study (Jakobson et al. 1977). Concentrations of the test substance in blood vs. time were reported. The study did report on the health of the animals (no animals died), but the skin was not examined for signs of irritation or damage. Overall, the study deviated significantly from current guidelines.
	Metric 15:	Consistency of outcome assessment	Low	Insufficient methodological details were reported to determine consistency across replicates.
	Metric 16:	Sampling adequacy and sensitivity	Medium	Sample sizes were provided in each figure, and the timing of blood collection was clearly reported. Blood was analyzed for concentrations of the test substance using gas chromatography.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Insufficient information was provided to determine whether confounding of bias may exist.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Neat 1,1,2-trichloroethane

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	No animals died during the study. The test substance was applied neat; therefore, solubility issues do not apply.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Uninformative	No statistical analysis was conducted. Mean concentrations in blood across time were presented, but no Kp or flux measurements were done. CV values were not provided, and means were presented without measures of variance, which is needed for an independent analysis.
	Metric 20:	Data interpretation	Uninformative	Data interpretation was restricted to comparing how the addition of surfactants or the use of emulsions altered absorption patterns in blood, compared with the neat test substance. The missing study details and lack of data reporting make it impossible for EPA to draw any absorption values with confidence.
	Metric 21:	Reporting of Data	Medium	The reported results appear to be consistent with the purposes of the study. Means were reported without measures of variance.

Overall Quality Determination Uninformative

Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Emulsion of 22.5% 1,1,2-TCE with 4.6% Triton X-100 and 0.4% SDS

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure were provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substance was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups.
	Metric 5:	Standards for Tests	Uninformative	No criteria were stated in the study. The study did not measure recovery or report CV values, and insufficient information is provided to conduct an independent analysis. Therefore, the study does not meet the basic standard for an in vivo dermal absorption study.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Medium	The methods used to generate the emulsions were described and included vibration and ultrasonication. Emulsions of the test substance with water and Triton X-100 were stable with the addition of SDS into the system.
	Metric 7:	Consistency of exposure administration	Low	Limited details were provided. The study referenced two other publications for methodological details (Jakobson et al., 1977 HERO ID 5465271, and Bowmann et al., 1989 – Not in HERO). The first reference was reviewed; it also had minimal details and cites yet another reference (Wahlberg, 1976; HERO ID 74541), which was reviewed. Bowman et al. 1989 is not available for review. One reference (HERO ID 74541) indicated that the exposure area (3.1 cm2) was ~0.7% of the total body area of the guinea pigs (370 to 378 g in that reference); OECD Guidelines suggest 5-10% of an animal's body surface is ideal. Based on the lack of information, the consistency of application cannot be assessed.
	Metric 8:	Reporting of concentrations	Uninformative	The dose groups are confusing. Table 1 reports varying concentrations of the test substance in an emulsion with a set concentration of Triton X-100 and SDS. The table indicates these as the mixtures and emulsions investigated. The skin exposure area was 3.1 cm^2. The study did not report the dose in mg, or the volumes applied. Two of the references cited for methods (HERO IDs 5465271 and 781351) applied 1.0 mL of pure (e.g., neat) test substance to the skin depots. It is unclear whether the same volume was used in the current study for the emulsion samples, resulting in substantial ambiguity about the exposure dose.
	Metric 9:	Exposure duration	High	Based on the figures provided, animals were exposed for up to 360 minutes (6 hours). This duration is appropriate and consistent with current OECD guidelines.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Emulsion of 22.5% 1,1,2-TCE with 4.6% Triton X-100 and 0.4% SDS

Domain	Metric		Rating	Comments
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested the neat test substance as well as groups of emulsions containing three concentrations of the COI with surfactants, Triton X-100 and SDS. The authors stated that these compounds are typical additives added to vehicles in topical drug formulations.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	Guinea pigs were used; no further descriptive information was reported in the main study. One of the studies cited for methods (HERO ID 5465271) indicated that the animals were obtained from a commercial source, that both sexes were used, and animals weighed between 600 and 800g. The other study cited for methods HERO ID 781351) reported using female outbred albino and pigmented guinea pigs weighing 500-700g. It is clear what the characteristics of the test animals were that were used in THIS study.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Low	The number of animals per group was not reported in the study methods. However, based on figures provided in the study, data were reported for 3-4 animals per group. OECD guidelines recommend at least 4 animals per test preparation.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Insufficient details were provided. Given the lack of details, it is unclear whether an infinite or finite exposure scenario was used; however, if the same volume was used as reported in the cited methods papers (1mL), with a skin surface area of 3.1 cm2 this would be an infinite exposure scenario, the applicate rate would be 0.31 mL/cm2 (310 uL/cm2). It was not specified whether the sites were occluded. The only compartment analyzed was blood, and details of blood sampling were reported and also described in a referenced study (Jakobson et al. 1977). Concentrations of the test substance in blood vs. time were reported. The study did report on the health of the animals (no animals died), but the skin was not examined for signs of irritation or damage. Overall, the study deviated significantly from current guidelines.
	Metric 15:	Consistency of outcome assessment	Low	Insufficient methodological details were reported to determine consistency across replicates.
	Metric 16:	Sampling adequacy and sensitivity	Medium	Sample sizes were provided in each figure, and the timing of blood collection was clearly reported. Blood was analyzed for concentrations of the test substance using gas chromatography.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Insufficient information was provided to determine whether confounding of bias may exist.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	No animals died during the study. The test substance was in a stable emulsion containing two surfactants.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Emulsion of 22.5% 1,1,2-TCE with 4.6% Triton X-100 and 0.4% SDS

Domain	Metric	Rating	Comments
Domain 7: Data Presentation and Analysis			
	Metric 19: Data analysis	Uninformative	No statistical analysis was conducted. Mean concentrations in blood across time were presented, but no Kp or flux measurements were done. CV values were not provided, and means were presented without measures of variance, which is needed for an independent analysis.
	Metric 20: Data interpretation	Uninformative	Data interpretation was restricted to comparing how the addition of surfactants or the use of emulsions altered absorption patterns in blood, compared with the neat test substance. The missing study details and lack of data reporting make it impossible for EPA to draw any absorption values with confidence.
	Metric 21: Reporting of Data	Medium	The reported results appear to be consistent with the purposes of the study. Means were reported without measures of variance.

Overall Quality Determination Uninformative

Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Binary solution with 5% Triton X-45

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure were provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substance was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups.
	Metric 5:	Standards for Tests	Uninformative	No criteria were stated in the study. The study did not measure recovery or report CV values, and insufficient information is provided to conduct an independent analysis. Therefore, the study does not meet the basic standard for an in vivo dermal absorption study.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Low	Details describing the preparation of binary solutions were not provided. Storage details were not reported.
	Metric 7:	Consistency of exposure administration	Low	Limited details were provided. The study referenced two other publications for methodological details (Jakobson et al., 1977 HERO ID 5465271, and Bowmann et al., 1989 – Not in HERO). The first reference was reviewed; it also had minimal details and cites yet another reference (Wahlberg, 1976; HERO ID 74541), which was reviewed. Bowman et al. 1989 is not available for review. One reference (HERO ID 74541) indicated that the exposure area (3.1 cm2) was ~0.7% of the total body area of the guinea pigs (370 to 378 g in that reference); OECD Guidelines suggest 5-10% of an animal's body surface is ideal. Based on the lack of information, the consistency of application cannot be assessed.
	Metric 8:	Reporting of concentrations	Uninformative	The dose groups are confusing. Table 1 reports varying concentrations of the test substance in an emulsion with a set concentration of Triton X-100 and SDS. The table indicates these as the mixtures and emulsions investigated. Table 2 then reports completely different solutions specifying the surfactant or solvent concentrations, but not the concentration of the test substance. The skin exposure area was 3.1 cm^2. The study did not report the doses in mg, or the volumes applied. Two of the references cited for methods (HERO IDs 5465271 and 781351) applied 1.0 mL of pure (e.g., neat) test substance to the skin depots. It is unclear whether the same volume was used in the current study for the binary or emulsion samples. The metric is uninformative due to the lack of clear reporting of the dose groups used.
	Metric 9:	Exposure duration	High	Based on the figures provided, animals were exposed for up to 360 minutes (6 hours). This duration is appropriate and consistent with current OECD guidelines.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Binary solution with 5% Triton X-45

Domain	Metric		Rating	Comments
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested the neat test substance as well as groups of binary solutions or emulsions containing the COI with Triton X-100 ± SDS. The authors stated that these compounds are typical additives added to vehicles in topical drug formulations.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	Guinea pigs were used; no further descriptive information was reported in the main study. One of the studies cited for methods (HERO ID 5465271) indicated that the animals were obtained from a commercial source, that both sexes were used, and animals weighed between 600 and 800g. The other study cited for methods HERO ID 781351) reported using female outbred albino and pigmented guinea pigs weighing 500-700g. It is clear what the characteristics of the test animals were that were used in THIS study.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Medium	The number of animals per group or replicate was not reported in the study methods. However, based on figures provided in the study, data were reported for 4 animals per experiment. OECD guidelines recommend at least 4 animals per test preparation.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Insufficient details were provided. Given the lack of details, it is unclear whether an infinite or finite exposure scenario was used; however, if the same volume was used as reported in the cited methods papers (1mL), with a skin surface area of 3.1 cm2 this would be an infinite exposure scenario, the applicate rate would be 0.31 mL/cm2 (310 uL/cm2). It was not specified whether the sites were occluded. The only compartment analyzed was blood, and details of blood sampling were reported and also described in a referenced study (Jakobson et al. 1977). Concentrations of the test substance in blood vs. time were reported. The study did report on the health of the animals (no animals died), but the skin was not examined for signs of irritation or damage. Overall, the study deviated significantly from current guidelines.
	Metric 15:	Consistency of outcome assessment	Low	Insufficient methodological details were reported to determine consistency across replicates.
	Metric 16:	Sampling adequacy and sensitivity	Medium	Sample sizes were provided in each figure, and the timing of blood collection was clearly reported. Blood was analyzed for concentrations of the test substance using gas chromatography. Limits of detection were not reported.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Insufficient information was provided to determine whether confounding of bias may exist.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	No animals died during the study. No other information either to support or dismiss the suggestion that there were differences among groups in animal attrition, health outcomes unrelated to exposure, or solubility that could influence the outcome assessment.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Binary solution with 5% Triton X-45

Domain	Metric	Rating	Comments
Domain 7: Data Presentation and Analysis			
	Metric 19: Data analysis	Uninformative	No statistical analysis was conducted. Mean concentrations in blood across time were presented, but no Kp or flux measurements were done. CV values were not provided, and means were presented without measures of variance, which is needed for an independent analysis.
	Metric 20: Data interpretation	Uninformative	Data interpretation was restricted to comparing how the addition of surfactants or the use of emulsions altered absorption patterns in blood, compared with the neat test substance. The study design deviated significantly from standard OECD guidelines, and the missing study details and lack of data reporting make it impossible for EPA to draw any absorption values with confidence.
	Metric 21: Reporting of Data	Medium	The reported results appear to be consistent with the purposes of the study. Means were reported without measures of variance.

Overall Quality Determination — Uninformative

Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Emulsion containing 47.5% or 67.5% 1,1,2 TCE plus 4.6% Triton X-100 and 0.4% SDS

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure were provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substance was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups.
	Metric 5:	Standards for Tests	Uninformative	No criteria were stated in the study. The study did not measure recovery or report CV values, and insufficient information is provided to conduct an independent analysis. Therefore, the study does not meet the basic standard for an in vivo dermal absorption study.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Medium	The methods used to generate the emulsions were described and included vibration and ultrasonication. Emulsions of the test substance with water and Triton X-100 were stable with the addition of SDS into the system.
	Metric 7:	Consistency of exposure administration	Low	Limited details were provided. The study referenced two other publications for methodological details (Jakobson et al., 1977 HERO ID 5465271, and Bowmann et al., 1989 – Not in HERO). The first reference was reviewed; it also had minimal details and cites yet another reference (Wahlberg, 1976; HERO ID 74541), which was reviewed. Bowman et al. 1989 is not available for review. One reference (HERO ID 74541) indicated that the exposure area (3.1 cm2) was ~0.7% of the total body area of the guinea pigs (370 to 378 g in that reference); OECD Guidelines suggest 5-10% of an animal's body surface is ideal. Based on the lack of information, the consistency of application cannot be assessed.
	Metric 8:	Reporting of concentrations	Uninformative	The dose groups are confusing. Table 1 reports varying concentrations of the test substance in an emulsion with a set concentration of Triton X-100 and SDS. The table indicates these as the mixtures and emulsions investigated. The skin exposure area was 3.1 cm^2. The study did not report the dose in mg, or the volumes applied. Two of the references cited for methods (HERO IDs 5465271 and 781351) applied 1.0 mL of pure (e.g., neat) test substance to the skin depots. It is unclear whether the same volume was used in the current study for the emulsion samples, resulting in substantial ambiguity about the exposure dose.
	Metric 9:	Exposure duration	High	Based on the figures provided, animals were exposed for up to 360 minutes (6 hours). This duration is appropriate and consistent with current OECD guidelines.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Emulsion containing 47.5% or 67.5% 1,1,2 TCE plus 4.6% Triton X-100 and 0.4% SDS

Domain	Metric		Rating	Comments
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested the neat test substance as well as groups of emulsions containing three concentrations of the COI with surfactants, Triton X-100 and SDS. The authors stated that these compounds are typical additives added to vehicles in topical drug formulations.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	Guinea pigs were used; no further descriptive information was reported in the main study. One of the studies cited for methods (HERO ID 5465271) indicated that the animals were obtained from a commercial source, that both sexes were used, and animals weighed between 600 and 800g. The other study cited for methods HERO ID 781351) reported using female outbred albino and pigmented guinea pigs weighing 500-700g. It is clear what the characteristics of the test animals were that were used in THIS study.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Medium	The number of animals per group was not reported in the study methods. However, based on figures provided in the study, data were reported for 4 animals per group, which is appropriate. OECD guidelines recommend at least 4 animals per test preparation.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Insufficient details were provided. Given the lack of details, it is unclear whether an infinite or finite exposure scenario was used; however, if the same volume was used as reported in the cited methods papers (1mL), with a skin surface area of 3.1 cm2 this would be an infinite exposure scenario, the applicate rate would be 0.31 mL/cm2 (310 uL/cm2). It was not specified whether the sites were occluded. The only compartment analyzed was blood, and details of blood sampling were reported and also described in a referenced study (Jakobson et al. 1977). Concentrations of the test substance in blood vs. time were reported. The study did report on the health of the animals (no animals died), but the skin was not examined for signs of irritation or damage. Overall, the study deviated significantly from current guidelines.
	Metric 15:	Consistency of outcome assessment	Low	Insufficient methodological details were reported to determine consistency across replicates.
	Metric 16:	Sampling adequacy and sensitivity	Medium	Sample sizes were provided in each figure, and the timing of blood collection was clearly reported. Blood was analyzed for concentrations of the test substance using gas chromatography.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Insufficient information was provided to determine whether confounding of bias may exist.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	No animals died during the study. The test substance was in a stable emulsion containing two surfactants.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Emulsion containing 47.5% or 67.5% 1,1,2 TCE plus 4.6% Triton X-100 and 0.4% SDS

Domain	Metric	Rating	Comments
Domain 7: Data Presentation and Analysis			
	Metric 19: Data analysis	Uninformative	No statistical analysis was conducted. Mean concentrations in blood across time were presented, but no Kp or flux measurements were done. CV values were not provided, and means were presented without measures of variance, which is needed for an independent analysis.
	Metric 20: Data interpretation	Uninformative	Data interpretation was restricted to comparing how the addition of surfactants or the use of emulsions altered absorption patterns in blood, compared with the neat test substance. The missing study details and lack of data reporting make it impossible for EPA to draw any absorption values with confidence.
	Metric 21: Reporting of Data	Medium	The reported results appear to be consistent with the purposes of the study. Means were reported without measures of variance.

Overall Quality Determination Uninformative

Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Binary solution with 10% Triton X-45

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure were provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substance was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups.
	Metric 5:	Standards for Tests	Uninformative	No criteria were stated in the study. The study did not measure recovery or report CV values, and insufficient information is provided to conduct an independent analysis. Therefore, the study does not meet the basic standard for an in vivo dermal absorption study.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Low	Details describing the preparation of binary solutions were not provided. Storage details were not reported.
	Metric 7:	Consistency of exposure administration	Low	Limited details were provided. The study referenced two other publications for methodological details (Jakobson et al., 1977 HERO ID 5465271, and Bowmann et al., 1989 – Not in HERO). The first reference was reviewed; it also had minimal details and cites yet another reference (Wahlberg, 1976; HERO ID 74541), which was reviewed. Bowman et al. 1989 is not available for review. One reference (HERO ID 74541) indicated that the exposure area (3.1 cm2) was ~0.7% of the total body area of the guinea pigs (370 to 378 g in that reference); OECD Guidelines suggest 5-10% of an animal's body surface is ideal. Based on the lack of information, the consistency of application cannot be assessed.
	Metric 8:	Reporting of concentrations	Uninformative	The dose groups are confusing. Table 1 reports varying concentrations of the test substance in an emulsion with a set concentration of Triton X-100 and SDS. The table indicates these as the mixtures and emulsions investigated. Table 2 then reports completely different solutions specifying the surfactant or solvent concentrations, but not the concentration of the test substance. The skin exposure area was 3.1 cm^2. The study did not report the doses in mg, or the volumes applied. Two of the references cited for methods (HERO IDs 5465271 and 781351) applied 1.0 mL of pure (e.g., neat) test substance to the skin depots. It is unclear whether the same volume was used in the current study for the binary or emulsion samples. The metric is uninformative due to the lack of clear reporting of the dose groups used.
	Metric 9:	Exposure duration	High	Based on the figures provided, animals were exposed for up to 360 minutes (6 hours). This duration is appropriate and consistent with current OECD guidelines.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Binary solution with 10% Triton X-45

Domain	Metric		Rating	Comments
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested the neat test substance as well as groups of binary solutions or emulsions containing the COI with Triton X-100 ± SDS. The authors stated that these compounds are typical additives added to vehicles in topical drug formulations.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	Guinea pigs were used; no further descriptive information was reported in the main study. One of the studies cited for methods (HERO ID 5465271) indicated that the animals were obtained from a commercial source, that both sexes were used, and animals weighed between 600 and 800g. The other study cited for methods HERO ID 781351) reported using female outbred albino and pigmented guinea pigs weighing 500-700g. It is clear what the characteristics of the test animals were that were used in THIS study.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Low	The number of animals per group or replicate was not reported in the study methods. However, based on figures provided in the study, data were reported for 3 animals per experiment. OECD guidelines recommend at least 4 animals per test preparation.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Insufficient details were provided. Given the lack of details, it is unclear whether an infinite or finite exposure scenario was used; however, if the same volume was used as reported in the cited methods papers (1mL), with a skin surface area of 3.1 cm2 this would be an infinite exposure scenario, the applicate rate would be 0.31 mL/cm2 (310 uL/cm2). It was not specified whether the sites were occluded. The only compartment analyzed was blood, and details of blood sampling were reported and also described in a referenced study (Jakobson et al. 1977). Concentrations of the test substance in blood vs. time were reported. The study did report on the health of the animals (no animals died), but the skin was not examined for signs of irritation or damage. Overall, the study deviated significantly from current guidelines.
	Metric 15:	Consistency of outcome assessment	Low	Insufficient methodological details were reported to determine consistency across replicates.
	Metric 16:	Sampling adequacy and sensitivity	Medium	Sample sizes were provided in each figure, and the timing of blood collection was clearly reported. Blood was analyzed for concentrations of the test substance using gas chromatography. Limits of detection were not reported.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Insufficient information was provided to determine whether confounding of bias may exist.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	No animals died during the study. No other information either to support or dismiss the suggestion that there were differences among groups in animal attrition, health outcomes unrelated to exposure, or solubility that could influence the outcome assessment.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Binary solution with 10% Triton X-45

Domain	Metric	Rating	Comments
Domain 7: Data Presentation and Analysis			
	Metric 19: Data analysis	Uninformative	No statistical analysis was conducted. Mean concentrations in blood across time were presented, but no Kp or flux measurements were done. CV values were not provided, and means were presented without measures of variance, which is needed for an independent analysis.
	Metric 20: Data interpretation	Uninformative	Data interpretation was restricted to comparing how the addition of surfactants or the use of emulsions altered absorption patterns in blood, compared with the neat test substance. The study design deviated significantly from standard OECD guidelines, and the missing study details and lack of data reporting make it impossible for EPA to draw any absorption values with confidence.
	Metric 21: Reporting of Data	Medium	The reported results appear to be consistent with the purposes of the study. Means were reported without measures of variance.

Overall Quality Determination Uninformative

Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Binary solution with 5% or 10% Trition X-100

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure were provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substance was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups.
	Metric 5:	Standards for Tests	Uninformative	No criteria were stated in the study. The study did not measure recovery or report CV values, and insufficient information is provided to conduct an independent analysis. Therefore, the study does not meet the basic standard for an in vivo dermal absorption study.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Low	Details describing the preparation of binary solutions were not provided. Storage details were not reported.
	Metric 7:	Consistency of exposure administration	Low	Limited details were provided. The study referenced two other publications for methodological details (Jakobson et al., 1977 HERO ID 5465271, and Bowmann et al., 1989 – Not in HERO). The first reference was reviewed; it also had minimal details and cites yet another reference (Wahlberg, 1976; HERO ID 74541), which was reviewed. Bowman et al. 1989 is not available for review. One reference (HERO ID 74541) indicated that the exposure area (3.1 cm2) was ~0.7% of the total body area of the guinea pigs (370 to 378 g in that reference); OECD Guidelines suggest 5-10% of an animal's body surface is ideal. Based on the lack of information, the consistency of application cannot be assessed.
	Metric 8:	Reporting of concentrations	Uninformative	The dose groups are confusing. Table 1 reports varying concentrations of the test substance in an emulsion with a set concentration of Triton X-100 and SDS. The table indicates these as the mixtures and emulsions investigated. Table 2 then reports completely different solutions specifying the surfactant or solvent concentrations, but not the concentration of the test substance. The skin exposure area was 3.1 cm^2. The study did not report the doses in mg, or the volumes applied. Two of the references cited for methods (HERO IDs 5465271 and 781351) applied 1.0 mL of pure (e.g., neat) test substance to the skin depots. It is unclear whether the same volume was used in the current study for the binary or emulsion samples. The metric is uninformative due to the lack of clear reporting of the dose groups used.
	Metric 9:	Exposure duration	High	Based on the figures provided, animals were exposed for up to 360 minutes (6 hours). This duration is appropriate and consistent with current OECD guidelines.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Binary solution with 5% or 10% Trition X-100

Domain	Metric		Rating	Comments
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested the neat test substance as well as groups of binary solutions or emulsions containing the COI with Triton X-100 ± SDS. The authors stated that these compounds are typical additives added to vehicles in topical drug formulations.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	Guinea pigs were used; no further descriptive information was reported in the main study. One of the studies cited for methods (HERO ID 5465271) indicated that the animals were obtained from a commercial source, that both sexes were used, and animals weighed between 600 and 800g. The other study cited for methods HERO ID 781351) reported using female outbred albino and pigmented guinea pigs weighing 500-700g. It is clear what the characteristics of the test animals were that were used in THIS study.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Low	The number of animals per group or replicate was not reported in the study methods. However, based on figures provided in the study, data were reported for 2-3 animals per experiment. OECD guidelines recommend at least 4 animals per test preparation.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Insufficient details were provided. Given the lack of details, it is unclear whether an infinite or finite exposure scenario was used; however, if the same volume was used as reported in the cited methods papers (1mL), with a skin surface area of 3.1 cm2 this would be an infinite exposure scenario, the applicate rate would be 0.31 mL/cm2 (310 uL/cm2). It was not specified whether the sites were occluded. The only compartment analyzed was blood, and details of blood sampling were reported and also described in a referenced study (Jakobson et al. 1977). Concentrations of the test substance in blood vs. time were reported. The study did report on the health of the animals (no animals died), but the skin was not examined for signs of irritation or damage. Overall, the study deviated significantly from current guidelines.
	Metric 15:	Consistency of outcome assessment	Low	Insufficient methodological details were reported to determine consistency across replicates.
	Metric 16:	Sampling adequacy and sensitivity	Medium	Sample sizes were provided in each figure, and the timing of blood collection was clearly reported. Blood was analyzed for concentrations of the test substance using gas chromatography. Limits of detection were not reported.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Insufficient information was provided to determine whether confounding of bias may exist.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	No animals died during the study. No other information either to support or dismiss the suggestion that there were differences among groups in animal attrition, health outcomes unrelated to exposure, or solubility that could influence the outcome assessment.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Binary solution with 5% or 10% Trition X-100

Domain	Metric	Rating	Comments
Domain 7: Data Presentation and Analysis			
	Metric 19: Data analysis	Uninformative	No statistical analysis was conducted. Mean concentrations in blood across time were presented, but no Kp or flux measurements were done. CV values were not provided, and means were presented without measures of variance, which is needed for an independent analysis.
	Metric 20: Data interpretation	Uninformative	Data interpretation was restricted to comparing how the addition of surfactants or the use of emulsions altered absorption patterns in blood, compared with the neat test substance. The study design deviated significantly from standard OECD guidelines, and the missing study details and lack of data reporting make it impossible for EPA to draw any absorption values with confidence.
	Metric 21: Reporting of Data	Medium	The reported results appear to be consistent with the purposes of the study. Means were reported without measures of variance.

Overall Quality Determination — Uninformative

Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Emulsion with 25%, 50%, or 75% SDS/Triton X-100

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure were provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substance was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups.
	Metric 5:	Standards for Tests	Uninformative	No criteria were stated in the study. The study did not measure recovery or report CV values, and insufficient information is provided to conduct an independent analysis. Therefore, the study does not meet the basic standard for an in vivo dermal absorption study.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Low	Details describing the preparation of binary solutions were not provided. Storage details were not reported.
	Metric 7:	Consistency of exposure administration	Low	Limited details were provided. The study referenced two other publications for methodological details (Jakobson et al., 1977 HERO ID 5465271, and Bowmann et al., 1989 – Not in HERO). The first reference was reviewed; it also had minimal details and cites yet another reference (Wahlberg, 1976; HERO ID 74541), which was reviewed. Bowman et al. 1989 is not available for review. One reference (HERO ID 74541) indicated that the exposure area (3.1 cm2) was ~0.7% of the total body area of the guinea pigs (370 to 378 g in that reference); OECD Guidelines suggest 5-10% of an animal's body surface is ideal. Based on the lack of information, the consistency of application cannot be assessed.
	Metric 8:	Reporting of concentrations	Uninformative	The dose groups are confusing. Table 1 reports varying concentrations of the test substance in an emulsion with a set concentration of Triton X-100 and SDS. The table indicates these as the mixtures and emulsions investigated. Table 2 then reports completely different solutions specifying the surfactant or solvent concentrations, but not the concentration of the test substance. The skin exposure area was 3.1 cm^2. The study did not report the doses in mg, or the volumes applied. Two of the references cited for methods (HERO IDs 5465271 and 781351) applied 1.0 mL of pure (e.g., neat) test substance to the skin depots. It is unclear whether the same volume was used in the current study for the binary or emulsion samples. The metric is uninformative due to the lack of clear reporting of the dose groups used.
	Metric 9:	Exposure duration	High	Based on the figures provided, animals were exposed for up to 360 minutes (6 hours). This duration is appropriate and consistent with current OECD guidelines.

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Emulsion with 25%, 50%, or 75% SDS/Triton X-100

Domain	Metric		Rating	Comments
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested the neat test substance as well as groups of binary solutions or emulsions containing the COI with Triton X-100 ± SDS. The authors stated that these compounds are typical additives added to vehicles in topical drug formulations.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	Guinea pigs were used; no further descriptive information was reported in the main study. One of the studies cited for methods (HERO ID 5465271) indicated that the animals were obtained from a commercial source, that both sexes were used, and animals weighed between 600 and 800g. The other study cited for methods HERO ID 781351) reported using female outbred albino and pigmented guinea pigs weighing 500-700g. It is clear what the characteristics of the test animals were that were used in THIS study.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Low	The number of animals per group or replicate was not reported.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Insufficient details were provided. Given the lack of details, it is unclear whether an infinite or finite exposure scenario was used; however, if the same volume was used as reported in the cited methods papers (1mL), with a skin surface area of 3.1 cm2 this would be an infinite exposure scenario, the applicate rate would be 0.31 mL/cm2 (310 uL/cm2). It was not specified whether the sites were occluded. The only compartment analyzed was blood, and details of blood sampling were reported and also described in a referenced study (Jakobson et al. 1977). Concentrations of the test substance in blood vs. time were reported. The study did report on the health of the animals (no animals died), but the skin was not examined for signs of irritation or damage. Overall, the study deviated significantly from current guidelines.
	Metric 15:	Consistency of outcome assessment	Low	Insufficient methodological details were reported to determine consistency across replicates.
	Metric 16:	Sampling adequacy and sensitivity	Uninformative	Sample sizes were not reported for these groups. The only data are provided in Table 2.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Insufficient information was provided to determine whether confounding of bias may exist.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	No animals died during the study. No other information either to support or dismiss the suggestion that there were differences among groups in animal attrition, health outcomes unrelated to exposure, or solubility that could influence the outcome assessment.
Domain 7: Data Presentation and Analysis				

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Study Citation: Boman, A., Blute, I., Fernström, P., Carlfors, J., Rydhag, L. (1989). Percutaneous absorption of 4 organic solvents in the guinea pig (II). Effect of surfactants. Contact Dermatitis 21(2):92-104.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 660787
Unique ID: Emulsion with 25%, 50%, or 75% SDS/Triton X-100

Domain	Metric		Rating	Comments
	Metric 19:	Data analysis	Uninformative	No statistical analysis was conducted. Mean concentrations in blood across time were presented, but no Kp or flux measurements were done. CV values were not provided, and means were presented without measures of variance, which is needed for an independent analysis.
	Metric 20:	Data interpretation	Uninformative	Data interpretation was restricted to comparing how the addition of surfactants or the use of emulsions altered absorption patterns in blood, compared with the neat test substance. The study design deviated significantly from standard OECD guidelines, and the missing study details and lack of data reporting make it impossible for EPA to draw any absorption values with confidence.
	Metric 21:	Reporting of Data	Uninformative	Concentrations in blood vs. time were not reported for these samples.

Overall Quality Determination Uninformative

Study Citation: Jakobson, I., Holmberg, B., Wahlberg, J. E. (1977). Variations in the blood concentration of 1,1,2-trichloroethane by percutaneous absorption and other routes of administration in the guinea pig. Acta Pharmacologica et Toxicologica 41(5):497-506.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 5465271
Unique ID: 2-hr duration

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure was provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substances was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups
	Metric 5:	Standards for Tests	Uninformative	No criteria were stated in the study. The study did not measure recovery, or report CV values and insufficient information is provided to conduct an independent analysis. Therefore, the study does not meet the basic standard for an in vivo dermal absorption study.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Medium	Preparation and storage details were not provided; however, the test substance was applied neat so limited preparation was required and the lack of details are unlikely to have a significant impact on the study results.
	Metric 7:	Consistency of exposure administration	Low	Details of skin preparation were not provided. The study cited HERO ID 74541 for application methods. That reference specifies a skin area of 3.1 cm2, and the current study specifies application of 1mL of the neat test substance. The reference above indicated that the skin depot was covered with a glass covers slip. It is uncertain whether the current study followed the same parameters. The metric is scored a Low due to insufficient information on exposure administration.
	Metric 8:	Reporting of concentrations	Medium	The study reported applying a 1mL volume of neat material to the skin. The skin surface area was not reported in THIS study; however, a referenced citation for methods (HERO ID 74541) specified an area of 3.1 cm2. Animal body weights ranged from 600 – 800 g. A dose range (mg/kg) can be estimated using the density of the pure test substance. No analytical measurements were made.
	Metric 9:	Exposure duration	Low	Animals were exposed for 2, 6 or 12 hrs and the durations were appropriate for the study type. Measurements did not continue post-exposure to account for retained doses in the skin, and conditions of use were not specified.
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested as single undiluted (neat) dose. OECD guidelines recommend a minimum of 3 dose groups.
Domain 4: Test Model				

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Study Citation: Jakobson, I., Holmberg, B., Wahlberg, J. E. (1977). Variations in the blood concentration of 1,1,2-trichloroethane by percutaneous absorption and other routes of administration in the guinea pig. Acta Pharmacologica et Toxicologica 41(5):497-506.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 5465271
Unique ID: 2-hr duration

Domain	Metric		Rating	Comments
	Metric 11:	Test animal characteristics	Low	The study used guinea pigs of both sexes obtained from an unspecified commercial source. The range of animal body weights was provided; age was not specified.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Low	The number of animals per group was not specified in the study methods. Based on the figures provided. 6 animals each were exposed for either 2hrs or 6hrs of exposure. Data for the 12 hr exposure group was only from 2 animals. It is unclear whether this group contained fewer animals at the start of the study, or if, for other reasons, data were only collected from two animals. The number of animals per sex was not specified.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Outcome assessment was limited to blood sampling via the carotid artery. Urine, feces, and skin from the application site were not measured. The study did not collected blood for any period post-exposure. The handling of the samples following collection was reported. Concentrations in blood were measured using gas chromatography. The skin depots were covered with a coverslip which should be sufficient for occlusion. 1mL applied to an area of 3.1 cm2 is appropriate for an infinite exposure scenario. Skin was not examined for signs of irritation or damage.
	Metric 15:	Consistency of outcome assessment	Medium	There were some limitations in the methodological details provided. The frequency of collections was not specified in the methods, but could be determined by extracting data from the figures provided. It appears that the frequency of collection differed for each group (e.g., frequency of blood collection was greater for animals exposed for only two hours vs those exposed for 6 or 12 hrs). No justification was made for the frequencies of collection.
	Metric 16:	Sampling adequacy and sensitivity	Medium	The number and interval of collections was adequate for the outcome of interest. Sample sizes were appropriate (n = 6) for animals exposed for 2 or 6 hours. The sample size for animals exposed for 12 hours was small (n =2) and no explanation was provided by the study authors.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Starting animal body weights ranged from 600 to 800 g. Starting weights on a per-group basis were not reported. Other potentially confounding variables, including whether different batches were used or if there were any differences in skin (e.g., hairy or signs of damage), were not reported. There is no indication that there were differences in the area of skin exposed (3.1 cm^2 based on the information in the cited study (HERO 74541).
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	No animals died during the study. The test substance was applied neat; therefore, solubility issues do not apply. It is unclear if there was any damaged tissue; the study cited another report suggesting skin damage was likely: "...skin lesions were observed under the microscope as early as 15 minutes after the start of an epicutaneous exposure of guinea pigs to 1,1,2-trichloroethane (Kronevi et al. 1977)."

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Study Citation: Jakobson, I., Holmberg, B., Wahlberg, J. E. (1977). Variations in the blood concentration of 1,1,2-trichloroethane by percutaneous absorption and other routes of administration in the guinea pig. Acta Pharmacologica et Toxicologica 41(5):497-506.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 5465271
Unique ID: 2-hr duration

Domain	Metric	Rating	Comments
Domain 7: Data Presentation and Analysis			
	Metric 19: Data analysis	Uninformative	The study presented mean concentrations in blood across time. Regression analysis was performed on means from all three exposure times, as well as for all three sets together. Means and standard deviations for concentrations measured in blood over time were provided for the animals exposed for 6 hours. CV values were not reported, but could be calculated for the 6-hour exposure data provided. The study text indicated that the standard deviations were similar for the other durations, but did not include that data on the figures, so no independent analysis is possible. The study did not calculate flux or Kp values, but these could likely be calculated based on the data provided.
	Metric 20: Data interpretation	Low	The study did not explicitly state using infinite or finite exposure scenarios and did not report the endpoints typically associated with those scenarios (e.g., Kp, or absorption estimates), thus deviates significantly from standard OECD guidelines. The study did not report % recovery.
	Metric 21: Reporting of Data	Low	The study clearly calculated standard deviations for all groups but did only reported measures of variance for one group. The study did not measure or report all of the outcomes specified in OECD 427.

Overall Quality Determination Uninformative

Study Citation: Jakobson, I., Holmberg, B., Wahlberg, J. E. (1977). Variations in the blood concentration of 1,1,2-trichloroethane by percutaneous absorption and other routes of administration in the guinea pig. Acta Pharmacologica et Toxicologica 41(5):497-506.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 5465271
Unique ID: 6-hr duration

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure was provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substances was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups
	Metric 5:	Standards for Tests	Low	No criteria were stated in the study. The study did not measure recovery or report CV values; however, CV values for concentrations in blood vs. time could be determined by extracting the means and standard deviations from the figures provided.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Medium	Preparation and storage details were not provided; however, the test substance was applied neat so limited preparation was required and the lack of details are unlikely to have a significant impact on the study results.
	Metric 7:	Consistency of exposure administration	Low	Details of skin preparation were not provided. The study cited HERO ID 74541 for application methods. That reference specifies a skin area of 3.1 cm2, and the current study specifies application of 1mL of the neat test substance. The reference above indicated that the skin depot was covered with a glass covers slip. It is uncertain whether the current study followed the same parameters. The metric is scored a Low due to insufficient information on exposure administration.
	Metric 8:	Reporting of concentrations	Medium	The study reported applying a 1mL volume of neat material to the skin. The skin surface area was not reported in THIS study; however, a referenced citation for methods (HERO ID 74541) specified an area of 3.1 cm2. Animal body weights ranged from 600 – 800 g. A dose range (mg/kg) can be estimated using the density of the pure test substance. No analytical measurements were made.
	Metric 9:	Exposure duration	Low	Animals were exposed for 2, 6 or 12 hrs and the durations were appropriate for the study type. Measurements did not continue post-exposure to account for retained doses in the skin, and conditions of use were not specified.
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested as single undiluted (neat) dose. OECD guidelines recommend a minimum of 3 dose groups.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	The study used guinea pigs of both sexes obtained from an unspecified commercial source. The range of animal body weights was provided; age was not specified.

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Study Citation: Jakobson, I., Holmberg, B., Wahlberg, J. E. (1977). Variations in the blood concentration of 1,1,2-trichloroethane by percutaneous absorption and other routes of administration in the guinea pig. Acta Pharmacologica et Toxicologica 41(5):497-506.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 5465271
Unique ID: 6-hr duration

Domain	Metric		Rating	Comments
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Low	The number of animals per group was not specified in the study methods. Based on the figures provided. 6 animals each were exposed for either 2hrs or 6hrs of exposure. Data for the 12 hr exposure group was only from 2 animals. It is unclear whether this group contained fewer animals at the start of the study, or if, for other reasons, data were only collected from two animals. The number of animals per sex was not specified.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Outcome assessment was limited to blood sampling via the carotid artery. Urine, feces, and skin from the application site were not measured. The study did not collected blood for any period post-exposure. The handling of the samples following collection was reported. Concentrations in blood were measured using gas chromatography. The skin depots were covered with a coverslip which should be sufficient for occlusion. 1mL applied to an area of 3.1 cm2 is appropriate for an infinite exposure scenario. Skin was not examined for signs of irritation or damage.
	Metric 15:	Consistency of outcome assessment	Medium	There were some limitations in the methodological details provided. The frequency of collections was not specified in the methods, but could be determined by extracting data from the figures provided. It appears that the frequency of collection differed for each group (e.g., frequency of blood collection was greater for animals exposed for only two hours vs those exposed for 6 or 12 hrs). No justification was made for the frequencies of collection.
	Metric 16:	Sampling adequacy and sensitivity	Medium	The number and interval of collections was adequate for the outcome of interest. Sample sizes were appropriate (n = 6) for animals exposed for 2 or 6 hours. The sample size for animals exposed for 12 hours was small (n =2) and no explanation was provided by the study authors.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Starting animal body weights ranged from 600 to 800 g. Starting weights on a per-group basis were not reported. Other potentially confounding variables, including whether different batches were used or if there were any differences in skin (e.g., hairy or signs of damage), were not reported. There is no indication that there were differences in the area of skin exposed (3.1 cm^2 based on the information in the cited study (HERO 74541).
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	No animals died during the study. The test substance was applied neat; therefore, solubility issues do not apply. It is unclear if there was any damaged tissue; the study cited another report suggesting skin damage was likely: "...skin lesions were observed under the microscope as early as 15 minutes after the start of an epicutaneous exposure of guinea pigs to 1,1,2-trichloroethane (Kronevi et al. 1977)."
Domain 7: Data Presentation and Analysis				

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Study Citation: Jakobson, I., Holmberg, B., Wahlberg, J. E. (1977). Variations in the blood concentration of 1,1,2-trichloroethane by percutaneous absorption and other routes of administration in the guinea pig. Acta Pharmacologica et Toxicologica 41(5):497-506.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 5465271
Unique ID: 6-hr duration

Domain	Metric		Rating	Comments
	Metric 19:	Data analysis	Low	The study presented mean concentrations in blood across time. Regression analysis was performed on means from all three exposure times, as well as for all three sets together. Means and standard deviations for concentrations measured in blood over time were provided for the animals exposed for 6 hours. CV values were not reported, but could be calculated for the 6-hour exposure data provided. The study text indicated that the standard deviations were similar for the other durations, but did not include that data in the figures. The study did not calculate flux or Kp values, but these could likely be calculated based on the data provided.
	Metric 20:	Data interpretation	Low	The study did not explicitly state using infinite or finite exposure scenarios and did not report the endpoints typically associated with those scenarios (e.g., Kp, or absorption estimates), thus deviates significantly from standard OECD guidelines. The study did not report % recovery.
	Metric 21:	Reporting of Data	Low	The study reported means ± SD for concentrations of the test substance measured in blood over time. The study did not measure or report all of the outcomes specified in OECD 427.

Overall Quality Determination — Low

Study Citation: Jakobson, I., Holmberg, B., Wahlberg, J. E. (1977). Variations in the blood concentration of 1,1,2-trichloroethane by percutaneous absorption and other routes of administration in the guinea pig. Acta Pharmacologica et Toxicologica 41(5):497-506.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 5465271
Unique ID: 12-hr duration

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test material was identified by name as 1,1,2-trichloroethane. No CASRN or structure was provided.
	Metric 2:	Test substance source	Low	The test substance was obtained from Fluka; a batch or lot number was not specified. A certification would have been available at the time of purchase, but the details were not provided in the publication, and the test substances was not analytically verified by the performing laboratory.
	Metric 3:	Test substance purity	Low	The purity was not reported.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not mention how animals were allocated into groups
	Metric 5:	Standards for Tests	Uninformative	No criteria were stated in the study. The study did not measure recovery, or report CV values and insufficient information is provided to conduct an independent analysis. Therefore, the study does not meet the basic standard for an in vivo dermal absorption study.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Medium	Preparation and storage details were not provided; however, the test substance was applied neat so limited preparation was required and the lack of details are unlikely to have a significant impact on the study results.
	Metric 7:	Consistency of exposure administration	Low	Details of skin preparation were not provided. The study cited HERO ID 74541 for application methods. That reference specifies a skin area of 3.1 cm2, and the current study specifies application of 1mL of the neat test substance. The reference above indicated that the skin depot was covered with a glass covers slip. It is uncertain whether the current study followed the same parameters. The metric is scored a Low due to insufficient information on exposure administration.
	Metric 8:	Reporting of concentrations	Medium	The study reported applying a 1mL volume of neat material to the skin. The skin surface area was not reported in THIS study; however, a referenced citation for methods (HERO ID 74541) specified an area of 3.1 cm2. Animal body weights ranged from 600 – 800 g. A dose range (mg/kg) can be estimated using the density of the pure test substance. No analytical measurements were made.
	Metric 9:	Exposure duration	Low	Animals were exposed for 2, 6 or 12 hrs and the durations were appropriate for the study type. Measurements did not continue post-exposure to account for retained doses in the skin, and conditions of use were not specified.
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study tested as single undiluted (neat) dose. OECD guidelines recommend a minimum of 3 dose groups.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	The study used guinea pigs of both sexes obtained from an unspecified commercial source. The range of animal body weights was provided; age was not specified.

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Study Citation: Jakobson, I., Holmberg, B., Wahlberg, J. E. (1977). Variations in the blood concentration of 1,1,2-trichloroethane by percutaneous absorption and other routes of administration in the guinea pig. Acta Pharmacologica et Toxicologica 41(5):497-506.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 5465271
Unique ID: 12-hr duration

Domain	Metric		Rating	Comments
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry conditions were reported.
	Metric 13:	Number of animals per group	Low	The number of animals per group was not specified in the study methods. Based on the figures provided. 6 animals each were exposed for either 2hrs or 6hrs of exposure. Data for the 12 hr exposure group was only from 2 animals. It is unclear whether this group contained fewer animals at the start of the study, or if, for other reasons, data were only collected from two animals. The number of animals per sex was not specified.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	Outcome assessment was limited to blood sampling via the carotid artery. Urine, feces, and skin from the application site were not measured. The study did not collected blood for any period post-exposure. The handling of the samples following collection was reported. Concentrations in blood were measured using gas chromatography. The skin depots were covered with a coverslip which should be sufficient for occlusion. 1mL applied to an area of 3.1 cm2 is appropriate for an infinite exposure scenario. Skin was not examined for signs of irritation or damage.
	Metric 15:	Consistency of outcome assessment	Medium	There were some limitations in the methodological details provided. The frequency of collections was not specified in the methods, but could be determined by extracting data from the figures provided. It appears that the frequency of collection differed for each group (e.g., frequency of blood collection was greater for animals exposed for only two hours vs those exposed for 6 or 12 hrs). No justification was made for the frequencies of collection.
	Metric 16:	Sampling adequacy and sensitivity	Low	The number and interval of collections was adequate for the outcome of interest. The sample size for animals exposed for 12 hours was small (n =2) and no explanation was provided by the study authors.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Starting animal body weights ranged from 600 to 800 g. Starting weights on a per-group basis were not reported. Other potentially confounding variables, including whether different batches were used or if there were any differences in skin (e.g., hairy or signs of damage), were not reported. There is no indication that there were differences in the area of skin exposed (3.1 cm^2 based on the information in the cited study (HERO 74541).
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	No animals died during the study. The test substance was applied neat; therefore, solubility issues do not apply. It is unclear if there was any damaged tissue; the study cited another report suggesting skin damage was likely: "...skin lesions were observed under the microscope as early as 15 minutes after the start of an epicutaneous exposure of guinea pigs to 1,1,2-trichloroethane (Kronevi et al. 1977)."
Domain 7: Data Presentation and Analysis				

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Study Citation: Jakobson, I., Holmberg, B., Wahlberg, J. E. (1977). Variations in the blood concentration of 1,1,2-trichloroethane by percutaneous absorption and other routes of administration in the guinea pig. Acta Pharmacologica et Toxicologica 41(5):497-506.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Parent compound
HERO ID: 5465271
Unique ID: 12-hr duration

Domain	Metric		Rating	Comments
	Metric 19:	Data analysis	Uninformative	The study presented mean concentrations in blood across time. Regression analysis was performed on means from all three exposure times, as well as for all three sets together. Means and standard deviations for concentrations measured in blood over time were provided for the animals exposed for 6 hours. CV values were not reported, but could be calculated for the 6-hour exposure data provided. The study text indicated that the standard deviations were similar for the other durations, but did not include that data on the figures, so no independent analysis is possible. The study did not calculate flux or Kp values, but these could likely be calculated based on the data provided.
	Metric 20:	Data interpretation	Low	The study did not explicitly state using infinite or finite exposure scenarios and did not report the endpoints typically associated with those scenarios (e.g., Kp, or absorption estimates), thus deviates significantly from standard OECD guidelines. The study did not report % recovery.
	Metric 21:	Reporting of Data	Low	The study clearly calculated standard deviations for all groups but did only reported measures of variance for one group. The study did not measure or report all of the outcomes specified in OECD 427.

Overall Quality Determination Uninformative

Study Citation: Jakobson, I., Wahlberg, J. E., Holmberg, B., Johansson, G. (1982). Uptake via the blood and elimination of 10 organic solvents following epicutaneous exposure of anesthetized guinea pigs. Toxicology and Applied Pharmacology 63(2):181-187.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 94881
Unique ID: 1,1,1-Trichloroethane- uptake

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test material was identified asn 1,1,1-trichloroethane. The form (liquid or solid) of the test substance was not specified. It was not radiolabeled.
	Metric 2:	Test substance source	Low	The test material was sourced from Fisher Scientific Co. A batch or lot number was not specified. Certification was not provided. The exact material purchased from the supplier could not be determined (multiple products listed). Therefore, the chemical could not be verified on the supplier's website.
	Metric 3:	Test substance purity	Low	Reported to be inhibited - no further information was provided; a purity was not reported. Details could not be obtained from the supplier website.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not specify whether animals were randomized.
	Metric 5:	Standards for Tests	Uninformative	The study authors did not report whether the test met any pre-established criteria. This study did not employ the use of metabolism cages. Percutaneous uptake over time in an infinite exposure model was evaluated by measuring concentrations of the test substance in the blood. The study did not calculate or determine percent recovery. Graphs, presumably showing mean blood concentrations over time did not include any measures of variance. Measures of variance also were not provided in a table reporting quantitative values. This lack of data prevents the ability to determine the variance across means making it impossible to determine the validity of the test.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Low	Details of the test substance preparation and storage were not provided. No dilutions or use of vehicles were mentioned, so it is assumed that the materials were applied neat. Storage conditions of the purchased material were not reported, and the test material is a volatile chemical.
	Metric 7:	Consistency of exposure administration	High	Details of exposure administration were reported and based on the information provided, exposures were administered consistently across study groups. Glass rings (area 3.1 cm2) were glued onto the clipped skin on the backs of guinea pigs. A cover glass with a central hole was attached, and 1 mL of the test material was injected. The holes were covered to prevent leakage or evaporation.
	Metric 8:	Reporting of concentrations	Low	The study reported the volume applied (1mL per depot) and the skin surface area (3.1 cm2); equivalent to 0.322 mL/cm2. Using the density of the test material (1.32 g/mL), a dose in mg/cm2 can be determined. (2.17 g/mL) x 0.322 mL/cm2) = 0.425 g/cm2 (or 425mg/cm2). There is no indication that the purchased test material was analytically verified. The material was assumed to have been applied neat but no information on purity was provided.

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Study Citation: Jakobson, I., Wahlberg, J. E., Holmberg, B., Johansson, G. (1982). Uptake via the blood and elimination of 10 organic solvents following epicutaneous exposure of anesthetized guinea pigs. Toxicology and Applied Pharmacology 63(2):181-187.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 94881
Unique ID: 1,1,1-Trichloroethane- uptake

Domain	Metric		Rating	Comments
	Metric 9:	Exposure duration	High	Based on Figure 1 in the results, the exposure duration was 6 hours. The study authors did not provide justification for the duration of an uptake experiment. Other chemicals tested in the study were exposed for 12 hours. There is no indication that the 6-hour duration was insufficient.
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study included a single exposure group (animals exposed to 1 ml/3.1 cm2 (or 0.3225 mL/cm2). Separate sets of animals were used for elimination experiments (separate form). OECD TG 427 only specifies that a study will "normally involve several groups;" therefore, the number of groups in this study seems to be low. It is unclear whether the concentrations/dosing was appropriate. Exposure should mimic potential human exposure, which is typically up to 10 uL/cm2 for a liquid. The 322.5 uL/cm2 used in this study is significantly higher than recommended in OECD 427.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	The study used male and female guinea pigs (distribution within groups not specified) with starting body weights ranging between 600 and 1,000 g (a mean weight was not reported), and it is not known whether the weights of the animals within a group were within 20% of the mean weight. The animal strain, age, and source were not reported. Guinea pigs are an appropriate model as per OECD 427, although rats are more commonly used.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry details were provided.
	Metric 13:	Number of animals per group	Low	The number of animals per group was not reported in the methods. Based on Table 1, the study used a total of 4 animals per group. The methods indicated that both males and females were used, but the number of each sex/group was not specified. OECD TG 427 indicates that at least 4 animals of a single sex should be used, making this study critically deficient.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Uninformative	The outcome assessment methodology deviated significantly from OECD 427 guidelines. The surface area (3.1 cm2) is lower than the guideline recommendations and does not cover 10% of the animal surface area. Other than measuring the presence of the chemical in blood, the experiment did not evaluate the amount of chemical remaining in the excreta, carcass, skin, skin wash, or exhaled air. Therefore it cannot be used to determine skin absorption.
	Metric 15:	Consistency of outcome assessment	High	The outcome assessment methodology was reported, and, based on the available information was mostly consistent across groups.
	Metric 16:	Sampling adequacy and sensitivity	Low	None of the figures or data tables reported an "n." It is assumed that the data were generated from all 4 animals per group, but this was not explicitly stated. It is unclear if the frequency of blood collection is appropriate because it necessitated replacement with Marcodex.

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Study Citation: Jakobson, I., Wahlberg, J. E., Holmberg, B., Johansson, G. (1982). Uptake via the blood and elimination of 10 organic solvents following epicutaneous exposure of anesthetized guinea pigs. Toxicology and Applied Pharmacology 63(2):181-187.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 94881
Unique ID: 1,1,1-Trichloroethane- uptake

Domain	Metric	Rating	Comments
Domain 6: Confounding/Variable Control			
	Metric 17: Confounding variables in test design and procedures	Medium	The study did not report all information to determine whether confounding bias occurred (test substance batch, body weight changes, or body weight variations greater than 20%, compared to the mean, differences in rodent skin within the group).
	Metric 18: Confounding variables in outcomes unrelated to exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition, health outcomes unrelated to exposure, or solubility that could influence the outcome assessment.
Domain 7: Data Presentation and Analysis			
	Metric 19: Data analysis	Uninformative	This study did not determine absorption estimates. The only results were blood concentrations over time and these data were not statistically analyzed.
	Metric 20: Data interpretation	Uninformative	The study described the observed absorption pattern for the test material in blood. The concentration reached a peak within 1 hour and then plateaued, remaining constant throughout the rest of the exposure period. This study did not calculate the amount of test the chemical absorbed per cm2 of skin over time. The study cannot be used for estimating skin absorption due to significant deviations from standard guidelines.
	Metric 21: Reporting of Data	Uninformative	The data for all specified outcomes were presented. The plot of blood concentrations by time was reported. Only concentrations at 0.5 and 6 hours were provided in table format. None of the data provided in the study included measures of variance. Data were inadequate for evaluating the fraction of the chemical absorbed through skin.

Overall Quality Determination — Uninformative

Study Citation: Jakobson, I., Wahlberg, J. E., Holmberg, B., Johansson, G. (1982). Uptake via the blood and elimination of 10 organic solvents following epicutaneous exposure of anesthetized guinea pigs. Toxicology and Applied Pharmacology 63(2):181-187.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 94881
Unique ID: 1,1,1-trichloroethane - elimination

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test material was identified as 1,1,1-trichloroethane. The form (liquid or solid) of the test substance was not specified. It was not radiolabeled.
	Metric 2:	Test substance source	Low	The test material was sourced from Fisher Scientific Co. A batch or lot number was not specified. Certification was not provided. The exact material purchased from the supplier could not be determined (multiple products listed), therefore, the chemical could not be verified on the supplier's website.
	Metric 3:	Test substance purity	Low	Reported to be inhibited - no further information was provided; a purity was not reported. Details could not be obtained from the supplier website.
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Low	The study did not specify whether animals were randomized.
	Metric 5:	Standards for Tests	Uninformative	The study authors did not report whether the test met any pre-established criteria. This study did not employ the use of metabolism cages. Percutaneous uptake over time in an infinite exposure model was evaluated by measuring concentrations of the test substance in the blood. The study did not calculate or determine percent recovery. Graphs, presumably showing mean blood concentrations over time did not include any measures of variance. Measures of variance also were not provided in a table reporting quantitative values. This lack of data prevents the ability to determine the variance across means making it impossible to determine the validity of the test.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	Low	Details of the test substance preparation and storage were not provided. No dilutions or use of vehicles were mentioned, so it is assumed that the materials were applied neat. Storage conditions of the purchased material were not reported, and the test material is a volatile chemical.
	Metric 7:	Consistency of exposure administration	High	Details of exposure administration were reported and based on the information provided, exposures were administered consistently across study groups. Glass rings (area 3.1 cm2) were glued onto the clipped skin on the backs of guinea pigs. During elimination experiments, the seal on the chamber was removed, the test substance was aspirated off and skin dried.
	Metric 8:	Reporting of concentrations	Low	The study reported the volume applied (1mL per depot) and the skin surface area (3.1 cm2); equivalent to 0.322 mL/cm2. There is no indication that the purchased test material was analytically verified. The material was assumed to be applied neat but information purity was not provided.
	Metric 9:	Exposure duration	High	For the elimination part of the study, animals were percutaneously exposed for 4 hours. Blood samples were then taken during the following 2 hours. The duration was not justified but seemed to be appropriate for this part of the test.

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Study Citation: Jakobson, I., Wahlberg, J. E., Holmberg, B., Johansson, G. (1982). Uptake via the blood and elimination of 10 organic solvents following epicutaneous exposure of anesthetized guinea pigs. Toxicology and Applied Pharmacology 63(2):181-187.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 94881
Unique ID: 1,1,1-trichloroethane - elimination

Domain	Metric		Rating	Comments
	Metric 10:	Number of exposure groups and concentration spacing	Low	The study included a single exposure group (animals exposed to 1 ml/3.1 cm2 (or 0.3225 mL/cm2). Separate sets of animals were used for elimination experiments (separate form). OECD TG 427 only specifies that a study will "normally involve several groups;" therefore, the number of groups in this study seems to be low. It is unclear whether the concentrations/dosing was appropriate. Exposure should mimic potential human exposure, which is typically up to 10 uL/cm2 for a liquid. The 322.5 uL/cm2 used in this study is significantly higher than recommended in OECD 427.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Low	The study used male and female guinea pigs (distribution within groups not specified) with starting body weights ranging between 600 and 1,000 g (a mean weight was not reported), and it is not known whether the weights of the animals within a group were within 20% of the mean weight. The animal strain, age, and source were not reported. Guinea pigs are an appropriate model as per OECD 427, although rats are more commonly used.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Low	No animal husbandry details were provided.
	Metric 13:	Number of animals per group	Low	Although Table 1 identifies that total of 4 animals was used per group, which is consistent with OECD 427 guidelines, this appears to be for the uptake studies and not clear this number was used for elimination studies. The methods indicated that both males and females were used, but the number of each sex/group was not specified.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Uninformative	The outcome assessment methodology deviated significantly from OECD 427 guidelines. Based on the information provided (volume applied and surface area), a dose of 425 mg/cm2 was determined using a test substance density of 1.32 g/mL, indicating infinite dosing. The surface area (3.1 cm2) is lower than the guideline recommendations and does not cover 10% of the animal surface area. Other than measuring the chemical in blood, the experiment did not evaluate the chemical remaining in the excreta, carcass, skin, skin wash, or exhaled air. Therefore, it cannot be used to determine skin absorption.
	Metric 15:	Consistency of outcome assessment	High	The outcome assessment methodology was reported, and, based on the available information was mostly consistent across groups.
	Metric 16:	Sampling adequacy and sensitivity	Low	None of the figures or data tables reported an "n." It is assumed that the data were generated from all 4 animals per group, but this was not explicitly stated. It is unclear if the frequency of blood collection is appropriate because it necessitated replacement with Marcodex.
Domain 6: Confounding/Variable Control				

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Study Citation: Jakobson, I., Wahlberg, J. E., Holmberg, B., Johansson, G. (1982). Uptake via the blood and elimination of 10 organic solvents following epicutaneous exposure of anesthetized guinea pigs. Toxicology and Applied Pharmacology 63(2):181-187.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 94881
Unique ID: 1,1,1-trichloroethane - elimination

Domain	Metric		Rating	Comments
	Metric 17:	Confounding variables in test design and procedures	Medium	The study did not report all information to determine whether confounding bias occurred (test substance batch, body weight changes, or body weight variations greater than 20%, compared to the mean, differences in rodent skin within the group).
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition, health outcomes unrelated to exposure, or solubility that could influence the outcome assessment.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Uninformative	Nonlinear regression analysis was conducted on values obtained for the concentration of the test material in the blood. The study referenced Holmberg et al. 1977 for additional details (open access, reviewed for this assessment). This cited reference did not provide a significant amount of additional details. The data were fitted to an equation representing a simplified two-compartment kinetic model (Snyder et al. 1981). The study, however, cannot be used to measure absorption based on a lack of appropriate information.
	Metric 20:	Data interpretation	Uninformative	The study specified studying elimination, but only measured concentrations in blood for 2 hours post-exposure, and did not measure concentrations in other excreta. The study also did not calculate clearance from plasma, or report any elimination kinetics. This part of the study does not provide any useful information on absorption.
	Metric 21:	Reporting of Data	Uninformative	A figure shows elimination curves from blood drawn according to a two-compartment model. The ”n” was not reported and the data points had no measures of variance. Data were inadequate for evaluating the fraction of the chemical absorbed through skin.

Overall Quality Determination — Uninformative

Study Citation:	Morgan, D. L., Cooper, S. W., Carlock, D. L., Sykora, J. J., Sutton, B., Mattie, D. R., McDougal, J. N. (1991). Dermal absorption of neat and aqueous volatile organic chemicals in the Fischer 344 rat. Environmental Research 55(1):51-63.
Chemical:	1,1,2-Trichloroethane
Exposure Type:	Isomer
HERO ID:	200487; Linked HERO ID(s): 200487, 1070095
Unique ID:	1,1,1-trichloroethane - Neat

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test substance was identified as unlabeled 1,1,1-trichloroethane, obtained from Aldrich Chemical Co. It was stabilized with 0.05% low alkyl epoxides.
	Metric 2:	Test substance source	High	The test substance was obtained from Aldrich Chemical Co. The manufacturer, batch or lot number was not specified. The chemical purity was confirmed by gas chromatography by the performing laboratory.
	Metric 3:	Test substance purity	High	A purity of >99% was confirmed using gas chromatography
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Medium	The method of animal allocation was not specified, although, it was indicated that some normalization to body weight occurred (body weights of rats within the same dose group were all within a 10 g range).
	Metric 5:	Standards for Tests	Low	The study authors did not report whether the test met any pre-established criteria. This study did not employ the use of metabolism cages. Percutaneous uptake over time in an intended infinite exposure model was evaluated by measuring concentrations of the test substance in the blood. The study did not calculate or determine percent recovery. It was mentioned that there was no loss to head space in the exposure cells, or to evaporation. The study did not explicitly report coefficients of variance. Figures showing mean ± SEM blood concentrations over time that could be extracted. The "n" was reported as a range (n = 6-10); however, a later data table (Table 3) reports the actual number of animals per group. CVs for the volume of the chemical solution absorbed could easily be calculated based on the data provided. These CV values (calculated for this review and noted in Metric 19) were > 25%.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	High	No preparation of the neat chemical was required. Saturated aqueous solutions were prepared by mixing 10-20 mL of neat chemical with 200 mL of HPLC-grade water. Details of mixing and removal of any remaining immiscible chemicals were provided. The samples were stored at 5-10 degrees C in zero head-space vials for 24 -48 hours prior to use. The study text suggests that stability tests were performed, and the solutions were stable for at least three weeks. The saturated solutions were diluted with HPLC-grade water.

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Study Citation: Morgan, D. L., Cooper, S. W., Carlock, D. L., Sykora, J. J., Sutton, B., Mattie, D. R., McDougal, J. N. (1991). Dermal absorption of neat and aqueous volatile organic chemicals in the Fischer 344 rat. Environmental Research 55(1):51-63.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - Neat

Domain	Metric		Rating	Comments
	Metric 7:	Consistency of exposure administration	Medium	Most animals were consistently exposed using the same protocol. Briefly, glass exposure cells (20 mm diameter, skin area 3.1 cm2) were attached to the shaved backs of rats the day before exposure. 2 mL volumes of the test solution were added to each cell under occlusive conditions (2 mL/3.1 cm2 or 0.645 mL/cm2), and animals were exposed for 24 hours.The text indicated that one group of rats was exposed using an exposure cell that was completely filled, instead of leaving a small headspace. It wasn't specified if this was a completely separate group of animals, or if one of the 4 exposure groups was exposed in this way. The authors specified that the concentrations of 1,1,1-trichloroethane in the aqueous solutions were the same between the samples with headspace and the one without, so the difference is not expected to have a significant impact on results.
	Metric 8:	Reporting of concentrations	High	Animals were exposed to neat, 1/3 saturated (198 ug/mL), 2/3 saturated (335 ug/mL), or saturated (573 ug/mL) aqueous solutions. Saturated solutions were analyzed by GC to ensure that the concentrations were in the range of literature values for saturated aqueous solutions. The volume applied (2 mL) and skin surface area (3.1 cm2 dorsal skin) were reported.
	Metric 9:	Exposure duration	High	Animals were exposed for 24 hours, which is consistent with OECD 427 guidelines.
	Metric 10:	Number of exposure groups and concentration spacing	High	The study included 4 exposure groups. The concentration spacing was not explicitly justified, but the study wanted to determine if there were differences in the volume absorbed and in blood concentrations attained from different dilutions. The concentrations of the chemical in surface or groundwater were reported to be magnitudes lower than those used in this study.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Medium	The study used male Fisher 344 rats sourced from Charles River Breeding Laboratories. An initial body weight range (at purchase) was reported to be 201-215g. Animals were acclimated for a week. Body weights prior to exposure were reported to be between 215 and 300 g, with all rats within one dose group within a 10g range. The variation between groups is not clear. Animal age was not reported.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Medium	Housing, animals per cage, and food and water availability were reported. Additional animal husbandry details (e.g., temperature, humidity) were not specified.
	Metric 13:	Number of animals per group	Medium	The number of animals per group was not specified in the methods. Based on the data tables, the sample size ranged from 6 to 10. It is unclear whether all groups initially had 10 animals per group, or if the number per group was a range from 6-10 animals. OECD guidelines only require 4 animals per group, so overall, the number was more than required.
Domain 5: Outcome Assessment				

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Study Citation: Morgan, D. L., Cooper, S. W., Carlock, D. L., Sykora, J. J., Sutton, B., Mattie, D. R., McDougal, J. N. (1991). Dermal absorption of neat and aqueous volatile organic chemicals in the Fischer 344 rat. Environmental Research 55(1):51-63.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - Neat

Domain	Metric		Rating	Comments
	Metric 14:	Outcome assessment methodology	Low	The outcome assessment methodology was sufficient to address the intentions of this non-guideline study but deviated from a traditional dermal absorption study as per OECD 427. In brief, this study attempted infinite exposure under occlusion. The mass per area was >10 mg/cm2 for all exposure groups; however, exposure was only about 1% of the total rat skin surface area, which is less than the suggested 5-10% (OECD 28). The report also indicated that in most cases, "levels in the blood rapidly decreased to near control levels by 24 hrs, probably due to depletion of chemical from the exposure cell," although this was not seen with neat levels. Blood samples were collected during exposure at times 0, 0.5, 1, 2, 4, 8, and 24 hours. The collection vials were sealed and stored at 5 degrees until GC analysis. They were stable for at least 3 weeks. At the end of exposure, the volume of test solution remaining in the exposure cell was measured. The remaining volume was subtracted from the initial 2 mL used to obtain the volume absorbed. The methods suggest that these samples were stored for GC analysis, but no results reporting concentrations of the test substance in the unabsorbed fraction were reported. This study did not determine the % recovery or the percent absorbed, but these were not intended endpoints for this study. The study did not conduct any skin washes or a wash of the dermal cells. Concentrations in the skin, other bodily fluids, or in exhaled air were not analyzed. The sampling sizes were not specified in the methods but were provided in the data tables and figures. The figures reported sample sizes "n" as a range from 6-10. For the volume of aqueous chemical absorbed endpoint, the data table indicated exact sample sizes. It was noted that animals also absorbed ~0.18 mL of water during the 24-hour exposure period. It is unclear whether water in the aqueous solutions increased skin permeability.
	Metric 15:	Consistency of outcome assessment	Medium	Blood samples were collected during exposure at times 0, 0.5, 1, 2, 4, 8, and 24 hours from 6-10 animals per group. Sample volumes were reported to be 50 or 100 uL; it is unclear if different volumes were collected from animals within a group, or across groups for a single chemical. This inconsistency could have an impact on the study results. Other aspects of outcome assessment (e.g., the timing of blood collection and study termination) were consistent across groups. The volume of aqueous solution remaining in the exposure cells at the end of the experiment was also measured from each replicate.
	Metric 16:	Sampling adequacy and sensitivity	High	Details of sampling were reported; VOC concentrations in blood were measured using GC with flame ionization for halogenated VOCs and electron capture for nonhalogenated VOCs from three repetitive samplings from each collection. Samples were stable for 3 weeks under the storage conditions specified. The sampling was appropriate for the endpoint of interest.

Domain 6: Confounding/Variable Control

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Study Citation: Morgan, D. L., Cooper, S. W., Carlock, D. L., Sykora, J. J., Sutton, B., Mattie, D. R., McDougal, J. N. (1991). Dermal absorption of neat and aqueous volatile organic chemicals in the Fischer 344 rat. Environmental Research 55(1):51-63.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - Neat

Domain	Metric		Rating	Comments
	Metric 17:	Confounding variables in test design and procedures	Medium	Animal body weights at the start of exposure remained within 10 g within a group. Overall, weights ranged from 215-300 g. A mean was not specified, so it is not known if these ranges fall within 20% of the mean. It was noted that some exposure cells with low volumes of neat test chemicals were assumed to have leaked. The study tested multiple chemicals and did not specify what chemicals or how many samples were affected by this. It was noted that these cells were not used in the calculation of the mean absorption volume. The text also indicated that there was a small amount of headspace in the exposure cells; however, the authors said the headspace was too small to lower the exposure concentration. They confirmed this by exposing one group of rats to saturated 1,1,1-trichloroethane using a cell completely filled (no headspace). After 24 hours, the concentration of 1,1,1-trichloroethane was still depleted to an amount similar to samples that had a headspace, indicating no loss to headspace occurred.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition, health outcomes unrelated to exposure, or solubility that could influence the outcome assessment. Solubility was noted as a factor affecting absorption, where absorption of neat chemicals decreased as their water solubility decreased, but this was not a confounding factor.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	The coefficient of variation could only be determined for the volume of chemical solution absorbed. The study authors noted a significant amount of variation, and the CV (calculated for this review) was 37%, 28%, 68%, and 74% for the neat, saturated, 2/3 saturated, and 1/3 saturated solutions, respectively. Sufficient information (mean, SD and sample size) is provided for EPA to calculate an alternate upper-end value to account for variability in the results. Levels in blood over time were graphically displayed showing means ± SEM. The figures report n as a range (6-10), but exact n values can be obtained from another data table. No statistical analysis was conducted.
	Metric 20:	Data interpretation	Low	This study was not conducted according to OECD 427, or in a manner allowing the determination of recovery or the calculation of absorption estimates. The only tissue compartment analyzed was blood/plasma. Absorption volumes were also determined, but not the total percent absorbed. The authors found no correlation between blood levels and absorption volumes. Although the authors intended to create an infinite exposure scenario, less than 1% of the initial concentration was purportedly present in the exposure cells after 24 hours (chemical-specific quantitative values were not provided). This indicated rapid absorption and depletion from the aqueous solutions. The authors believed evaporation of the chemical was unlikely because the exposure cells were sealed, and the Teflon-coated caps were found not to absorb the test chemicals. The usefulness of this study is limited to demonstrating absorption through the skin occurs upon exposure to lower dilutions in aqueous solutions.

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - Neat

Domain	Metric	Rating	Comments
	Metric 21: Reporting of Data	Medium	Data were reported for all of the outcomes specified in the methods and included concentrations in blood over time and volume of test solution absorbed for each group. Data were presented as means ± either SE or SD. The number of samples was provided either as a range, or a specific numerical value. Individual animal data were not provided. Because a range was reported for some data (blood concentrations), CV values could not be calculated for those endpoints, which significantly reduces the ability to interpret the data.

Overall Quality Determination Medium

Study Citation: Morgan, D. L., Cooper, S. W., Carlock, D. L., Sykora, J. J., Sutton, B., Mattie, D. R., McDougal, J. N. (1991). Dermal absorption of neat and aqueous volatile organic chemicals in the Fischer 344 rat. Environmental Research 55(1):51-63.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - Saturated

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test substance was identified as unlabeled 1,1,1-trichloroethane, obtained from Aldrich Chemical Co. It was stabilized with 0.05% low alkyl epoxides.
	Metric 2:	Test substance source	High	The test substance was obtained from Aldrich Chemical Co. The manufacturer, batch or lot number was not specified. The chemical purity was confirmed by gas chromatography by the performing laboratory.
	Metric 3:	Test substance purity	High	A purity of >99% was confirmed using gas chromatography
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Medium	The method of animal allocation was not specified, although, it was indicated that some normalization to body weight occurred (body weights of rats within the same dose group were all within a 10 g range).
	Metric 5:	Standards for Tests	Low	The study authors did not report whether the test met any pre-established criteria. This study did not employ the use of metabolism cages. Percutaneous uptake over time in an intended infinite exposure model was evaluated by measuring concentrations of the test substance in the blood. The study did not calculate or determine percent recovery. It was mentioned that there was no loss to head space in the exposure cells, or to evaporation. The study did not explicitly report coefficients of variance. Figures showing mean ± SEM blood concentrations over time that could be extracted. The "n" was reported as a range (n = 6-10); however, a later data table (Table 3) reports the actual number of animals per group. CVs for the volume of the chemical solution absorbed could easily be calculated based on the data provided. These CV values (calculated for this review and noted in Metric 19) were > 25%.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	High	No preparation of the neat chemical was required. Saturated aqueous solutions were prepared by mixing 10-20 mL of neat chemical with 200 mL of HPLC-grade water. Details of mixing and removal of any remaining immiscible chemicals were provided. The samples were stored at 5-10 degrees C in zero head-space vials for 24 -48 hours prior to use. The study text suggests that stability tests were performed, and the solutions were stable for at least three weeks. The saturated solutions were diluted with HPLC-grade water.

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - Saturated

Domain	Metric		Rating	Comments
	Metric 7:	Consistency of exposure administration	Medium	Most animals were consistently exposed using the same protocol. Briefly, glass exposure cells (20 mm diameter, skin area 3.1 cm2) were attached to the shaved backs of rats the day before exposure. 2 mL volumes of the test solution were added to each cell under occlusive conditions (2 mL/3.1 cm2 or 0.645 mL/cm2), and animals were exposed for 24 hours.The text indicated that one group of rats was exposed using an exposure cell that was completely filled, instead of leaving a small headspace. It wasn't specified if this was a completely separate group of animals, or if one of the 4 exposure groups was exposed in this way. The authors specified that the concentrations of 1,1,1-trichloroethane in the aqueous solutions were the same between the samples with headspace and the one without, so the difference is not expected to have a significant impact on results.
	Metric 8:	Reporting of concentrations	High	Animals were exposed to neat, 1/3 saturated (198 ug/mL), 2/3 saturated (335 ug/mL), or saturated (573 ug/mL) aqueous solutions. Saturated solutions were analyzed by GC to ensure that the concentrations were in the range of literature values for saturated aqueous solutions. The volume applied (2 mL) and skin surface area (3.1 cm2 dorsal skin) were reported.
	Metric 9:	Exposure duration	High	Animals were exposed for 24 hours, which is consistent with OECD 427 guidelines.
	Metric 10:	Number of exposure groups and concentration spacing	High	The study included 4 exposure groups. The concentration spacing was not explicitly justified, but the study wanted to determine if there were differences in the volume absorbed and in blood concentrations attained from different dilutions. The concentrations of the chemical in surface or groundwater were reported to be magnitudes lower than those used in this study.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Medium	The study used male Fisher 344 rats sourced from Charles River Breeding Laboratories. An initial body weight range (at purchase) was reported to be 201-215g. Animals were acclimated for a week. Body weights prior to exposure were reported to be between 215 and 300 g, with all rats within one dose group within a 10g range. The variation between groups is not clear. Animal age was not reported.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Medium	Housing, animals per cage, and food and water availability were reported. Additional animal husbandry details (e.g., temperature, humidity) were not specified.
	Metric 13:	Number of animals per group	Medium	The number of animals per group was not specified in the methods. Based on the data tables, the sample size ranged from 6 to 10. It is unclear whether all groups initially had 10 animals per group, or if the number per group was a range from 6-10 animals. OECD guidelines only require 4 animals per group, so overall, the number was more than required.
Domain 5: Outcome Assessment				

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - Saturated

Domain	Metric		Rating	Comments
	Metric 14:	Outcome assessment methodology	Low	The outcome assessment methodology was sufficient to address the intentions of this non-guideline study but deviated from a traditional dermal absorption study as per OECD 427. In brief, this study attempted infinite exposure under occlusion. The mass per area was >10 mg/cm2 for all exposure groups; however, exposure was only about 1% of the total rat skin surface area, which is less than the suggested 5-10% (OECD 28). The report also indicated that in most cases, "levels in the blood rapidly decreased to near control levels by 24 hrs, probably due to depletion of chemical from the exposure cell," although this was not seen with neat levels. Blood samples were collected during exposure at times 0, 0.5, 1, 2, 4, 8, and 24 hours. The collection vials were sealed and stored at 5 degrees until GC analysis. They were stable for at least 3 weeks. At the end of exposure, the volume of test solution remaining in the exposure cell was measured. The remaining volume was subtracted from the initial 2 mL used to obtain the volume absorbed. The methods suggest that these samples were stored for GC analysis, but no results reporting concentrations of the test substance in the unabsorbed fraction were reported. This study did not determine the % recovery or the percent absorbed, but these were not intended endpoints for this study. The study did not conduct any skin washes or a wash of the dermal cells. Concentrations in the skin, other bodily fluids, or in exhaled air were not analyzed. The sampling sizes were not specified in the methods but were provided in the data tables and figures. The figures reported sample sizes "n" as a range from 6-10. For the volume of aqueous chemical absorbed endpoint, the data table indicated exact sample sizes. It was noted that animals also absorbed ~0.18 mL of water during the 24-hour exposure period. It is unclear whether water in the aqueous solutions increased skin permeability.
	Metric 15:	Consistency of outcome assessment	Medium	Blood samples were collected during exposure at times 0, 0.5, 1, 2, 4, 8, and 24 hours from 6-10 animals per group. Sample volumes were reported to be 50 or 100 uL; it is unclear if different volumes were collected from animals within a group, or across groups for a single chemical. This inconsistency could have an impact on the study results. Other aspects of outcome assessment (e.g., the timing of blood collection and study termination) were consistent across groups. The volume of aqueous solution remaining in the exposure cells at the end of the experiment was also measured from each replicate.
	Metric 16:	Sampling adequacy and sensitivity	High	Details of sampling were reported; VOC concentrations in blood were measured using GC with flame ionization for halogenated VOCs and electron capture for nonhalogenated VOCs from three repetitive samplings from each collection. Samples were stable for 3 weeks under the storage conditions specified. The sampling was appropriate for the endpoint of interest.

Domain 6: Confounding/Variable Control

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Study Citation: Morgan, D. L., Cooper, S. W., Carlock, D. L., Sykora, J. J., Sutton, B., Mattie, D. R., McDougal, J. N. (1991). Dermal absorption of neat and aqueous volatile organic chemicals in the Fischer 344 rat. Environmental Research 55(1):51-63.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - Saturated

Domain	Metric		Rating	Comments
	Metric 17:	Confounding variables in test design and procedures	Medium	Animal body weights at the start of exposure remained within 10 g within a group. Overall, weights ranged from 215-300 g. A mean was not specified, so it is not known if these ranges fall within 20% of the mean. It was noted that some exposure cells with low volumes of neat test chemicals were assumed to have leaked. The study tested multiple chemicals and did not specify what chemicals or how many samples were affected by this. It was noted that these cells were not used in the calculation of the mean absorption volume. The text also indicated that there was a small amount of headspace in the exposure cells; however, the authors said the headspace was too small to lower the exposure concentration. They confirmed this by exposing one group of rats to saturated 1,1,1-trichloroethane using a cell completely filled (no headspace). After 24 hours, the concentration of 1,1,1-trichloroethane was still depleted to an amount similar to samples that had a headspace, indicating no loss to headspace occurred.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition, health outcomes unrelated to exposure, or solubility that could influence the outcome assessment. Solubility was noted as a factor affecting absorption, where absorption of neat chemicals decreased as their water solubility decreased, but this was not a confounding factor.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	The coefficient of variation could only be determined for the volume of chemical solution absorbed. The study authors noted a significant amount of variation, and the CV (calculated for this review) was 37%, 28%, 68%, and 74% for the neat, saturated, 2/3 saturated, and 1/3 saturated solutions, respectively. Sufficient information (mean, SD and sample size) is provided for EPA to calculate an alternate upper-end value to account for variability in the results. Levels in blood over time were graphically displayed showing means ± SEM. The figures report n as a range (6-10), but exact n values can be obtained from another data table. No statistical analysis was conducted.
	Metric 20:	Data interpretation	Low	This study was not conducted according to OECD 427, or in a manner allowing the determination of recovery or the calculation of absorption estimates. The only tissue compartment analyzed was blood/plasma. Absorption volumes were also determined, but not the total percent absorbed. The authors found no correlation between blood levels and absorption volumes. Although the authors intended to create an infinite exposure scenario, less than 1% of the initial concentration was purportedly present in the exposure cells after 24 hours (chemical-specific quantitative values were not provided). This indicated rapid absorption and depletion from the aqueous solutions. The authors believed evaporation of the chemical was unlikely because the exposure cells were sealed, and the Teflon-coated caps were found not to absorb the test chemicals. The usefulness of this study is limited to demonstrating absorption through the skin occurs upon exposure to lower dilutions in aqueous solutions.

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - Saturated

Domain	Metric	Rating	Comments
	Metric 21: Reporting of Data	Medium	Data were reported for all of the outcomes specified in the methods and included concentrations in blood over time and volume of test solution absorbed for each group. Data were presented as means ± either SE or SD. The number of samples was provided either as a range, or a specific numerical value. Individual animal data were not provided. Because a range was reported for some data (blood concentrations), CV values could not be calculated for those endpoints, which significantly reduces the ability to interpret the data.

Overall Quality Determination Medium

Study Citation: Morgan, D. L., Cooper, S. W., Carlock, D. L., Sykora, J. J., Sutton, B., Mattie, D. R., McDougal, J. N. (1991). Dermal absorption of neat and aqueous volatile organic chemicals in the Fischer 344 rat. Environmental Research 55(1):51-63.
Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - 2/3 Saturated

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test substance was identified as unlabeled 1,1,1-trichloroethane, obtained from Aldrich Chemical Co. It was stabilized with 0.05% low alkyl epoxides.
	Metric 2:	Test substance source	High	The test substance was obtained from Aldrich Chemical Co. The manufacturer, batch or lot number was not specified. The chemical purity was confirmed by gas chromatography by the performing laboratory.
	Metric 3:	Test substance purity	High	A purity of >99% was confirmed using gas chromatography
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Medium	The method of animal allocation was not specified, although, it was indicated that some normalization to body weight occurred (body weights of rats within the same dose group were all within a 10 g range).
	Metric 5:	Standards for Tests	Low	The study authors did not report whether the test met any pre-established criteria. This study did not employ the use of metabolism cages. Percutaneous uptake over time in an intended infinite exposure model was evaluated by measuring concentrations of the test substance in the blood. The study did not calculate or determine percent recovery. It was mentioned that there was no loss to head space in the exposure cells, or to evaporation. The study did not explicitly report coefficients of variance. Figures showing mean ± SEM blood concentrations over time that could be extracted. The "n" was reported as a range (n = 6-10); however, a later data table (Table 3) reports the actual number of animals per group. CVs for the volume of the chemical solution absorbed could easily be calculated based on the data provided. These CV values (calculated for this review and noted in Metric 19) were > 25%.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	High	No preparation of the neat chemical was required. Saturated aqueous solutions were prepared by mixing 10-20 mL of neat chemical with 200 mL of HPLC-grade water. Details of mixing and removal of any remaining immiscible chemicals were provided. The samples were stored at 5-10 degrees C in zero head-space vials for 24 -48 hours prior to use. The study text suggests that stability tests were performed, and the solutions were stable for at least three weeks. The saturated solutions were diluted with HPLC-grade water.

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - 2/3 Saturated

Domain	Metric		Rating	Comments
	Metric 7:	Consistency of exposure administration	Medium	Most animals were consistently exposed using the same protocol. Briefly, glass exposure cells (20 mm diameter, skin area 3.1 cm2) were attached to the shaved backs of rats the day before exposure. 2 mL volumes of the test solution were added to each cell under occlusive conditions (2 mL/3.1 cm2 or 0.645 mL/cm2), and animals were exposed for 24 hours.The text indicated that one group of rats was exposed using an exposure cell that was completely filled, instead of leaving a small headspace. It wasn't specified if this was a completely separate group of animals, or if one of the 4 exposure groups was exposed in this way. The authors specified that the concentrations of 1,1,1-trichloroethane in the aqueous solutions were the same between the samples with headspace and the one without, so the difference is not expected to have a significant impact on results.
	Metric 8:	Reporting of concentrations	High	Animals were exposed to neat, 1/3 saturated (198 ug/mL), 2/3 saturated (335 ug/mL), or saturated (573 ug/mL) aqueous solutions. Saturated solutions were analyzed by GC to ensure that the concentrations were in the range of literature values for saturated aqueous solutions. The volume applied (2 mL) and skin surface area (3.1 cm2 dorsal skin) were reported.
	Metric 9:	Exposure duration	High	Animals were exposed for 24 hours, which is consistent with OECD 427 guidelines.
	Metric 10:	Number of exposure groups and concentration spacing	High	The study included 4 exposure groups. The concentration spacing was not explicitly justified, but the study wanted to determine if there were differences in the volume absorbed and in blood concentrations attained from different dilutions. The concentrations of the chemical in surface or groundwater were reported to be magnitudes lower than those used in this study.
Domain 4: Test Model				
	Metric 11:	Test animal characteristics	Medium	The study used male Fisher 344 rats sourced from Charles River Breeding Laboratories. An initial body weight range (at purchase) was reported to be 201-215g. Animals were acclimated for a week. Body weights prior to exposure were reported to be between 215 and 300 g, with all rats within one dose group within a 10g range. The variation between groups is not clear. Animal age was not reported.
	Metric 12:	Adequacy and consistency of animal husbandry conditions	Medium	Housing, animals per cage, and food and water availability were reported. Additional animal husbandry details (e.g., temperature, humidity) were not specified.
	Metric 13:	Number of animals per group	Medium	The number of animals per group was not specified in the methods. Based on the data tables, the sample size ranged from 6 to 10. It is unclear whether all groups initially had 10 animals per group, or if the number per group was a range from 6-10 animals. OECD guidelines only require 4 animals per group, so overall, the number was more than required.
Domain 5: Outcome Assessment				

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Chemical: 1,1,2-Trichloroethane
Exposure Type: Isomer
HERO ID: 200487; Linked HERO ID(s): 200487, 1070095
Unique ID: 1,1,1-trichloroethane - 2/3 Saturated

Domain	Metric		Rating	Comments
	Metric 14:	Outcome assessment methodology	Low	The outcome assessment methodology was sufficient to address the intentions of this non-guideline study but deviated from a traditional dermal absorption study as per OECD 427. In brief, this study attempted infinite exposure under occlusion. The mass per area was >10 mg/cm2 for all exposure groups; however, exposure was only about 1% of the total rat skin surface area, which is less than the suggested 5-10% (OECD 28). The report also indicated that in most cases, "levels in the blood rapidly decreased to near control levels by 24 hrs, probably due to depletion of chemical from the exposure cell," although this was not seen with neat levels. Blood samples were collected during exposure at times 0, 0.5, 1, 2, 4, 8, and 24 hours. The collection vials were sealed and stored at 5 degrees until GC analysis. They were stable for at least 3 weeks. At the end of exposure, the volume of test solution remaining in the exposure cell was measured. The remaining volume was subtracted from the initial 2 mL used to obtain the volume absorbed. The methods suggest that these samples were stored for GC analysis, but no results reporting concentrations of the test substance in the unabsorbed fraction were reported. This study did not determine the % recovery or the percent absorbed, but these were not intended endpoints for this study. The study did not conduct any skin washes or a wash of the dermal cells. Concentrations in the skin, other bodily fluids, or in exhaled air were not analyzed. The sampling sizes were not specified in the methods but were provided in the data tables and figures. The figures reported sample sizes "n" as a range from 6-10. For the volume of aqueous chemical absorbed endpoint, the data table indicated exact sample sizes. It was noted that animals also absorbed ~0.18 mL of water during the 24-hour exposure period. It is unclear whether water in the aqueous solutions increased skin permeability.
	Metric 15:	Consistency of outcome assessment	Medium	Blood samples were collected during exposure at times 0, 0.5, 1, 2, 4, 8, and 24 hours from 6-10 animals per group. Sample volumes were reported to be 50 or 100 uL; it is unclear if different volumes were collected from animals within a group, or across groups for a single chemical. This inconsistency could have an impact on the study results. Other aspects of outcome assessment (e.g., the timing of blood collection and study termination) were consistent across groups. The volume of aqueous solution remaining in the exposure cells at the end of the experiment was also measured from each replicate.
	Metric 16:	Sampling adequacy and sensitivity	High	Details of sampling were reported; VOC concentrations in blood were measured using GC with flame ionization for halogenated VOCs and electron capture for nonhalogenated VOCs from three repetitive samplings from each collection. Samples were stable for 3 weeks under the storage conditions specified. The sampling was appropriate for the endpoint of interest.

Domain 6: Confounding/Variable Control

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Domain	Metric		Rating	Comments
	Metric 17:	Confounding variables in test design and procedures	Medium	Animal body weights at the start of exposure remained within 10 g within a group. Overall, weights ranged from 215-300 g. A mean was not specified, so it is not known if these ranges fall within 20% of the mean. It was noted that some exposure cells with low volumes of neat test chemicals were assumed to have leaked. The study tested multiple chemicals and did not specify what chemicals or how many samples were affected by this. It was noted that these cells were not used in the calculation of the mean absorption volume. The text also indicated that there was a small amount of headspace in the exposure cells; however, the authors said the headspace was too small to lower the exposure concentration. They confirmed this by exposing one group of rats to saturated 1,1,1-trichloroethane using a cell completely filled (no headspace). After 24 hours, the concentration of 1,1,1-trichloroethane was still depleted to an amount similar to samples that had a headspace, indicating no loss to headspace occurred.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition, health outcomes unrelated to exposure, or solubility that could influence the outcome assessment. Solubility was noted as a factor affecting absorption, where absorption of neat chemicals decreased as their water solubility decreased, but this was not a confounding factor.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	The coefficient of variation could only be determined for the volume of chemical solution absorbed. The study authors noted a significant amount of variation, and the CV (calculated for this review) was 37%, 28%, 68%, and 74% for the neat, saturated, 2/3 saturated, and 1/3 saturated solutions, respectively. Sufficient information (mean, SD and sample size) is provided for EPA to calculate an alternate upper-end value to account for variability in the results. Levels in blood over time were graphically displayed showing means ± SEM. The figures report n as a range (6-10), but exact n values can be obtained from another data table. No statistical analysis was conducted.
	Metric 20:	Data interpretation	Low	This study was not conducted according to OECD 427, or in a manner allowing the determination of recovery or the calculation of absorption estimates. The only tissue compartment analyzed was blood/plasma. Absorption volumes were also determined, but not the total percent absorbed. The authors found no correlation between blood levels and absorption volumes. Although the authors intended to create an infinite exposure scenario, less than 1% of the initial concentration was purportedly present in the exposure cells after 24 hours (chemical-specific quantitative values were not provided). This indicated rapid absorption and depletion from the aqueous solutions. The authors believed evaporation of the chemical was unlikely because the exposure cells were sealed, and the Teflon-coated caps were found not to absorb the test chemicals. The usefulness of this study is limited to demonstrating absorption through the skin occurs upon exposure to lower dilutions in aqueous solutions.

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Unique ID: 1,1,1-trichloroethane - 2/3 Saturated

Domain	Metric	Rating	Comments
	Metric 21: Reporting of Data	Medium	Data were reported for all of the outcomes specified in the methods and included concentrations in blood over time and volume of test solution absorbed for each group. Data were presented as means ± either SE or SD. The number of samples was provided either as a range, or a specific numerical value. Individual animal data were not provided. Because a range was reported for some data (blood concentrations), CV values could not be calculated for those endpoints, which significantly reduces the ability to interpret the data.

Overall Quality Determination Medium

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Unique ID: 1,1,1-trichloroethane - 1/3 Saturated

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	Medium	The test substance was identified as unlabeled 1,1,1-trichloroethane, obtained from Aldrich Chemical Co. It was stabilized with 0.05% low alkyl epoxides.
	Metric 2:	Test substance source	High	The test substance was obtained from Aldrich Chemical Co. The manufacturer, batch or lot number was not specified. The chemical purity was confirmed by gas chromatography by the performing laboratory.
	Metric 3:	Test substance purity	High	A purity of >99% was confirmed using gas chromatography
Domain 2: Test Design				
	Metric 4:	Randomized allocation of animals	Medium	The method of animal allocation was not specified, although, it was indicated that some normalization to body weight occurred (body weights of rats within the same dose group were all within a 10 g range).
	Metric 5:	Standards for Tests	Low	The study authors did not report whether the test met any pre-established criteria. This study did not employ the use of metabolism cages. Percutaneous uptake over time in an intended infinite exposure model was evaluated by measuring concentrations of the test substance in the blood. The study did not calculate or determine percent recovery. It was mentioned that there was no loss to head space in the exposure cells, or to evaporation. The study did not explicitly report coefficients of variance. Figures showing mean ± SEM blood concentrations over time that could be extracted. The "n" was reported as a range (n = 6-10); however, a later data table (Table 3) reports the actual number of animals per group. CVs for the volume of the chemical solution absorbed could easily be calculated based on the data provided. These CV values (calculated for this review and noted in Metric 19) were > 25%.
Domain 3: Exposure Characterization				
	Metric 6:	Preparation and storage of test substance (chemical)	High	No preparation of the neat chemical was required. Saturated aqueous solutions were prepared by mixing 10-20 mL of neat chemical with 200 mL of HPLC-grade water. Details of mixing and removal of any remaining immiscible chemicals were provided. The samples were stored at 5-10 degrees C in zero head-space vials for 24 -48 hours prior to use. The study text suggests that stability tests were performed, and the solutions were stable for at least three weeks. The saturated solutions were diluted with HPLC-grade water.

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	Metric 9:	Exposure duration	High	Animals were exposed for 24 hours, which is consistent with OECD 427 guidelines.
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Domain 6: Confounding/Variable Control

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Overall Quality Determination Medium