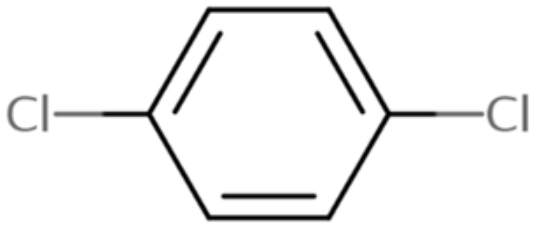
United States
Environmental Protection Agency

April 2026
Office of Chemical Safety and
Pollution Prevention

Draft Data Quality Evaluation Information for Dermal Absorption for *p*-Dichlorobenzene

Systematic Review Support Document for the Draft Risk Evaluation

CASRN 106-46-7



April 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 p-Dichlorobenzene* and were used to characterize dermal absorption. EPA conducted data quality evaluations based on author-reported descriptions and results; additional analyses (*e.g.*, statisti-cal analyses performed during data integration for the risk evaluation) potentially conducted by EPA are not contained in this supplemental file. Key parameters and corresponding data for each condition were 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 will be described in the *Draft Systematic Review Protocol for p-Dichlorobenzene*.

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 more appropriately. No OQD is determined for each reference as a whole, if it contains data from more than one condition. A single reference may evaluate only a limited number of conditions (*e.g.*, use of only the neat compound). If all other methods and results are adequate, the study may be considered acceptable for certain conditions of use. However, the study may still be limited for use in the risk evaluation because it may not address other uses (*e.g.*, lower concentrations, certain solvents/diluents).

Table of Contents

Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: Neat 10% in acetone

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test substance was definitively identified by name (p-dichlorobenzene; pDCB). Chemical structures were provided, and the position of the radiolabel [14C-pDCB] was shown.
	Metric 2:	Test substance source	High	The source of both the radiolabeled test substance was reported. The unlabeled test substance was supplied by the sponsor (American Chemicals Council). Batch numbers were reported and certificates of analysis were provided in an appendix.
	Metric 3:	Test substance purity	Medium	The reported purity of the unlabeled test substance was 99.9% and the purity of the radiolabeled test substance was 99.4% when received and 97.7% just prior to the start of the study. Radiochromatograms were provided.
Domain 2: Test Design				
	Metric 4:	Reference compounds	Medium	Use of a reference compound was not reported. The study did not include a description on whether the testing laboratory was proficient in conducting dermal absorption studies; however, the experiments were conducted by Charles River Laboratories, and they routinely conduct dermal absorption experiments and have used reference compounds in the past.
	Metric 5:	Assay procedures	High	All assay methods and procedures were described in detail and generally followed OECD TG 428. The receptor fluid was PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v). 6.4 uL of the test solution was applied (10 uL/cm2). The test substance was extremely volatile and volatility tests were conducted prior to the start of the study to determine the effectiveness of the occlusion and the carbon traps. Terminal procedures were described; quantification of radioactivity from all relevant samples and washes was done using a liquid scintillation counter. Limits of reliable measurements were determined.
	Metric 6:	Standards for tests	Medium	Criteria used to determine the validity acceptability, reliability, and/or quality of the experiment (e.g., percent recovery, and skin integrity were assessed. CV values were not provided in the study report but can be calculated based on the data shown.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	High	Preparation of the test solutions were described in detail, and radioactivity of the solutions was determined. Stability and solubility of the test substance in the vehicles (acetone, IPM, or HHN) were tested. The test substance was soluble in acetone. The radioactivity of each solution was determined. The static diffusion cell set up was described in detail. Conditions of use were not discussed; however, the study tested the test substance neat, and at least 3 dilutions each in two separate vehicles.
	Metric 8:	Consistency of exposure administration	Medium	Details of exposure administration were adequately reported and there was consistency across groups (e.g., consistent skin thickness, surface area, and volumes added)

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Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: Neat 10% in acetone

Domain	Metric		Rating	Comments
	Metric 9:	Reporting of concentrations	High	The test substance was applied neat at 1 or 5 mg/cm2 evaporated from acetone. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	The exposure duration was 8 hours prior to washing, and post-washing monitoring continued to 24 hours. The duration is appropriate for an occupational condition of use. A shorter period of time would have been appropriate as absorption was deemed to be complete within the first half of the exposure period.
	Metric 11:	Number of exposure groups and concentration spacing	High	In total, the study tested more than 3 dose groups as per OECD recommendations. This included 10% and 50% w/v neat in acetone, 50%, 10%, and 1% in IPM, and 40%, 10%, and 1% in HHN. The application of the test substance in acetone was followed by a sodium chloride application. This was reported to be representative of an exposure mixed with sweat; however, no specific justification of the 10% and 50% concentrations were provided.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	Abdominal skin was obtained from 11 female donors (aged 32 – 62) sourced from two different suppliers. Samples arrived on dry ice and were stored at -20 degrees C until use. The samples were dermatomed and the prepared split thickness skin was 390-400um thick.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates per dose/concentration group was reported and was appropriate. The study included a total of 8 samples per group, obtained from 4 different donors.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	Appropriate outcomes (e.g., total % absorbed) were assessed for finite exposure scenarios, and were conducted according to OECD 428. The study reported measurements from all components of the test system. The selected formulations are reasonable for the chemical of interest and would result in a sufficiently conservative estimate representative range of conditions of use for the chemical of interest (e.g., use of IPM diluent).
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment methods were reported, and the same protocol was applied across groups. The same receptor fluid. PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v) was used, and all groups shared the same durations and sampling periods.
	Metric 16:	Sampling adequacy and sensitivity	High	Sampling size and sampling intervals were adequate for the outcomes of interest. The study identified the limit of reliable measurement (LoRM) as 30 d.p.m. above background. Any counts below the LoRM were noted in the study results.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	High	Skin integrity was assessed by measuring TEWL and by conducting an electrical resistance barrier integrity test. No criteria were applied to the TEWL results. Any skin samples exhibiting resistance lower than 10.9 k ohms were excluded. TEWL measurements were also made 24 hrs after application. The neat test substance had no significant impact on skin integrity.

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Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: Neat 10% in acetone

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	Solubility in the receptor fluid was tested and the receptor fluid was not rate-limiting for skin absorption. There were no reported differences among replicates or groups in the test model unrelated to exposure.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Total percent absorption estimates were presented across time from relevant compartments. The study clearly described the reasoning behind the exclusion of outliers when determining mass balance and absorption estimates. Since data were sufficiently reported, an alternate analysis could be done if previously excluded datasets were wanted to be reconsidered. 1-2 datasets from the neat groups were excluded due to recovery issues. The CV values for recovery (mass balance were all <25%). The CV for total absorption was high (>50%) for the neat 50% solution, but data are available for EPA to calculate an alternate (upper end) value to account for variability in the results (mean, standard deviation, and number of replicates; per OECD NO. 156)
	Metric 20:	Data interpretation	High	Recovery was within 100 ± 20% for all replicates that were not excluded. One replicate from the 10% neat group and two from the 50% neat group were excluded due to exceptionally low recoveries. The total absorbed dose was determined for a finite exposure scenario and was the sum recovered in receptor fluid and in the receptor chamber wash. The study also determined a "dermal delivery" dose, which was the sum of the total absorbed and what was recovered from exposed skin; the first two tape strips were included in this measurement. Individual replicates and sample results were provided for EPA to calculate values as well.
	Metric 21:	Reporting of data	High	Data were reported for all outcomes (means and standard deviations) and in detail along with individual replicates.

Overall Quality Determination High

Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: Neat 50% in acetone

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test substance was definitively identified by name (p-dichlorobenzene; pDCB). Chemical structures were provided, and the position of the radiolabel [14C-pDCB] was shown.
	Metric 2:	Test substance source	High	The source of both the radiolabeled test substance was reported. The unlabeled test substance was supplied by the sponsor (American Chemicals Council). Batch numbers were reported and certificates of analysis were provided in an appendix.
	Metric 3:	Test substance purity	Medium	The reported purity of the unlabeled test substance was 99.9% and the purity of the radiolabeled test substance was 99.4% when received and 97.7% just prior to the start of the study. Radiochromatograms were provided.
Domain 2: Test Design				
	Metric 4:	Reference compounds	Medium	Use of a reference compound was not reported. The study did not include a description on whether the testing laboratory was proficient in conducting dermal absorption studies; however, the experiments were conducted by Charles River Laboratories, and they routinely conduct dermal absorption experiments and have used reference compounds in the past.
	Metric 5:	Assay procedures	High	All assay methods and procedures were described in detail and generally followed OECD TG 428. The receptor fluid was PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v). 6.4 uL of the test solution was applied (10 uL/cm2). The test substance was extremely volatile and volatility tests were conducted prior to the start of the study to determine the effectiveness of the occlusion and the carbon traps. Terminal procedures were described; quantification of radioactivity from all relevant samples and washes was done using a liquid scintillation counter. Limits of reliable measurements were determined.
	Metric 6:	Standards for tests	Medium	Criteria used to determine the validity acceptability, reliability, and/or quality of the experiment (e.g., percent recovery, and skin integrity were assessed. CV values were not provided in the study report but can be calculated based on the data shown.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	High	Preparation of the test solutions were described in detail, and radioactivity of the solutions was determined. Stability and solubility of the test substance in the vehicles (acetone, IPM, or HHN) were tested. The test substance was soluble in acetone. The radioactivity of each solution was determined. The static diffusion cell set up was described in detail. Conditions of use were not discussed; however, the study tested the test substance neat, and at least 3 dilutions each in two separate vehicles.
	Metric 8:	Consistency of exposure administration	Medium	Details of exposure administration were adequately reported and there was consistency across groups (e.g., consistent skin thickness, surface area, and volumes added)
	Metric 9:	Reporting of concentrations	High	The test substance was applied neat at 1 or 5 mg/cm2 evaporated from acetone. Individual cells are reported independently. Nominal and analytical doses are reported.

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Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: Neat 50% in acetone

Domain	Metric		Rating	Comments
	Metric 10:	Exposure frequency	High	The exposure duration was 8 hours prior to washing, and post-washing monitoring continued to 24 hours. The duration is appropriate for an occupational condition of use. A shorter period of time would have been appropriate as absorption was deemed to be complete within the first half of the exposure period.
	Metric 11:	Number of exposure groups and concentration spacing	High	In total, the study tested more than 3 dose groups as per OECD recommendations. This included 10% and 50% w/v neat in acetone, 50%, 10%, and 1% in IPM, and 40%, 10%, and 1% in HHN. The application of the test substance in acetone was followed by a sodium chloride application. This was reported to be representative of an exposure mixed with sweat; however, no specific justification of the 10% and 50% concentrations were provided.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	Abdominal skin was obtained from 11 female donors (aged 32 – 62) sourced from two different suppliers. Samples arrived on dry ice and were stored at -20 degrees C until use. The samples were dermatomed and the prepared split thickness skin was 390-400um thick.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates per dose/concentration group was reported and was appropriate. The study included a total of 8 samples per group, obtained from 4 different donors.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	Appropriate outcomes (e.g., total % absorbed) were assessed for finite exposure scenarios, and were conducted according to OECD 428. The study reported measurements from all components of the test system. The selected formulations are reasonable for the chemical of interest and would result in a sufficiently conservative estimate representative range of conditions of use for the chemical of interest (e.g., use of IPM diluent).
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment methods were reported, and the same protocol was applied across groups. The same receptor fluid. PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v) was used, and all groups shared the same durations and sampling periods.
	Metric 16:	Sampling adequacy and sensitivity	High	Sampling size and sampling intervals were adequate for the outcomes of interest. The study identified the limit of reliable measurement (LoRM) as 30 d.p.m. above background. Any counts below the LoRM were noted in the study results.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	High	Skin integrity was assessed by measuring TEWL and by conducting an electrical resistance barrier integrity test. No criteria were applied to the TEWL results. Any skin samples exhibiting resistance lower than 10.9 k ohms were excluded. TEWL measurements were also made 24 hrs after application. The neat test substance had no significant impact on skin integrity.

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Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: Neat 50% in acetone

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	Solubility in the receptor fluid was tested and the receptor fluid was not rate-limiting for skin absorption. There were no reported differences among replicates or groups in the test model unrelated to exposure.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	High	Total percent absorption estimates were presented across time from relevant compartments. The study clearly described the reasoning behind the exclusion of outliers when determining mass balance and absorption estimates. Since data were sufficiently reported, an alternate analysis could be done if previously excluded datasets were wanted to be reconsidered. 1-2 datasets from the neat groups were excluded due to recovery issues. The CV values for recovery (mass balance were all <25%). The CV for total absorption was <25% for the neat (10% in acetone) solution.
	Metric 20:	Data interpretation	High	Recovery was within 100 ± 20% for all replicates that were not excluded. One replicate from the 10% neat group and two from the 50% neat group were excluded due to exceptionally low recoveries. The total absorbed dose was determined for a finite exposure scenario and was the sum recovered in receptor fluid and in the receptor chamber wash. The study also determined a "dermal delivery" dose, which was the sum of the total absorbed and what was recovered from exposed skin; the first two tape strips were included in this measurement. Individual replicates and sample results were provided for EPA to calculate values as well.
	Metric 21:	Reporting of data	High	Data were reported for all outcomes (means and standard deviations) and in detail along with individual replicates.

Overall Quality Determination High

Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 50% in IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test substance was definitively identified by name (p-dichlorobenzene; pDCB). Chemical structures were provided, and the position of the radiolabel [14C-pDCB] was shown.
	Metric 2:	Test substance source	High	The source of both the radiolabeled test substance was reported. The unlabeled test substance was supplied by the sponsor (American Chemicals Council). Batch numbers were reported and certificates of analysis were provided in an appendix.
	Metric 3:	Test substance purity	Medium	The reported purity of the unlabeled test substance was 99.9% and the purity of the radiolabeled test substance was 99.4% when received and 97.7% just prior to the start of the study. Radiochromatograms were provided.
Domain 2: Test Design				
	Metric 4:	Reference compounds	Medium	Use of a reference compound was not reported. The study did not include a description on whether the testing laboratory was proficient in conducting dermal absorption studies; however, the experiments were conducted by Charles River Laboratories, and they routinely conduct dermal absorption experiments and have used reference compounds in the past.
	Metric 5:	Assay procedures	High	All assay methods and procedures were described in detail and generally followed OECD TG 428. The receptor fluid was PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v). 6.4 uL of the test solution was applied (10 uL/cm2). The test substance was extremely volatile and volatility tests were conducted prior to the start of the study to determine the effectiveness of the occlusion and the carbon traps. Terminal procedures were described; quantification of radioactivity from all relevant samples and washes was done using a liquid scintillation counter. Limits of reliable measurements were determined.
	Metric 6:	Standards for tests	Medium	Criteria used to determine the validity acceptability, reliability, and/or quality of the experiment (e.g., percent recovery, and skin integrity were assessed. CV values were not provided in the study report but can be calculated based on the data shown.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	Medium	Preparation of the test solutions was described in detail, and the radioactivity of the solutions was determined. Stability and solubility of the test substance in the vehicles (acetone, IPM, or HHN) were tested. Solubility tests showed that IPM test solutions formed a cloudy suspension with small, evenly dispersed particles, indicating some concern for solubility. The radioactivity of each solution was determined. The static diffusion cell set up was described in detail. Conditions of use were not discussed; however, the study tested the test substance neat and at least 3 dilutions each in two separate vehicles.
	Metric 8:	Consistency of exposure administration	Medium	Details of exposure administration were adequately reported and there was consistency across groups (e.g., consistent skin thickness, surface area, and volumes added)

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Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 50% in IPM

Domain	Metric		Rating	Comments
	Metric 9:	Reporting of concentrations	High	The test substance was applied at an application rate of 10 uL/cm2, which is appropriate for a finite exposure scenario. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	The exposure duration was 8 hours prior to washing, and post-washing monitoring continued to 24 hours. The duration is appropriate for an occupational condition of use. A shorter period of time would have been appropriate as absorption was deemed to be complete within the first half of the exposure period.
	Metric 11:	Number of exposure groups and concentration spacing	High	In total, the study tested more than 3 dose groups as per OECD recommendations. This included 10% and 50% w/v neat in acetone, 50%, 10%, and 1% in IPM, and 40%, 10%, and 1% in HHN. The application of the test substance in acetone was followed by a sodium chloride application. This was reported to be representative of an exposure mixed with sweat; however, no specific justification of the 10% and 50% concentrations were provided.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	Abdominal skin was obtained from 11 female donors (aged 32 – 62) sourced from two different suppliers. Samples arrived on dry ice and were stored at -20 degrees C until use. The samples were dermatomed and the prepared split thickness skin was 390-400um thick.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates per dose/concentration group was reported and was appropriate. The study included a total of 8 samples per group, obtained from 4 different donors.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	Appropriate outcomes (e.g., total % absorbed) were assessed for finite exposure scenarios, and were conducted according to OECD 428. The study reported measurements from all components of the test system. The selected formulations are reasonable for the chemical of interest and would result in a sufficiently conservative estimate representative range of conditions of use for the chemical of interest (e.g., use of IPM diluent).
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment methods were reported, and the same protocol was applied across groups. The same receptor fluid. PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v) was used, and all groups shared the same durations and sampling periods.
	Metric 16:	Sampling adequacy and sensitivity	High	Sampling size and sampling intervals were adequate for the outcomes of interest. The study identified the limit of reliable measurement (LoRM) as 30 d.p.m. above background. Any counts below the LoRM were noted in the study results.
Domain 6: Confounding/Variable Control				

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Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 50% in IPM

Domain	Metric		Rating	Comments
	Metric 17:	Confounding variables in test design and procedures	Medium	Skin integrity was assessed by measuring TEWL and by conducting an electrical resistance barrier integrity test. No criteria were applied to the TEWL results. Any skin samples exhibiting resistance lower than 10.9 k ohms were excluded. TEWL measurements were also made 24 hrs after application. The 24 hr TEWL measurements were increased from initial values, and the study authors noted that exposure to IPM may adversely affect the barrier integrity of the skin samples.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	Solubility in the receptor fluid was tested and the receptor fluid was not rate-limiting for skin absorption. There were no reported differences among replicates or groups in the test model unrelated to exposure.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Total percent absorption estimates were presented across time from relevant compartments. The study clearly described the reasoning behind the exclusion of outliers when determining mass balance and absorption estimates. Since data were sufficiently reported, an alternate analysis could be done if previously excluded datasets were wanted to be reconsidered. 1-2 datasets from the neat groups were excluded due to recovery issues. The CV values for recovery (mass balance were all $<$25%). CV values for total absorption (all dilutions) were $>$25% and $<$50%; data are available for EPA to calculate an alternate (upper end) value to account for variability in the results (mean, standard deviation, and number of replicates; per OECD NO. 156)
	Metric 20:	Data interpretation	Medium	The mean mass balance was 79.55% for the 50% in IPM group, which is slightly less than the 100 $\pm$ 20% noted for volatile substances in OECD 428. 4/4 replicates had mass balances below 80%. One of the replicates with an exceptionally low mass balance was excluded. The total absorbed dose was determined for a finite exposure scenario and was the sum recovered in receptor fluid and in the receptor chamber wash. The study also determined a “dermal delivery” dose, which was the sum of the total absorbed and what was recovered from exposed skin; the first two tape strips were included in this measurement. Individual replicates and sample results were provided for EPA to calculate values as well.
	Metric 21:	Reporting of data	High	Data were reported for all outcomes (means and standard deviations) and in detail along with individual replicates.

Overall Quality Determination — High

Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 10% and 1% in IPM

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test substance was definitively identified by name (p-dichlorobenzene; pDCB). Chemical structures were provided, and the position of the radiolabel [14C-pDCB] was shown.
	Metric 2:	Test substance source	High	The source of both the radiolabeled test substance was reported. The unlabeled test substance was supplied by the sponsor (American Chemicals Council). Batch numbers were reported and certificates of analysis were provided in an appendix.
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Domain 2: Test Design				
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	Metric 5:	Assay procedures	High	All assay methods and procedures were described in detail and generally followed OECD TG 428. The receptor fluid was PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v). 6.4 uL of the test solution was applied (10 uL/cm2). The test substance was extremely volatile and volatility tests were conducted prior to the start of the study to determine the effectiveness of the occlusion and the carbon traps. Terminal procedures were described; quantification of radioactivity from all relevant samples and washes was done using a liquid scintillation counter. Limits of reliable measurements were determined.
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	Metric 8:	Consistency of exposure administration	Medium	Details of exposure administration were adequately reported and there was consistency across groups (e.g., consistent skin thickness, surface area, and volumes added)

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Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 10% and 1% in IPM

Domain	Metric		Rating	Comments
	Metric 9:	Reporting of concentrations	High	The test substance was applied at an application rate of 10 uL/cm2, which is appropriate for a finite exposure scenario. Individual cells are reported independently. Nominal and analytical doses are reported.
	Metric 10:	Exposure frequency	High	The exposure duration was 8 hours prior to washing, and post-washing monitoring continued to 24 hours. The duration is appropriate for an occupational condition of use. A shorter period of time would have been appropriate as absorption was deemed to be complete within the first half of the exposure period.
	Metric 11:	Number of exposure groups and concentration spacing	High	In total, the study tested more than 3 dose groups as per OECD recommendations. This included 10% and 50% w/v neat in acetone, 50%, 10%, and 1% in IPM, and 40%, 10%, and 1% in HHN. The application of the test substance in acetone was followed by a sodium chloride application. This was reported to be representative of an exposure mixed with sweat; however, no specific justification of the 10% and 50% concentrations were provided.
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	Metric 12:	Test model (skin)	High	Abdominal skin was obtained from 11 female donors (aged 32 – 62) sourced from two different suppliers. Samples arrived on dry ice and were stored at -20 degrees C until use. The samples were dermatomed and the prepared split thickness skin was 390-400um thick.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates per dose/concentration group was reported and was appropriate. The study included a total of 8 samples per group, obtained from 4 different donors.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	Appropriate outcomes (e.g., total % absorbed) were assessed for finite exposure scenarios, and were conducted according to OECD 428. The study reported measurements from all components of the test system. The selected formulations are reasonable for the chemical of interest and would result in a sufficiently conservative estimate representative range of conditions of use for the chemical of interest (e.g., use of IPM diluent).
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment methods were reported, and the same protocol was applied across groups. The same receptor fluid. PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v) was used, and all groups shared the same durations and sampling periods.
	Metric 16:	Sampling adequacy and sensitivity	High	Sampling size and sampling intervals were adequate for the outcomes of interest. The study identified the limit of reliable measurement (LoRM) as 30 d.p.m. above background. Any counts below the LoRM were noted in the study results.
Domain 6: Confounding/Variable Control				

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Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 10% and 1% in IPM

Domain	Metric		Rating	Comments
	Metric 17:	Confounding variables in test design and procedures	Medium	Skin integrity was assessed by measuring TEWL and by conducting an electrical resistance barrier integrity test. No criteria were applied to the TEWL results. Any skin samples exhibiting resistance lower than 10.9 k ohms were excluded. TEWL measurements were also made 24 hrs after application. The 24 hr TEWL measurements were increased from initial values, and the study authors noted that exposure to IPM may adversely affect the barrier integrity of the skin samples.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	Solubility in the receptor fluid was tested and the receptor fluid was not rate-limiting for skin absorption. There were no reported differences among replicates or groups in the test model unrelated to exposure.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Total percent absorption estimates were presented across time from relevant compartments. The study clearly described the reasoning behind the exclusion of outliers when determining mass balance and absorption estimates. Since data were sufficiently reported, an alternate analysis could be done if previously excluded datasets were wanted to be reconsidered. 1-2 datasets from the neat groups were excluded due to recovery issues. The CV values for recovery (mass balance were all $<$25%). CV values for total absorption (all dilutions) were $>$25% and $<$50%; data are available for EPA to calculate an alternate (upper end) value to account for variability in the results (mean, standard deviation, and number of replicates; per OECD NO. 156)
	Metric 20:	Data interpretation	Medium	The mean mass balances were 100 $\pm$ 20% which is acceptable for volatile substances in OECD 428. 4/4 replicates in each dilution had mass balances below 80%. One of the replicates with an exceptionally low mass balance was excluded. The total absorbed dose was determined for a finite exposure scenario and was the sum recovered in receptor fluid and in the receptor chamber wash. The study also determined a "dermal delivery" dose, which was the sum of the total absorbed and what was recovered from exposed skin; the first two tape strips were included in this measurement. Individual replicates and sample results were provided for EPA to calculate values as well.
	Metric 21:	Reporting of data	High	Data were reported for all outcomes (means and standard deviations) and in detail along with individual replicates.

Overall Quality Determination — High

Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 40% in HHN

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test substance was definitively identified by name (p-dichlorobenzene; pDCB). Chemical structures were provided, and the position of the radiolabel [14C-pDCB] was shown.
	Metric 2:	Test substance source	High	The source of both the radiolabeled test substance was reported. The unlabeled test substance was supplied by the sponsor (American Chemicals Council). Batch numbers were reported and certificates of analysis were provided in an appendix.
	Metric 3:	Test substance purity	Medium	The reported purity of the unlabeled test substance was 99.9% and the purity of the radiolabeled test substance was 99.4% when received and 97.7% just prior to the start of the study. Radiochromatograms were provided.
Domain 2: Test Design				
	Metric 4:	Reference compounds	Medium	Use of a reference compound was not reported. The study did not include a description on whether the testing laboratory was proficient in conducting dermal absorption studies; however, the experiments were conducted by Charles River Laboratories, and they routinely conduct dermal absorption experiments and have used reference compounds in the past.
	Metric 5:	Assay procedures	High	All assay methods and procedures were described in detail and generally followed OECD TG 428. The receptor fluid was PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v). 6.4 uL of the test solution was applied (10 uL/cm2). The test substance was extremely volatile and volatility tests were conducted prior to the start of the study to determine the effectiveness of the occlusion and the carbon traps. Terminal procedures were described; quantification of radioactivity from all relevant samples and washes was done using a liquid scintillation counter. Limits of reliable measurements were determined.
	Metric 6:	Standards for tests	Medium	Criteria used to determine the validity acceptability, reliability, and/or quality of the experiment (e.g., percent recovery, and skin integrity were assessed. CV values were not provided in the study report but can be calculated based on the data shown.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	High	Preparation of the test solutions was described in detail, and the radioactivity of the solutions was determined. Stability and solubility of the test substance in the vehicles (acetone, IPM, or HHN) were tested. The test substance was soluble in HHN. The radioactivity of each solution was determined. The static diffusion cell set up was described in detail. Conditions of use were not discussed; however, the study tested the test substance neat and at least 3 dilutions each in two separate vehicles.
	Metric 8:	Consistency of exposure administration	Medium	Details of exposure administration were adequately reported and there was consistency across groups (e.g., consistent skin thickness, surface area, and volumes added)
	Metric 9:	Reporting of concentrations	High	The test substance was applied at an application rate of 10 uL/cm2, which is appropriate for a finite exposure scenario. Individual cells are reported independently. Nominal and analytical doses are reported.

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Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 40% in HHN

Domain	Metric		Rating	Comments
	Metric 10:	Exposure frequency	High	The exposure duration was 8 hours prior to washing, and post-washing monitoring continued to 24 hours. The duration is appropriate for an occupational condition of use. A shorter period of time would have been appropriate as absorption was deemed to be complete within the first half of the exposure period.
	Metric 11:	Number of exposure groups and concentration spacing	High	In total, the study tested more than 3 dose groups as per OECD recommendations. This included 10% and 50% w/v neat in acetone, 50%, 10%, and 1% in IPM, and 40%, 10%, and 1% in HHN. The application of the test substance in acetone was followed by a sodium chloride application. This was reported to be representative of an exposure mixed with sweat; however, no specific justification of the 10% and 50% concentrations were provided.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	Abdominal skin was obtained from 11 female donors (aged 32 – 62) sourced from two different suppliers. Samples arrived on dry ice and were stored at -20 degrees C until use. The samples were dermatomed and the prepared split thickness skin was 390-400um thick.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates per dose/concentration group was reported and was appropriate. The study included a total of 8 samples per group, obtained from 4 different donors.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	Appropriate outcomes (e.g., total % absorbed) were assessed for finite exposure scenarios, and were conducted according to OECD 428. The study reported measurements from all components of the test system. The selected formulations are reasonable for the chemical of interest and would result in a sufficiently conservative estimate representative range of conditions of use for the chemical of interest (e.g., use of IPM diluent).
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment methods were reported, and the same protocol was applied across groups. The same receptor fluid. PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v) was used, and all groups shared the same durations and sampling periods.
	Metric 16:	Sampling adequacy and sensitivity	High	Sampling size and sampling intervals were adequate for the outcomes of interest. The study identified the limit of reliable measurement (LoRM) as 30 d.p.m. above background. Any counts below the LoRM were noted in the study results.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Skin integrity was assessed by measuring TEWL and by conducting an electrical resistance barrier integrity test. No criteria were applied to the TEWL results. Any skin samples exhibiting resistance lower than 10.9 k ohms were excluded. TEWL measurements were also made 24 hrs after application. TEWEL measurements conducted at 24 hrs were inconsistent, so it was not possible to predict the effect of exposure to HHN on barrier integrity.

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Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 40% in HHN

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	Solubility in the receptor fluid was tested and the receptor fluid was not rate-limiting for skin absorption. There were no reported differences among replicates or groups in the test model unrelated to exposure.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	High	Total percent absorption estimates were presented across time from relevant compartments. The study clearly described the reasoning behind the exclusion of outliers when determining mass balance and absorption estimates. Since data were sufficiently reported, an alternate analysis could be done if previously excluded datasets were wanted to be reconsidered. 1-2 datasets from the neat groups were excluded due to recovery issues. The CV values for recovery (mass balance were all <25%). The CV value for total absorption was low (<25%) in the 40% in HHN group.
	Metric 20:	Data interpretation	High	The mean mass balance for all dilutions in HHN were 100 ± 20%, which is sufficient for volatile substances according to OECD 128. The total absorbed dose was determined for a finite exposure scenario and was the sum recovered in receptor fluid and in the receptor chamber wash. The study also determined a "dermal delivery" dose, which was the sum of the total absorbed and what was recovered from exposed skin; the first two tape strips were included in this measurement. Individual replicates and sample results were provided for EPA to calculate values as well.
	Metric 21:	Reporting of data	High	Data were reported for all outcomes (means and standard deviations) and in detail along with individual replicates.

Overall Quality Determination High

Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 10% and 1% in HHN

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test substance was definitively identified by name (p-dichlorobenzene; pDCB). Chemical structures were provided, and the position of the radiolabel [14C-pDCB] was shown.
	Metric 2:	Test substance source	High	The source of both the radiolabeled test substance was reported. The unlabeled test substance was supplied by the sponsor (American Chemicals Council). Batch numbers were reported and certificates of analysis were provided in an appendix.
	Metric 3:	Test substance purity	Medium	The reported purity of the unlabeled test substance was 99.9% and the purity of the radiolabeled test substance was 99.4% when received and 97.7% just prior to the start of the study. Radiochromatograms were provided.
Domain 2: Test Design				
	Metric 4:	Reference compounds	Medium	Use of a reference compound was not reported. The study did not include a description on whether the testing laboratory was proficient in conducting dermal absorption studies; however, the experiments were conducted by Charles River Laboratories, and they routinely conduct dermal absorption experiments and have used reference compounds in the past.
	Metric 5:	Assay procedures	High	All assay methods and procedures were described in detail and generally followed OECD TG 428. The receptor fluid was PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v). 6.4 uL of the test solution was applied (10 uL/cm2). The test substance was extremely volatile and volatility tests were conducted prior to the start of the study to determine the effectiveness of the occlusion and the carbon traps. Terminal procedures were described; quantification of radioactivity from all relevant samples and washes was done using a liquid scintillation counter. Limits of reliable measurements were determined.
	Metric 6:	Standards for tests	Medium	Criteria used to determine the validity acceptability, reliability, and/or quality of the experiment (e.g., percent recovery, and skin integrity were assessed. CV values were not provided in the study report but can be calculated based on the data shown.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and storage of test substance (chemical)	High	Preparation of the test solutions was described in detail, and the radioactivity of the solutions was determined. Stability and solubility of the test substance in the vehicles (acetone, IPM, or HHN) were tested. The test substance was soluble in HHN. The radioactivity of each solution was determined. The static diffusion cell set up was described in detail. Conditions of use were not discussed; however, the study tested the test substance neat and at least 3 dilutions each in two separate vehicles.
	Metric 8:	Consistency of exposure administration	Medium	Details of exposure administration were adequately reported and there was consistency across groups (e.g., consistent skin thickness, surface area, and volumes added)
	Metric 9:	Reporting of concentrations	High	The test substance was applied at an application rate of 10 uL/cm2, which is appropriate for a finite exposure scenario. Individual cells are reported independently. Nominal and analytical doses are reported.

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Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 10% and 1% in HHN

Domain	Metric		Rating	Comments
	Metric 10:	Exposure frequency	High	The exposure duration was 8 hours prior to washing, and post-washing monitoring continued to 24 hours. The duration is appropriate for an occupational condition of use. A shorter period of time would have been appropriate as absorption was deemed to be complete within the first half of the exposure period.
	Metric 11:	Number of exposure groups and concentration spacing	High	In total, the study tested more than 3 dose groups as per OECD recommendations. This included 10% and 50% w/v neat in acetone, 50%, 10%, and 1% in IPM, and 40%, 10%, and 1% in HHN. The application of the test substance in acetone was followed by a sodium chloride application. This was reported to be representative of an exposure mixed with sweat; however, no specific justification of the 10% and 50% concentrations were provided.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	Abdominal skin was obtained from 11 female donors (aged 32 – 62) sourced from two different suppliers. Samples arrived on dry ice and were stored at -20 degrees C until use. The samples were dermatomed and the prepared split thickness skin was 390-400um thick.
	Metric 13:	Number/Replicates per group	Medium	The number of replicates per dose/concentration group was reported and was appropriate. The study included a total of 8 samples per group, obtained from 4 different donors.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	Appropriate outcomes (e.g., total % absorbed) were assessed for finite exposure scenarios, and were conducted according to OECD 428. The study reported measurements from all components of the test system. The selected formulations are reasonable for the chemical of interest and would result in a sufficiently conservative estimate representative range of conditions of use for the chemical of interest (e.g., use of IPM diluent).
	Metric 15:	Consistency of outcome assessment	High	Details of outcome assessment methods were reported, and the same protocol was applied across groups. The same receptor fluid. PBS containing polyoxyethylene 20 oleyl ether (PEG, ca 6%, w/v) was used, and all groups shared the same durations and sampling periods.
	Metric 16:	Sampling adequacy and sensitivity	High	Sampling size and sampling intervals were adequate for the outcomes of interest. The study identified the limit of reliable measurement (LoRM) as 30 d.p.m. above background. Any counts below the LoRM were noted in the study results.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	Skin integrity was assessed by measuring TEWL and by conducting an electrical resistance barrier integrity test. No criteria were applied to the TEWL results. Any skin samples exhibiting resistance lower than 10.9 k ohms were excluded. TEWL measurements were also made 24 hrs after application. TEWEL measurements conducted at 24 hrs were inconsistent, so it was not possible to predict the effect of exposure to HHN on barrier integrity.

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Study Citation: Charles River Laboratories, (2025). The in vitro percutaneous absorption of radiolabelled p-dichlorobenzene (pDCB) in eight dose scenarios through human split-thickness skin.
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 12392282
Unique ID: 10% and 1% in HHN

Domain	Metric		Rating	Comments
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	Solubility in the receptor fluid was tested and the receptor fluid was not rate-limiting for skin absorption. There were no reported differences among replicates or groups in the test model unrelated to exposure.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Total percent absorption estimates were presented across time from relevant compartments. The study clearly described the reasoning behind the exclusion of outliers when determining mass balance and absorption estimates. Since data were sufficiently reported, an alternate analysis could be done if previously excluded datasets were wanted to be reconsidered. 1-2 datasets from the neat groups were excluded due to recovery issues. The CV values for recovery (mass balance were all <25%). CV values were >25% and <50%; data are available for EPA to calculate an alternate (upper end) value to account for variability in the results (mean, standard deviation, and number of replicates; per OECD NO. 156)
	Metric 20:	Data interpretation	High	The mean mass balance for all dilutions in HHN were 100 ± 20%, which is sufficient for volatile substances according to OECD 128. The total absorbed dose was determined for a finite exposure scenario and was the sum recovered in receptor fluid and in the receptor chamber wash. The study also determined a "dermal delivery" dose, which was the sum of the total absorbed and what was recovered from exposed skin; the first two tape strips were included in this measurement. Individual replicates and sample results were provided for EPA to calculate values as well.
	Metric 21:	Reporting of data	High	Data were reported for all outcomes (means and standard deviations) and in detail along with individual replicates.

Overall Quality Determination High

Study Citation:	CPA, (2005). Letter to OPPT Document Control Office, USEPA, from Lynne Jones, Manager, Chlorobenzene Producers Association, re: Study entitled "p-Dichlorobenzene: In Vitro Dermal Absorption Rate Testing".
Chemical:	p-Dichlorobenzene
Exposure Type:	Parent compound
HERO ID:	7978648
Unique ID:	Infinite exposure

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test substance was identified as p-Dichlorobenzene (CASRN 106-46-7); colorless crystals. The study used both unlabeled and 14C radiolabeled test substances. A structure was provided and the radiolabel was reported to be uniform.
	Metric 2:	Test substance source	High	The unlabeled and radiolabeled test substance was supplied by Sigma-Aldrich. The certificates of analysis were provided in the study Appendices.
	Metric 3:	Test substance purity	High	The purity of the unlabeled test substance was 99.7%. The radiolabeled substance had a radiochemical purity of 95.7%. When the test material was incorporated into the isopropyl myristate vehicle, the radiochemical purity was 95.3%. The specific activity was also reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	Low	The study did not include any of the specified concurrent controls (caffeine, testosterone, or benzoic acid). Although it is likely that the performing laboratory (Haskell Laboratory) likely has an established history of performing these types of tests, this was not explicitly stated.
	Metric 5:	Assay procedures	High	An infinite dosing study was conducted according to OECD TG 428 and 28. Details of the assay procedures were well described. In brief, studies were conducted under static, occluded conditions. The test material was applied in an isopropyl myristate vehicle to human stratum corneum mounted onto diffusion cells at a volume of 100uL/cm2., where the surface area was 0.64 cm2. The specific activity of the radiolabel was clearly reported. The receptor fluid was 0.9% saline with 6% PEG 20 oleyl ether which was appropriate for a lipophilic compound. The chambers were held at 32 degrees C. Humidity was not reported. The exposure duration was 30 hours. Receptor fluid was collected at reported intervals during the exposure period. After exposure, the skin was washed with a 2% Ivory soap solution, then water. Radioactivity in the receptor fluid, skin washes, donor chamber rinses, and skin was assessed by scintillation counting. Quantification was sensitive and the LOD was reported. The number of scintillation counts was specified.
	Metric 6:	Standards for tests	Low	Skin integrity was confirmed by electrical impedance both before and after exposure. Skin samples were considered to be acceptable for use if they had an electrical conductance of 217 k-ohms. This appears to be a typo as no samples have a value that high, and published guidance suggests that >17 is a potential cutoff. Percent recoveries were reported. The recovery of the applied dose was >76%. Sufficient data were provided to determine the coefficients of variation (see metric 19 for more details).
Domain 3: Exposure Characterization				

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Study Citation: CPA, (2005). Letter to OPPT Document Control Office, USEPA, from Lynne Jones, Manager, Chlorobenzene Producers Association, re: Study entitled "p-Dichlorobenzene: In Vitro Dermal Absorption Rate Testing".
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 7978648
Unique ID: Infinite exposure

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Low	The unlabeled and radiolabeled test substances were mixed with isopropyl myristate to a target concentration of 100 mg/mL. Details of mixing were not specified, but homogeneity and the specific activity were assessed by scintillation counting. The test substance was reported to be stable under the conditions of the study. Solubility in the receptor fluid was confirmed prior to the start of the study. The maximum solubility in the receptor fluid was 2,352 ug/mL, which was 29-fold the maximum solubility in water. No details on storage were provided and the test substance is volatile.
	Metric 8:	Consistency of exposure administration	Medium	Based on the available information, the same duration of exposure, and receptor fluid collection times were applied to all of the replicates. A skin thickness range was 39 to 71 um. It is unclear whether potential differences in thickness could have had an impact on the results.
	Metric 9:	Reporting of concentrations	High	100 uL/cm2 was applied to a skin surface area of 0.64 cm2. The target concentration was 100 mg/mL. The specific activity of the test solution was determined by scintillation counting. The analytical concentration of the test substance in the isopropyl myristate vehicle was 98.4 mg/mL. The specific activity was reported to be 0.0.3118 uCi/mg, which is presumed to be a typographical error. A mass per surface area of 9.84 mg/cm2 was calculated for this review.
	Metric 10:	Exposure frequency	High	Exposures were conducted for 30 hours in an infinite exposure scenario to assure a steady state was reached. Shorter durations (<24 hrs) are typically desired, but longer durations are sometimes required for lipophilic substances, and there were no effects on skin integrity for the duration of the study.
	Metric 11:	Number of exposure groups and concentration spacing	Low	The study used a single infinite exposure which allowed the determination of a Kp. No justification was provided for the concentration selected (~10% w/v).
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	Tests were conducted on human cadaver abdominal skin obtained from the National Disease Research Interchange. The samples were frozen at -20 degrees C and were used within 3 months. Skin was heat-treated to allow separation of layers, and the stratum corneum, with a thickness ranging from 39 to 71 um, was mounted onto static diffusion cells. Six replicates were obtained from 3 donors. Epidermal membranes are acceptable for this study type.
	Metric 13:	Number/Replicates per group	Medium	The infinite test used 6 replicates (obtained from 3 donors). Current test guidelines specify at least 4 replicates.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	High	The study was conducted according to OECD TG 428 and 28. Receptor fluid was collected at 0.5, 1,2,3,4,5,6, 8, 10, 12, 18,24, and 30 hours. The receptor fluid was replaced with an equal volume to maintain a total volume of 5 mL. Kp was derived from an infinite dose. The dose volume (100uL/cm2) is typical for an infinite dose study.
	Metric 15:	Consistency of outcome assessment	Medium	Details of the outcome assessment were provided. Exposure times, receptor fluid collection times, and handling of replicates were consistent. It was not specified how soon after the collection of receptor fluids was scintillation counts performed.

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Study Citation: CPA, (2005). Letter to OPPT Document Control Office, USEPA, from Lynne Jones, Manager, Chlorobenzene Producers Association, re: Study entitled "p-Dichlorobenzene: In Vitro Dermal Absorption Rate Testing".
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 7978648
Unique ID: Infinite exposure

Domain	Metric		Rating	Comments
	Metric 16:	Sampling adequacy and sensitivity	High	The study reported adequate sampling for the outcome(s) of interest including number of evaluations per exposure group, and measurement sensitivity. The number of scintillation counts per sample was reported and the LOD was defined as twice the background disintegration rate from blank samples.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study included a single exposure group. Human abdominal skin samples were tested for integrity, and the integrity tests were acceptable. The ratio of post EI to pre-EI values was 1.20, indicating there was no loss of integrity during the course of exposure overall, however, the higher post-EI values were attributed to a rise in skin hydration and occlusion of the skin surface by residual test material not removed by washing. 1 cell dropped to 0.07 of the original (4.30) and should be excluded from results; it was excluded from calculating the EI ratio but NOT the absorption results.The % total recovery varied across replicates by up to 11.8%; it is unclear whether the number of replicates per donor (assuming 2) was adequate. However, the variation in recovery is not expected to have a significant impact on Kp determinations. Occlusion, especially with stratum corneum membranes, can cause overhydration which was mentioned as a possible issue in the study.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	No issues with solubility or test substance stability were identified. There were no reported differences among replicates that were unrelated to exposure.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Details of Kp determination were provided, and the Kp was determined based on a linear/steady-state portion of the absorption curve containing at least 4 data points. The absorption estimates in the receptor fluid were presented across time. The coefficients of variation for the steady state Kp and flux were 27% (calculated from SD), which is greater than the guideline limit of 25%, however all results are available. If the damaged cell (from wash) is excluded, CV is reduced.
	Metric 20:	Data interpretation	Medium	Recovery of the applied radioactive dose was 76.2%, which is less than the acceptable range of 100 $\pm$ 10% as per OECD guidelines. However, recovery determination is generally not relevant for infinite dose applications because only measurements in receptor fluid are required to determine a Kp (OECD TG 28). An infinite dose scenario was used for Kp determination. This does indicate that the occlusion was not complete however, so confidence is reduced a bit.
	Metric 21:	Reporting of data	Low	Data were adequately reported as means $\pm$ SD, and concentrations in receptor fluid vs. time were also graphically displayed.There are also several typos that make interpretation more difficult.

Overall Quality Determination Medium

Study Citation: CPA, (2005). Letter to OPPT Document Control Office, USEPA, from Lynne Jones, Manager, Chlorobenzene Producers Association, re: Study entitled "p-Dichlorobenzene: In Vitro Dermal Absorption Rate Testing".
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 7978648
Unique ID: 10-min flux

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test substance was identified as p-Dichlorobenzene (CASRN 106-46-7); colorless crystals. The study used both unlabeled and 14C radiolabeled test substances. A structure was provided and the radiolabel was reported to be uniform.
	Metric 2:	Test substance source	High	The unlabeled and radiolabeled test substance was supplied by Sigma-Aldrich. The certificates of analysis were provided in the study Appendices.
	Metric 3:	Test substance purity	High	The purity of the unlabeled test substance was 99.7%. The radiolabeled substance had a radiochemical purity of 95.7%. When the test material was incorporated into the isopropyl myristate vehicle, the radiochemical purity was 95.3%. The specific activity was also reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	Low	The study did not include any of the specified concurrent controls (caffeine, testosterone, or benzoic acid). Although it is likely that the performing laboratory (Haskell Laboratory) likely has an established history of performing these types of tests, this was not explicitly stated.
	Metric 5:	Assay procedures	High	A finite study was conducted according to OECD TG 428 and 28. Details of the assay procedures were well described. In brief, studies were conducted under static, occluded conditions. The test material was applied in an isopropyl myristate vehicle to human stratum corneum mounted onto diffusion cells at a volume of 30uL/cm2., where the surface area was 0.64 cm2. 0.9% saline with 6% PEG 20 oleyl ether was used as the receptor fluid and was appropriate for a lipophilic compound. The chambers were held at 32 degrees C. Humidity was not reported. The exposure durations were 10 minutes and 60 minutes. Receptor fluid was collected at the end of the exposure periods. After exposure, skin was washed with a 2% Ivory soap solution, then water. radioactivity in the receptor fluid, skin washes, donor chamber rinses, and skin was assessed by scintillation counting. Quantification was sensitive and the LOD was reported. The number of scintillation counts was specified.
	Metric 6:	Standards for tests	Medium	Skin integrity was confirmed by electrical impedance both before and after exposure. Skin samples were considered to be acceptable for use if they had an electrical conductance of 217 k-ohms. This appears to be a typo as no samples have a value that high, and published guidance suggests that >17 is a potential cutoff. Percent recoveries were reported. The recovery of the applied dose was 81.2% (10 minutes) and 73.7% (60 minutes). Sufficient data were provided to determine the coefficients of variation (see metric 19 for more details).
Domain 3: Exposure Characterization				

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Study Citation: CPA, (2005). Letter to OPPT Document Control Office, USEPA, from Lynne Jones, Manager, Chlorobenzene Producers Association, re: Study entitled "p-Dichlorobenzene: In Vitro Dermal Absorption Rate Testing".
Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 7978648
Unique ID: 10-min flux

Domain	Metric		Rating	Comments
	Metric 7:	Preparation and storage of test substance (chemical)	Low	The unlabeled and radiolabeled test substances were mixed with isopropyl myristate to a target concentration of 100 mg/mL. Details of mixing were not specified, but homogeneity and the specific activity were assessed by scintillation counting. The test substance was reported to be stable under the conditions of the study. Solubility in the receptor fluid was confirmed prior to the start of the study. The maximum solubility in the receptor fluid was 2,352 ug/mL, which was 29-fold the maximum solubility in water. No details on storage were provided and the test substance is volatile.
	Metric 8:	Consistency of exposure administration	Medium	Based on the available information, the same duration of exposure, and receptor fluid collection times were applied to all of the replicates. A skin thickness range was 39 to 71 um. It is unclear whether potential differences in thickness could have had an impact on the results.
	Metric 9:	Reporting of concentrations	High	30 uL/cm2 was applied to a skin surface area of 0.64 cm2. The target concentration was 100 mg/mL. The specific activity of the test solution was determined by scintillation counting.
	Metric 10:	Exposure frequency	High	Exposures were conducted for 10 or 60 minutes. No justification was provided for the durations tested and the % recovery in the skin washes indicates that the majority of the test substance was not absorbed. This can be useful for identifying peak flux over short durations, however, and since it is used for Kp/flux measurements only this is ok.
	Metric 11:	Number of exposure groups and concentration spacing	Low	The study only used a single exposure group. Typically, three groups are preferred for an absorption study.
Domain 4: Test Model				
	Metric 12:	Test model (skin)	High	Tests were conducted on human cadaver abdominal skin obtained from the National Disease Research Interchange. The samples were frozen at -20 degrees C and were used within 3 months. Skin was heat-treated to allow separation of layers, and the stratum corneum, with a thickness ranging from 39 to 71 um, was mounted onto static diffusion cells. Four replicates were obtained from a single donor. Epidermal membranes are acceptable for this study type.
	Metric 13:	Number/Replicates per group	Medium	Three separate fininte tests were conducted each using 4 replicates from a unique donor (each test: 2 replicates each for 10 or 60 minute exposure times). The number of replicates (4 from one donor) is the minimum number required as per OECD TG 428.
Domain 5: Outcome Assessment				
	Metric 14:	Outcome assessment methodology	Low	The outcome assessment methodologies were clearly described including the method of scintillation counting. The dose applied in a finite study (30ul/cm2) is larger than typically recommended (10 uL/cm2). These scenarios were considered 'finite' but are more likely infinite/nondepletable over the short timeline.
	Metric 15:	Consistency of outcome assessment	Medium	Details of the outcome assessment were provided. Exposure times and handling of replicates were consistent within groups.

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Domain	Metric		Rating	Comments
	Metric 16:	Sampling adequacy and sensitivity	High	The number of scintillation counts per sample was reported and the LOD was defined as twice the background disintegration rate from blank samples. The study indicated that larger aliquots of receptor fluid were taken (0.5mL) in order to increase sensitivity in the shorter exposure durations.
Domain 6: Confounding/Variable Control				
	Metric 17:	Confounding variables in test design and procedures	Medium	The study included a single exposure group. Human abdominal skin samples were tested for integrity, and the integrity tests were acceptable. The ratio of post EI to pre-EI values were 1.02 and 0.82 for the 10 minute and 60-minute exposures, respectively. 2 cells for the 10min and one cell for the 60 min assay were $<$ 17 kohms after testing; the 10min (but not 60min) were excluded from this ratio calculation but were still used for absorption calculations. Based on the recovery data for individual replicates reported in data tables on pg. 50/98, the recovery in skin, receptor fluid etc., and the total % recovery varied by more than 10% after both the 10 min and 60 min exposures. The results may not be reliable for estimating actual absorption. Additionally, occlusion, especially with stratum corneum membranes, can cause overhydration which was mentioned as possible issue in the study.
	Metric 18:	Confounding variables in outcomes unrelated to exposure	High	No issues with solubility or test substance stability were identified. There were no reported differences among replicates that were unrelated to exposure.
Domain 7: Data Presentation and Analysis				
	Metric 19:	Data analysis	Low	Details of data analysis were adequately reported. Absorption rates were calculated by dividing the sum of the ug equivalents in the receptor fluids and skin by the skin exposure area and exposure time. Total recovery was determined from radioactivity measurements taken from the receptor fluid, skin and donor chamber washes, and in skin. The standard deviations relative to the mean were >25% for % recoveries in skin and/or receptor fluid, but would be lower with exclusion of damaged replicates (damaged during wash, after absorption).
	Metric 20:	Data interpretation	Low	Recovery of the applied radioactive dose was 81.2% for the 10-minute and 73.7% for the 60-minute exposure groups. This is less than the 100 $\pm$ 10% specified in OECD guidelines. Fractional absorption results were derived from a finite dose scenario; however, the study calculated penetration rates which may have been inappropriate for a finite study.
	Metric 21:	Reporting of data	Medium	Data were adequately reported as means $\pm$ SD, and concentrations in receptor fluid vs. time were also graphically displayed.There is an issue with the printing of the study that confuses units (pg with ug), and has several typos that makes it difficult to confidently interpret results.

Overall Quality Determination Medium

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Chemical: p-Dichlorobenzene
Exposure Type: Parent compound
HERO ID: 7978648
Unique ID: 60-min flux

Domain	Metric		Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test substance identity	High	The test substance was identified as p-Dichlorobenzene (CASRN 106-46-7); colorless crystals. The study used both unlabeled and 14C radiolabeled test substances. A structure was provided and the radiolabel was reported to be uniform.
	Metric 2:	Test substance source	High	The unlabeled and radiolabeled test substance was supplied by Sigma-Aldrich. The certificates of analysis were provided in the study Appendices.
	Metric 3:	Test substance purity	High	The purity of the unlabeled test substance was 99.7%. The radiolabeled substance had a radiochemical purity of 95.7%. When the test material was incorporated into the isopropyl myristate vehicle, the radiochemical purity was 95.3%. The specific activity was also reported.
Domain 2: Test Design				
	Metric 4:	Reference compounds	Low	The study did not include any of the specified concurrent controls (caffeine, testosterone, or benzoic acid). Although it is likely that the performing laboratory (Haskell Laboratory) likely has an established history of performing these types of tests, this was not explicitly stated.
	Metric 5:	Assay procedures	High	A finite study was conducted according to OECD TG 428 and 28. Details of the assay procedures were well described. In brief, studies were conducted under static, occluded conditions. The test material was applied in an isopropyl myristate vehicle to human stratum corneum mounted onto diffusion cells at a volume of 30uL/cm2., where the surface area was 0.64 cm2. 0.9% saline with 6% PEG 20 oleyl ether was used as the receptor fluid and was appropriate for a lipophilic compound. The chambers were held at 32 degrees C. Humidity was not reported. The exposure durations were 10 minutes and 60 minutes. Receptor fluid was collected at the end of the exposure periods. After exposure, skin was washed with a 2% Ivory soap solution, then water. radioactivity in the receptor fluid, skin washes, donor chamber rinses, and skin was assessed by scintillation counting. Quantification was sensitive and the LOD was reported. The number of scintillation counts was specified.
	Metric 6:	Standards for tests	Medium	Skin integrity was confirmed by electrical impedance both before and after exposure. Skin samples were considered to be acceptable for use if they had an electrical conductance of 217 k-ohms. This appears to be a typo as no samples have a value that high, and published guidance suggests that >17 is a potential cutoff. Percent recoveries were reported. The recovery of the applied dose was 81.2% (10 minutes) and 73.7% (60 minutes). Sufficient data were provided to determine the coefficients of variation (see metric 19 for more details).
Domain 3: Exposure Characterization				

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