皮膚等障害化学物質の選定のための検討会

報告書

令和5年4月 19 日

独立行政法人労働者健康安全機構
労働安全衛生総合研究所

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第 1 検討会の趣旨・目的等

1. 背景

我が国における化学物質による健康障害事案 (休業 4 日以上: がん等遅発性疾病除く)は年間 200～400 件ほどで推移しているが、この障害事案の中では、経皮ばく露による皮膚障害が最も多く、続いて眼障害であり、皮膚障害においては、吸入・経口ばく露による障害発生件数の約 4 倍にのぼる[1]。この皮膚障害数は、主に、化学物質の刺激性・腐食性に起因する障害事例が数字として出ていると考えられるが、最近では、オルト-トルイジンや MOCA(4,4'-メチレンビス (2-クロロアニリン))と言った、皮膚刺激性はないが、ヒトや動物に対する発がん性が認められている物質が皮膚から吸収され発がん (膀胱がん)に至ったと疑われる事案も発生している[2,3]。このような背景を受け、令和4年厚生労働省令第 91 号(令和4年5月 31 日公布)において、労働安全衛生規則の一部が改正され、化学物質による皮膚等への障害を防止することを目的とした以下規則が設定された (第 594 条の 2、及び第 594 条の 3)

第 594 条の2 (令和 6 年 4 月 1 日施行)
事業者は、化学物質又は化学物質を含有する製剤(皮膚若しくは眼に障害を与えるおそれの又は皮膚から吸収される、若しくは皮膚に侵入して、健康障害を生ずるおそれがあることが明らかなものに限る。以下「皮膚等障害化学物質等」という。)を製造し、又は取り扱う業務(法及びこれに基づく命令の規定により労働者に保護具を使用させなければならない業務及び皮膚障害化学物質等を密閉して製造し、又は取り扱う業務を除く。)に労働者を従事させるときは、不浸透性の保護衣、保護手袋、履物又は保護眼鏡等適切な保護具を使用させなければならない。

第 594 条の3 (令和 5 年 4 月 1 日時点においては第 594 条の 2)
事業者は、化学物質又は化学物質を含有する製剤(皮膚等障害化学物質等及び皮膚若しくは眼に障害を与えるおそれ又は皮膚から吸収され、若しくは皮膚に侵入して、健康障害を生ずるおそれがないことが明らかなものを除く。)を製造し、又は取り扱う業務(法及びこれに基づく命令の規定により労働者に保護具を使用させなければならない業務及びこれらの物を密閉して製造し、又は取り扱う業務を除く。)に労働者を従事させるときは、当該労働者に保護衣、保護手袋、履物又は保護眼鏡等適切な保護具を使用させるよう努めなければならない。

ここで、皮膚若しくは眼に障害を与えるおそれの又は皮膚から吸収される、若しくは皮膚に侵入して、健康障害を生ずるおそれがあることが明らかな皮膚等障害化学物質等にはどのような化学物質が該当し、保護具使用の義務対象になるのか、逆に、健康障害を生ずるおそれがないことが明らかな物質にはどのような化学物質が該当し、当該義務等の対象から除かれるのか、その判定基準や、その他必要なガイドライン等については未整備であり、皮膚等障害化学物質等の選定のための考え方を整理する必要がある。

そのため、本検討会では、皮膚等障害化学物質による労働者の障害防止のために、当該規則を円滑に運用できるように必要な事項について検討を行う (ただし、本検討会では、化学物質に限定し、物理的因子、生物学的因子は含まない)。

2. 検討会の目的

基発 0531 第 9 号 (令和 4 年 5 月 31 日)において、「皮膚等障害化学物質」には、国が公表するGHS 分類の結果及び譲渡提供者より提供された SDS 等に記載された有害性情報のうち「皮膚
腐食性・刺激性」、「眼に対する重篤な損傷性・眼刺激性」及び「呼吸器感作性又は皮膚感作性」のいずれかで区分 1 に分類されているもの及び別途示すものが含まれることとされている。一方で、「皮膚から吸収され、若しくは皮膚に侵入して、健康障害を生ずるおそれがあることが明らかな」物質 (以下、皮膚吸収性有害物質)については、GHS に分類がなく、どのような物質が「皮膚吸収性有害物質」に該当するのかを参照することができない。そこで、本検討会では、皮膚等障害化学物質のうち、皮膚吸収性有害物質に該当するものを、どのように決定すべきかを中心に議論し、皮膚吸収性有害物質を選定することを目的とする。

3. 検討会の開催日時、及び主要な議題

- 第 1 回皮膚等障害化学物質の選定のための検討会
  開催日時:2022 年 10 月 18 日(火) 10 時 00 分～12 時 00 分
  開催場所:Microsoft Teams による web および労働安全衛生総合研究所2階会議室
  主議題:皮膚吸収性有害物質の考え方について
- 第2回皮膚等障害化学物質の選定のための検討会
  開催日時:2023 年 12 月6日(火) 10 時 00 分～12 時 00 分
  開催場所:Microsoft Teams による web および労働安全衛生総合研究所2階会議室
  主議題: 第 594 条の 2 (義務化)に該当する物質の選定について
- 第 3 回皮膚等障害化学物質の選定のための検討会
  開催日時:2023 年 1 月 24 日(火) 10 時 00 分～12 時 00 分
  開催場所:Microsoft Teams による web および労働安全衛生総合研究所2階会議室
  議題:第 594 条の 3 (努力義務)に該当する物質の選定について
- 第4回皮膚等障害化学物質の選定のための検討会
  開催日時:2023 年 3 月 16 日(火) 10 時 00 分～12 時 00 分
  開催場所:Microsoft Teams による web および労働安全衛生総合研究所2階会議室
  議題: 皮膚吸収性有害物質の更新、保護具等衛生管理について

4. 検討会委員構成

- 岩澤 聡子
  防衛医科大学校医学教育部医学科衛生学公衆衛生学 講師
- 王 瑞生
  独立行政法人 労働者健康安全機構 労働安全衛生総合研究所 化学物質情報管理研究センター 有害性評価研究部 部長
- 甲田 茂樹
  独立行政法人 労働者健康安全機構 労働安全衛生総合研究所 所長代理
- 豊岡 達士
  独立行政法人 労働者健康安全機構 労働安全衛生総合研究所 化学物質情報管理研究センター 有害性評価研究部 上席研究員
- 中原 浩彦
  独立行政法人 労働者健康安全機構 労働安全衛生総合研究所 化学物質情報管理研究センター
- 宮内 博幸
  産業医科大学 産業保健学部 作業環境計測制御学講座 教授
- 柳場 由絵
  独立行政法人 労働者健康安全機構 労働安全衛生総合研究所 化学物質情報管理研究センター 有害性評価研究部 上席研究員

（50音順 令和４年度所属）

オブザーバー

- 山口 修
  一般社団法人 日本化学工業協会 環境安全部
- 安井 省侍郎
  厚生労働省労働基準局安全衛生部化学物質対策課 課長
- 平川 秀樹
  厚生労働省労働基準局安全衛生部化学物質対策課 環境改善室長

（令和４年度所属）

第 2 検討内容

1. 皮膚吸収性有害物質について

(1) 皮膚吸収性有害物質の概念と Skin Notation

条文中における皮膚吸収性有害物質の毒性学的概念は、「皮膚から吸収され、若しくは皮膚に侵入して、健康障害を生ずるおそれがある物質」であり、法令上では、そのことが明らかな物質と定義されている。

皮膚吸収性有害物質と同様の毒性学的概念は、ばく露限界等を提案する諸機関において、Skin Notation として提案されている。Skin Notation は、1961 年に 米国産業衛生専門家会議 (ACGIH)が、「液体化合物が正常皮膚を透過して全身に影響を及ぼす可能性がある（当時定義）」ことを警告するために、許容濃度(TLV)に併記する形で初めて使用された [4]。

本検討会では、法令上の皮膚吸収性有害物質を選定するための参考情報として、諸機関: ACGIH、米国労働安全衛生研究所 (NIOSH)、米国労働安全衛生庁（OSHA）、ドイツ学術振興会 (DFG) [8]、英国安全衛生庁 (HSE)、日本産業衛生学会 (産衛) における Skin Notation の概念、化学物質に Skin Notation を付す際の基準等について確認した [5-10]。

(2) 諸機関における Skin Notation の概念と評価基準について

以下では、Skin Notation が付される物質の定義、及び基準等が明示されていた ACGIH、NIOSH、DFG について記す。

- **ACGIH**

Skin Notation 物質の定義

蒸気、液体、固体との接触により、粘膜や目を含む皮膚からのばく露が、全体のばく露に大きく寄与する可能性がある物質 (ただし、皮膚に限定した刺激性、腐食性、感作性を引き起こす化学物質には Skin Notation を適用しない)

評価基準

- 特に許容濃度 (TLV: Threshold limit value) が低い物質について、現場作業で手や前腕から吸収される可能性が大きいことを示唆する情報がある場合は Skin Notation を適用する。
- 経皮ばく露による動物急性毒性試験において、半数致死量 (LD50)が 1,000mg/kg 体重以下の物質には、Skin Notation を適用する。
- 物性情報から化学物質が皮膚浸透しやすく（水オクタノール分配係数：log *Kow* が高い等）、毒性影響に経皮吸収が重要であることが示唆される場合は Skin Notation の適用が考慮される。
- 経皮ばく露により呼吸器感作性を引き起こす物質については、Skin Notation に感作性表記 (SEN：sensitization)を伴うことがある。

- **NIOSH**

Skin Notation 物質の定義

皮膚から吸収され、全身毒性につながる可能性があることが科学的に証明された物質

＊NIOSH における経皮吸収による全身毒性があることを示す表記は SK:SYS (Skin: Systemic)であり、皮膚に限定した刺激性 (Irritation)、腐食性 (Corrosion)、感作性 (Sensitization)については、それぞれ、SK：IRR、SK：COR、SK：SEN の別表記となる。

評価基準

- 疫学情報等、経皮ばく露によるヒト健康障害の証拠が認められる場合、Skin Notation (SK:SYS)を適用する。
- 経皮ばく露による動物急性毒性試験において，半数致死量 LD50<2,000 mg/kg 体重以下である場合，SK：SYS を適用する．特に，LD50<200 mg/kg 体重以下の場合は，SK: SYS (FETAL)の表記とする。
- 経皮ばく露(短～長期)による動物毒性試験において、全身毒性に基づく NOAEL (無毒性量)が 1,000 mg/kg 体重/日未満の場合、SK：SYS を適用する．

  ＊全身毒性には，血液学的指標の変化，各種臓器に対する病理組織学的変化や生化学的指標等の変化，免疫系，生殖および発達への影響，生物学的機能等への影響を含む．

  ＊NOAEL を見出すことが困難な場合，LOAEL (最小毒性量)で代用できる．
- 経皮ばく露により，皮膚を除く臓器・組織において発がんの証拠 (全身吸収した証拠)がある場合，SK：SYS を適用する。
- In vitro における皮膚吸収試験，物質の物理化学的特性を使用した数理モデル等から皮膚吸収が予想される物質は，SK 表記の適用候補となる．

  ＊皮膚吸収のみでは SK：SYS は適用されない．
- 毒性実験データが存在しない場合、トキシコキネティクスモデルの利用が可能であり、職業ばく露限界値に基づき算出される吸入ばく露量を、予想される経皮ばく露量で除した値 (SI ratio)が 0. 1 以上となる場合 SK：SYS を適用するための補助とすることができる．

- **DFG**

SK 物質の定義

皮膚吸収が全身ばく露量に大きく寄与することがあり、ばく露限界値 (MAK)の遵守だけでは、健康障害の防止が保証されなくなった物質

評価基準

以下のいずれかに該当する場合に Skin Notation (H)を適用する。ただし皮膚に限定した刺激性や腐食性、感作性を引き起こす化学物質には適用しない。

- 現場調査や疫学調査の事例から、化学物質を扱う作業者の経皮吸収が大きいことが科学的に証明され、毒性作用に寄与する可能性がある場合

- 動物実験において、皮膚吸収性が証明され、毒性影響が観察された場合
- 毒性作用に寄与しうる経皮吸収が、公知の方法 (フランツセル法等、In vitro 皮膚吸収性試験)で定量化されている場合。
- 類似物質のデータまたは数学的モデルによる計算に基づいて、適切なレベルの経皮吸収が予想できる場合。

(3) 諸機関における Skin Notation 付与パターンについて

(2)により、物質に Skin Notation を付す際に利用される情報は以下のように分類でき、その付与パターンを図 1 に示す。

① ヒトに関する情報 (疫学研究、症例報告、被験者実験)

② 動物に関する情報 (in vivo 経皮ばく露毒性情報、in vivo 経皮ばく露動態情報＋ばく露限界値・毒性を考慮した計算予測)

③ in vitro での情報 (動物摘出皮膚・三次元培養皮膚吸収性情報＋ばく露限界値・毒性を考慮した計算予測)

④ Skin Notation が既に付されている物質との構造類似性や、ばく露限界値や毒性情報を利用したモデル計算

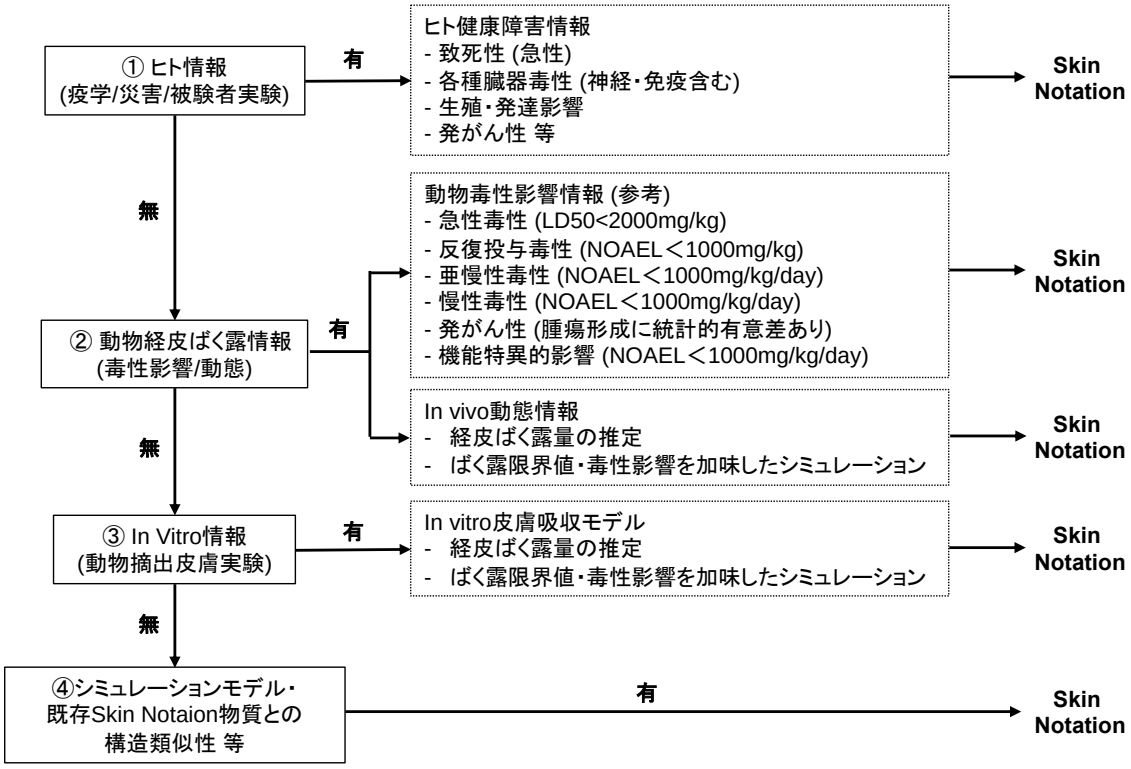

図 1 Skin Notation の付与パターン

いずれの機関も、情報の優先度は①～④の番号順に扱われ、ある物質に①経皮ばく露が疑われるヒト健康障害の証拠がある場合、②動物経皮ばく露による毒性影響の証拠がある場合には、その物質に Skin Notation が付すことになっている。ただし、②動物経皮ばく露毒性影響について、毒性を示す物質の濃度を考慮するか否かは評価機関ごとにそれぞれ異なる。また、動物経皮ばく露動態情報のみをもって Skin Notation が付されることはなく、動態情報を基にしたシミュレーションモデル (吸収速度や組織分布量等の推定)に、ばく露限界値や動物毒性情報 (経皮ばく露以外も可)を加味し、Skin Notation を判断することになっている。同様に③動物摘出皮膚等を使用した皮膚吸収性試験においても、その結果のみで Skin Notation が付されることはなく、結果を基に吸収速度や組織分布量等を推定し、ばく露限界値や動物毒性情報を加味した計算予測により、Skin Notation が判断される。④については、その情報のみをもって Skin Notation を判断するか否かは機関ごとに考え方が異なる。

2. 第 594 条の 2 (義務化)に該当する皮膚吸収性有害物質の選定について

(1) 候補物質群について

基発 0531 第 9 号において、皮膚等障害化学物質のうち、「皮膚/眼刺激性・腐食性物質」、「皮膚感作性物質」は、国が公表する GHS 分類の結果から、区分 1 に分類されるものが該当することが示されているため、皮膚吸収性有害物質の候補物質についても同様に GHS 分類対象化学物質から選定する。GHS 分類対象化学物質は、独立行政法人製品評価技術基盤機構から入手できるリスト (令和 4 年度版)を使用し、CAS 番号が付されている化学物質約 3000 物質とした。 なお、GHS 分類対象物質の内、環境影響のみに区分があり、ヒトへの健康影響が区分に該当しない、若しくは、分類できない物質約 290 種類は除いて考えるとしたが、これら物質についても、後述の皮膚吸収性有害物質の判定基準に照らし合わせ、別途確認することにした。

(2) 選定プロセス、基準等について

第 594 条の 2 (義務化)に該当する皮膚吸収性有害物質を、以下便宜的に皮膚吸収性有害物質 Group 1 と呼ぶ。本検討会では、Group1 候補物質を、原則、諸機関 (ACGIH, NIOSH, OSHA, DFG, HSE, 産衛)において、職業ばく露限界値の設定がなされているものから選定していくことにした。ここで、職業ばく露限界値の設定がある物質から選定していくことにした理由は、皮膚吸収性有害物質は法令上、皮膚から吸収され、若しくは皮膚に侵入して、健康障害を生ずるおそれがあることが、「明らかである」とされることから、Group 1 に該当する物質は、物質の物理化学的特性、体内動態・代謝、各種毒性影響に関する文献等、少なくとも職業ばく露限界値を設定しうる相当の根拠が存在するものの中から選定することが妥当であると考えられたからである。これに加えて、前記の通り、諸機関において、Skin Notation は職業ばく露限界値を勘案して付されることがあり、職業ばく露限界値と Skin Notation はセットで提示されることが一般的であることも考慮に入れた。

GHS 分類対象化学物質の中で、諸機関 (ACGIH, NIOSH, OSHA, DFG, HSE, 産衛)において、職業ばく露限界値が設定されえている物質数は、令和４年度時点において、ACGIH (約 700 物質)、NIOSH (約 580 物質)、OSHA (約 420 物質)、DFG (約 400 物質)、HSE (約 120 物質)、産衛 (約 220 物質)である。各評価機関で物質に重複があるため、いずれか１つ以上の評価機関において、職業ばく露限界値が設定されている物質数としては、約 870 物質になり、これを「Group 1 候補物質群」とすることにした。なお、発がん性物質については、ばく露限界値を設定しない (設定できない)とする機関があるため、そのような物質については、別途確認の上、検討することとした。

本検討会では皮膚吸収性有害物質 Group 1 候補物質群約 870 物質について、ACGIH の評価書を中心にレビューし、経皮ばく露に関する情報が存在する場合は、それを 1(3)に示した以下 4 つに分けて整理することにした。また、Group 1 候補物質の中には、Skin Notation が付されている物質を含むために、それら物質については、別途、Skin Notation を付す理由についても整理した。

① ヒトに関する情報 (疫学研究、症例報告、被験者実験)
② 動物に関する情報 (in vivo 経皮ばく露毒性情報、in vivo 経皮ばく露動態情報＋ばく露限界値・毒性を考慮した計算予測)
③ in vitro での情報 (動物摘出皮膚・三次元培養皮膚吸収性情報＋ばく露限界値・毒性を考慮した計算予測)
④ Skin Notation が既に付されている物質との構造類似性や、ばく露限界値や毒性情報を利用したモデル計算

レビューの結果は別添1に示す通りであり、Group1 対象候補物質の中で、経皮ばく露に関する情報が得られたのは、約 420 物質であった。検討会では上記①～④の経皮ばく露に関する情報を検討した。

①に関しては、候補物質によって引き起こされたヒト健康障害に、経皮ばく露が関与することが、学術論文や報告書等、相応の根拠をもって、科学的に明らかにされている場合、その物質はヒト健康障害を生ずるおそれがあることが明らか（Group 1 に該当する）と判断できるとした。

②に関して、動物毒性影響から、ヒト健康障害を推定する手法 (ヒトへの外挿)は、長年研究されており、相応の根拠の蓄積があるため、候補物質による動物経皮毒性が一定の濃度範囲 (下記参照)において観察されていることが科学的に明らかにされている場合、その物質はヒト健康障害を生ずるおそれがあることが明らか (Group 1 に該当する)であると判断できるとした。また、候補物質を動物に経皮ばく露した後の体内動態 (吸収速度、組織分布、代謝等)が明らかになっている場合、体内動態における種差、及び、ばく露限界値等を関連させて、経皮ばく露によるヒト健康障害を科学的根拠をもって評価できるため、その候補物質は Group 1 に該当すると判断できるとした。

③については、動物摘出皮膚等において、候補物質の皮膚吸収性や透過性を評価することはできるものの、組織分布の評価はできず、ばく露限界値等を考慮した上で、ヒト健康障害を生ずるおそれが明らかであると断定するには科学的根拠がやや弱く、Group 1 に該当する根拠としては不十分であると判断した。

④については、候補物質が、Skin Notation が既に付されている物質と化学構造が類似している場合 (異性体、官能基の種類や数のみが異なる等)、「類似した化合物は類似した性質を示す」という類似性原則は示されているが、その候補物質が、実際に類似性質を示すという相応の科学的根拠がない限り、経皮ばく露によるヒト健康障害のおそれがあることが明らかとは断定することは難しく、Group 1 に該当する根拠としては不十分と判断した。また、物質の物性情報、ばく露限界値や毒性情報を利用したモデル計算から、その物質の経皮吸収の程度、及び、健康障害の可能性を推測することはできるものの、これはあくまでも、経皮ばく露によりヒト健康障害のおそれがある可能性のある物質を示唆するに留まるものであり、このことを実際に示す相応の科学的根拠がない限り、Group 1 に該当する根拠としては不十分と判断した。

以上のことを踏まえて、本検討会では、皮膚吸収性有害物質 Group 1 の物質に該当するには、職業ばく露限界値が原則定められていることを前提に、以下のいずれかに合致することを条件とした。

皮膚吸収性有害物質 Group 1 に該当する条件

- ヒトにおいて、経皮ばく露が関与する健康障害を示す情報 (疫学研究、症例報告、被験者実験等)があること
- 動物において、経皮ばく露による毒性影響を示す情報があること
- 動物において、経皮ばく露による体内動態情報があり、併せて職業ばく露限界値を用いたモデル計算等により経皮ばく露による毒性影響を示す情報があること

ここで、ヒトに対する経皮ばく露による健康障害とは、致死性 (急性)、各種臓器毒性 (神経・免疫毒性含む)、生殖・発達影響、発がん性等を想定し、動物において経皮ばく露による毒性影響を示すとは、急性毒性 (LD50<2000 mg/kg)、反復投与毒性 (NOAEL < 1000mg/kg)、亜慢性毒性 (NOAEL < 1000mg/kg/day)、慢性毒性 (NOAEL < 1000mg/kg/day)、発がん性 (腫瘍形成に統計的有意差あり)、機能特異的影響 (NOAEL< 1000mg/kg/day)を参考にすることが妥当であると考えられた。また、発がんに関して、皮膚がんは皮膚に限定した影響であるが、本検討会では皮膚を一つの臓器と見なし、経皮ばく露によりヒトまたは動物に皮膚発がんを示す物質は、皮膚吸収性有害物質に含まれるとした。検討会では、経皮ばく露に関する情報が得られた約 420 物質の内、皮膚吸収性有害物質 Group1 に該当する物質として、356 物質を選定した (別表 1)。

【留意事項】

- **ばく露限界値の設定がない発がん性物質(特に皮膚発がん)について**

次の物質、クリセン (CAS: 218-01-9)、ベンゾ[a]ピレン (CAS: 50-32-8)、ベンゾ[a]アントラセン (CAS: 56-55-3)、ジベンゾ［a,i］ピレン (CAS: 189-55-9)、ジベンゾ［a,h］ピレン (CAS: 189-64-0)、インデノ［1,2,3-cd］ピレン (CAS: 193-39-5)、ベンゾ［j］フルオランテン (CAS: 205-82-3)、ベンゾ[e]フルオラセン (CAS: 205-99-2)、ベンゾ［k］フルオランテン (CAS: 207-08-9)、ジベンゾ［a,h］アントラセン (CAS: 53-70-3)、フェナントレン (CAS: 85-01-8)は、動物において、経皮ばく露による皮膚発がんが認められており、発がん性物質のために、ばく露限界値の設定がいずれの評価機関においてもなされていなかったため、別途検討した。本検討会では、前述の通り、皮膚を一つの臓器とみなした場合、皮膚に吸収され発がん性を示すおそれがある物質は、皮膚吸収性有害物質に含まれると判断したため、これら物質をGroup 1 に選定した。

- **環境影響のみに GHS 区分がある物質約 290 種類と Group 1 選定物質について**

皮膚吸収性有害物質 Group 1 には、安息香酸 (CAS: 65-85-0)が含まれているところであるが、別途、GHS 区分が環境影響のみである物質リストを確認すると、安息香酸カリウム (CAS: 532-25-2)が含まれていた。両物質は水溶液の状態では、解離し、いずれも安息香酸イオン ($C_6H_5COO^-$)の形で存在する。安息香酸の経皮ばく露による健康障害のおそれは安息香酸イオンによるものと解することが科学的に自然であるため、検討会では、安息香酸カリウムについても、Group 1 に含めることにした。

以上のことを踏まえ、皮膚吸収性有害物質 Group1 の選定に係るプロセスの概略を図 2 にまとめた。

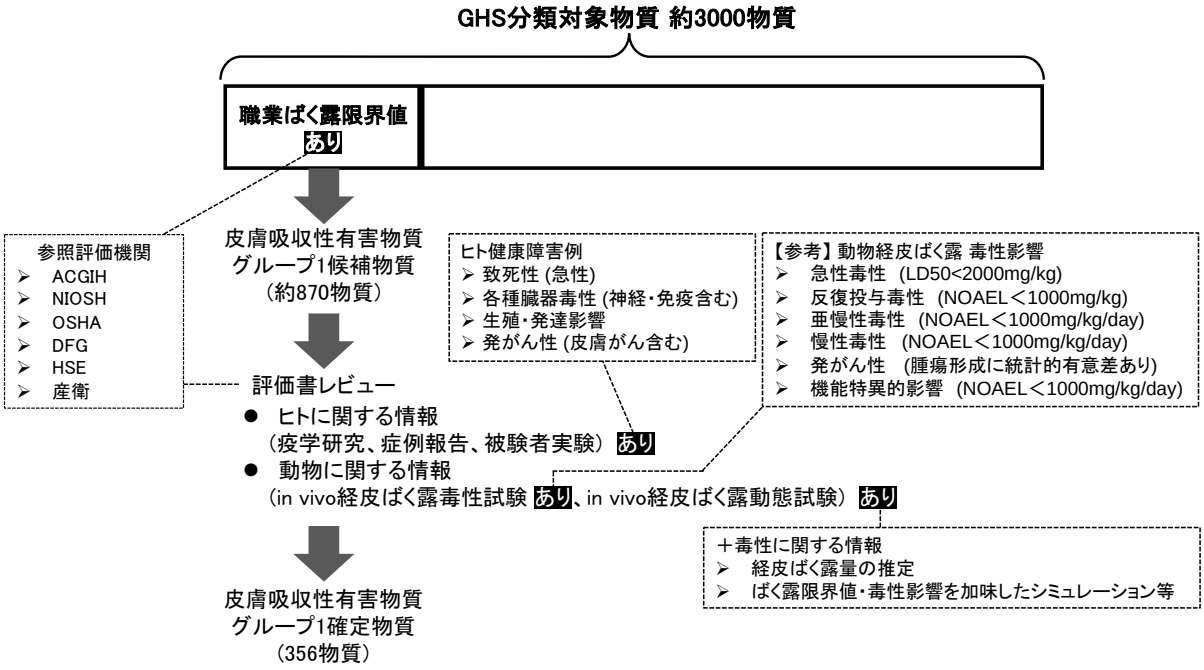

図 2 皮膚吸収性有害物質 Group 1 に該当する物質の選定プロセス概略

3. 第 594 条の 3 (努力義務)に該当する皮膚吸収性有害物質の選定について

(1) 物質候補群

第 594 条の 3 (努力義務)に該当する皮膚吸収性有害物質を、以下便宜的に Group 2 と呼ぶ。Group2 の候補群は、GHS 対象物質から Group1 確定物質 (356 物質)を除いたものになる。また、Group2 の候補群のうち、経皮ばく露に関する情報が得られたが、その情報が、「in vitro での情報 (動物摘出皮膚・三次元培養皮膚吸収性試験)」、若しくは、「Skin Notation が既に付されている物質との構造類似性や、ばく露限界値を利用したモデル計算の情報」であり、Group 1 にするには根拠が弱いとした約 70 物質について、本検討会では Group2 の確定物質とするのが妥当であるとした。

(2) 皮膚吸収性有害物質 Group 2 に該当する物質の法的解釈について

Group2 に該当する物質は、法令上、皮膚から吸収され、若しくは皮膚に侵入して、健康障害を生ずるおそれがないことが明らかな物質以外は全てと解釈ずることができる。すなわち、Group 2 を確定することは、「経皮ばく露によって健康障害が生じるおそれがない」ことが「明らか」であることを、適切な根拠をもって判断することと同義となる。なお、Group 2 の毒性学的概念は、Group 1 と同様に「皮膚から吸収され、若しくは皮膚に侵入して、健康障害を生ずるおそれがある物質」と解釈することができる (ただし、法令上の解釈をするときに、その「おそれ」が、相当の根拠をもって「明らか」であるとまでは要求されない)。

(3) 皮膚吸収性有害物質 Group 2 該当物質と、経皮ばく露によって健康障害が生じるおそれがない物質について

Group 1 に該当する物質は、少なくとも 1 機関以上の化学物質評価機関において、ばく露限界値が原則設定されていることを前提に、その評価書をレビューし経皮ばく露に関連する情報を取捨選択することで決定してきた。一方で、Group 2 候補群となる物質には、GHS分類はされているが、諸機関の評価書内に経皮ばく露に関する情報がない (ばく露限界値はある)物質や、評価書自体がない物質 (ばく露限界値もない)等が含まれる。

したがって、検討会では、下図 3 に示すように、化学物質の物性情報から経皮ばく露の可能性、及び、GHS 分類の結果から、経皮ばく露による毒性影響を推定し、Group 2 該当物質、若しくは、経皮ばく露によって健康障害が生じるおそれが「ないことが明らかな物質」を特定することができるのか否かを試みることにした。

- **GHS 分類を利用した皮膚吸収性有害物質 Group 2 該当物質の絞り込み**

図 3 に示すスキームは、Group 2 該当物質を絞り込むために作成したが、見方を変えるとGroup 1 の取りこぼし物質を見つけるプロセスと見ることもできる。また一方では、このプロセスにおいて Group 2 に確定しなかった物質を、「経皮ばく露によって健康障害が生じるおそれがない物質」としてよいのか否かについて議論する必要が生じた。

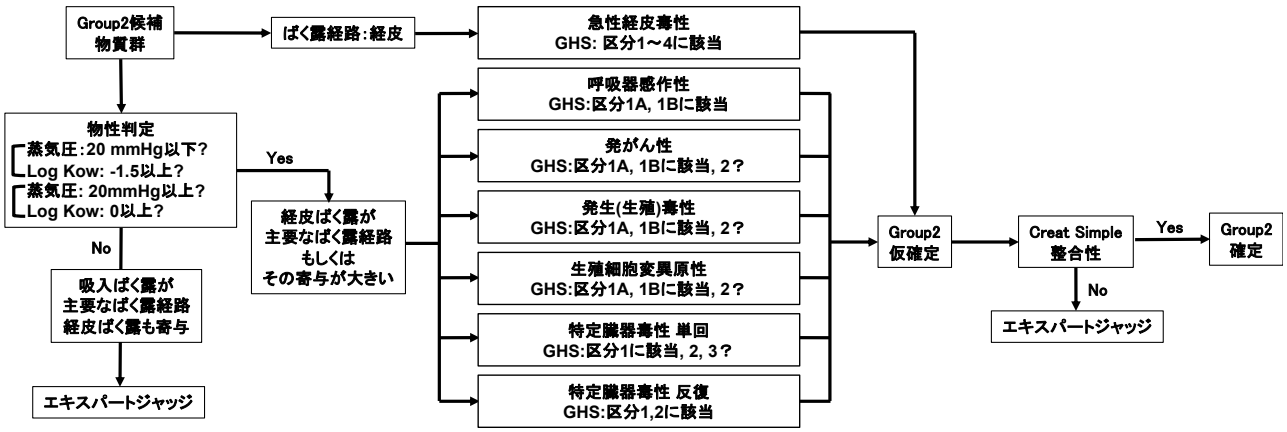

図 3 皮膚吸収性有害物質 Group 2 に該当する物質の選定プロセス概略

前者について、例えば、Group2 候補物質において、ばく露経路が間違いなく経皮ばく露であり、その毒性情報が存在するのは、急性経皮毒性である。Group 1 物質を確定するための参考条件の一つに、動物急性経皮毒性 (LD50<2000 mg/kg 体重) があり、実際に、その結果を根拠に、Group 1 に分類した物質があるため、検討会では、Group 2 候補物質群の中で、GHS 動物急性経皮毒性区分 1 (LD50<50 mg/kg 体重)に該当する物質について、まず検証した。その結果、GHS 対象物質中 (約 3200 物質)、動物急性経皮毒性区分 1 に該当する物質は 42 物質あり、このうち、24 物質は、既に Group 1 に分類されていたが、別添 2 に示す 18 物質は Group 1 に分類されていなかった。この 18 物質は、Group 1 の取りこぼしである可能性を否定できないため、検討会では、これらについて職業ばく露限界値の有無、急性経皮毒性区分 1 に分類した根拠を確認した。

18 物質の中では、2 物質 (CAS: 107-16-4 グリコロニトリル、CAS: 12185-10-3 黄リン)にばく露限界値の設定があり、区分 1 に分類した根拠論文についても入手可能なものがいくつか存在した。グリコロニトリルについては、根拠論文が 2 報存在したものの、一つは皮下投与の LD50 であり、実質 1 報のみであること、及び発行年数が古いこともあり、現時点では積極的に Group 1 に分類する強い理由は見当たらないとした。他方、黄リン (黄リンマッチの製造は禁止されているが、他用途で使われている)については、皮膚接触による重度のやけどが報告されていたが、皮膚吸収性有害物質の毒性学的概念と合致せず、Group 1 に分類する理由はないと判断した。その他、16 物質については、ばく露限界値が設定されていないため、限界値を定めるに足りる毒性情報が蓄積されていないという判断 (発がん物質でもない)から、現時点では Group 1 に分類する根拠が不十分であると判断した。この16物質については行政の専門家検討会に判断を仰ぐべきである。

GHS 急性経皮毒性は、ばく露経路が間違いなく経皮ばく露であると言えるが、その他の GHS 分類による毒性情報を利用し、経皮ばく露による健康障害が生じるおそれについて論

じるためには、図 3 に示すとおり、物質の物性を基に、経皮ばく露の可能性から検証していく必要がある。

一般に物質の蒸気圧が低ければ低いほど、その物質は気中に出にくくなるため、ばく露経路としては、経皮ばく露の可能性が高まる。また、物質のオクタノール水分配係数 (Log *Kow*)は、物質の親水性 (水溶性)・疎水性 (脂溶性) を判断する物質特有の値であり、数値が大きいほど脂溶性が高く、数値が低いほど水溶性が高い。皮膚の最表面にある角層は全体として、疎水性の膜であるため、一般に、物質の Log *Kow* が 1~4 程度の場合に、皮膚吸収性が高くなると言われている。したがって、蒸気圧が低く、Log *Kow* が 1~4 程度の物質は、経皮ばく露によって、物質を皮膚吸収する可能性が高いと推測される。

しかしながら、経皮ばく露により物質を吸収する可能性が高いであろうことまでは推測できるが、その吸収量と GHS 分類の結果を利用し、「健康障害を生ずるおそれがあることが明らか」であると断言することは、現時点での情報量では困難である。これらのことより、検討会では、図 3 に示す G2 候補物質群の中から、Group 1 に分類すべき物質は現段階では見当たらないという結論に達した。

- **経皮ばく露によって健康障害が生じるおそれがないことが明らかな物質について**

Group 2 に確定しなかった物質を、「経皮ばく露によって健康障害が生じるおそれがないことが明らかな物質」としてよいのか否かについて、検討会で議論した結果、Group 2 に確定しなかった物質であっても、経皮ばく露によって健康障害が生じるおそれがない物質とは言い切れないと判断した。例えば、ある物質の蒸気圧が非常に高く、主なばく露経路は吸入ばく露である場合であっても、気体状の物質が皮膚に付着し、皮膚吸収が生じないことを否定することは難しい (特に、Log *Kow* が高い値の場合)。実際、図 4 に示すように、皮膚吸収性有害物質 Group 1 の蒸気圧と Log *Kow* の関係について検証したところ、ばく露経路として、経皮・吸入の両方が問題になるであろう蒸気圧：20 mmHg から、吸入ばく露が主となる 1000 mmHg までの領域 (薄ピンク)に、約 20%の物質が含まれていることがわかる。さらには、皮膚にほぼ吸収されることはない (あっても極微量)と考えられる Log *Kow* (-1.5 以下)を有する物質も存在する。このように、経皮ばく露によって健康障害が生じるおそれがないことが明らかな物質を特定することは現時点では困難である。

また、上記は、物性情報、及び GHS 分類情報があることを前提に記述したが、実際には Group 2 候補群 (約 2700 物質)おいて、物性情報として、蒸気圧・Log *Kow* の両方が揃っているのは約 1500 物質であり、残り半分弱は情報が不完全若しくは全くない状態である。GHS 分類についても同様に情報がない、若しくは利用できないものが多い。検討会では、このような物質についても、情報がないからこそ、安全とはいえないと結論した。

したがって、条文 594 条の 3 中の除外規定、「経皮ばく露によって健康障害が生じるおそれがないことが明らかな物質は除く」はその物質を現時点では特定できないため、GHS 分類対象物質中の皮膚吸収性有害物質 (Group 2)は、皮膚吸収性有害物質(Group 1)を除くすべての物質が該当する。

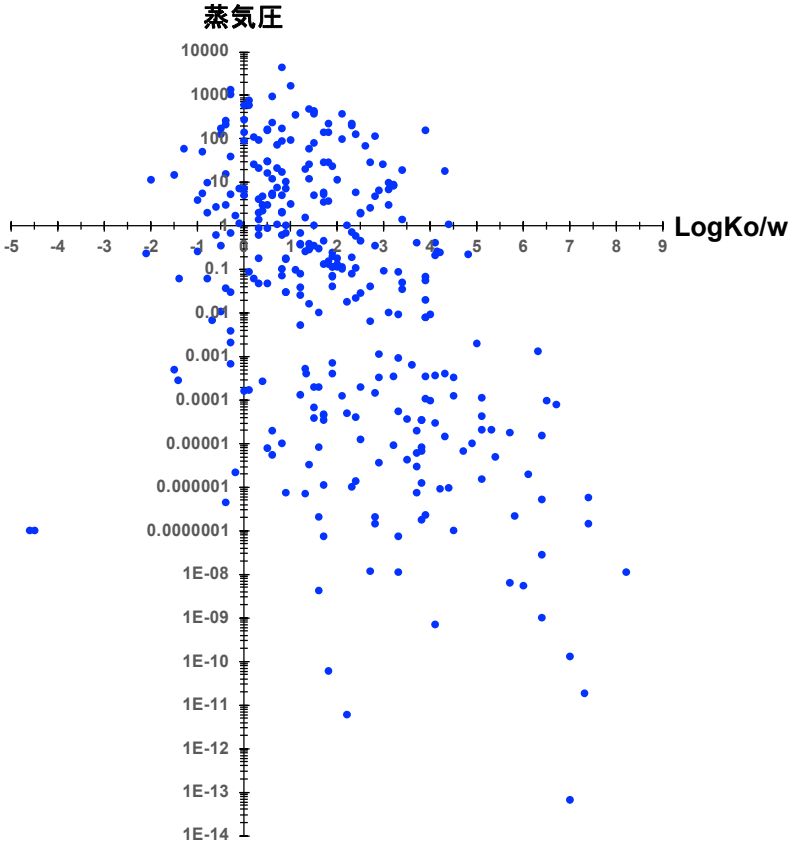

図 4 皮膚吸収性有害物質 Gropu 1 の蒸気圧と Log *Kow* の関係

第 3 皮膚吸収性有害物質の更新等について

本検討会では、皮膚吸収性有害物質 (Group 2)は、皮膚吸収性有害物質(Group 1)を除くすべての物質が該当するとした。この皮膚吸収性有害物質 Group 2 を構成する物質を、ばく露限界値、物性情報、GHS 毒性情報の有無によって分類すると以下のようになる。

- ばく露限界値の設定があり、経皮ばく露に関する in vitro (動物摘出皮膚等)の情報、及び/または、ばく露限界値を利用したモデル計算等に関する情報がある (諸機関において Skin Notation が付与されている物質を含む)
- ばく露限界値の設定があり、物性情報、及び GHS 毒性情報が存在する
- ばく露限界値の設定はないが、物性情報、及び GHS 毒性情報が存在する
- ばく露限界値の設定がなく、物性情報、若しくは GHS 毒性情報が不完全
- ばく露限界値の設定がなく、物性情報、及び GHS 毒性情報もない

このように、Group 2 を構成する物質は、限りなく Group 1 に近く、経皮ばく露により健康障害を生ずるおそれがあることが疑われる物質 (明らかとは断定できない)から、情報が全くなく、経皮ばく露により、どのような影響が生ずるか不明な物質まで含まれており、物質の経皮

毒性ポテンシャルにグラデーションがある状態である。これらGroup 2の物質は今後、Group 1 へ分類される可能性がある。

一つは研究の進展による更新がある。例えば、Group 1 に限りなく近い Group 2 物質に関しては、研究が進展し毒性情報 (特に動物)の追加がある可能性が高いと考えられるため、定期的なフォローアップを実施し、状況に応じた更新が適宜なされる可能性がある。次に、ばく露限界値の新たな設定、若しくは変更 (規制強化)に応じて、更新する可能性がある。例えば ACGIH や DFG では毎年、数物質にばく露限界値の設定、若しくは変更がなされている。また、我が国でも、化学物質の規制が、自律的な管理を基軸とする規制に変更していく一環で、化学物質の濃度基準値 (厚生労働大臣が定める濃度の基準)が、順次設定されていく運びとなっている。したがって、この濃度基準値も参考にして、更新をする可能性も検討する必要がある。

本検討会では、皮膚吸収性有害物質を諸機関の評価書に掲げられた文献をレビューする形式で選定したが、第 2, 3(3)で触れたように、GHS 分類の毒性情報を利用し、更新を検討する必要がある物質を見出す必要もある。前述の通り、皮膚吸収性有害物質 Group1 の該当条件の一つに、動物における経皮ばく露による急性毒性 (LD50<2000 mg/kg)が含まれており、これは、GHS 分類経皮急性毒性の区分 1～4 に該当する。下表には、GHS 対象物質約 3200 物質中の経皮急性毒性区分 1~5 に該当する物質数に対して、それが、Group 1 か Group 2 のどちらに含まれていたかの数を示している。

Acute Toxicity Estimate (ATE)：LD50 (推定値)

経皮急性毒性	区分 1	区分 2	区分 3	区分 4	区分 5
mg/kg 体重	ATE <50	50<ATE <200	200<ATE <1000	1000<ATE <2000	2000<ATE <5000
GHS 対象物質中	42	74	198	99	17
Group 1	24	28	66	29	2
Group 2	18	46	132	70	15

経皮急性毒性区分 1 の Group 2 に含まれていた 18 物質 (別添 2)については、検討会で検証した結果、現段階では Group 1 に更新しないとしたが、区分 2～区分 4 にも検証が必要な物質が存在する。これらについては、今後、専門家検討会等で、検証する必要があるものと考えられる。これに加えて、図 3 において、物性情報から主たるばく露経路が経皮ばく露であることが、合理的に判断できる物質については、経皮急性毒性以外の GHS 毒性情報を利用して、Group 2 から Group 1 へ更新する仕組み等を検討していくことが、経皮ばく露による健康障害の予防的観点からは重要であると考えられる。

第 4 皮膚吸収性有害物質に対する衛生管理、及び課題について

本検討会では、令和 6 年 4 月 1 日施行に施行される、労働安全衛生規則第 594 条の 2 において、その製造や取り扱い時に、不浸透性の保護衣、保護手袋等の保護具使用が義務となる 356 種類の化学物質を皮膚等障害化学物質：皮膚吸収性有害物質)として選定した。これら、皮膚吸収性有害物質は、経皮ばく露により皮膚から吸収され、健康障害を生ずるおそれがあることが明らかな物質である。皮膚吸収性有害物質の経皮ばく露を防止するためには、設備の自動化や密閉化、適切な治具の使用等で有害化学物質との接触機会の低減を図る等の作業環境管理の実施、さらに、作業時間の短縮、ばく露を低減しうる作業手法の工夫等の作業管理を実施することが、まずは基本となる。一方で、作業の性質やコスト面での問題等で、本質的なばく露防止対策を取れない場合、化学防護手袋等の保護具を使用する必要があるが、これは最終的な手段となる。検討会では、保護具使用が義務となる皮膚吸収性有害物質が設定されることに伴い生ずる課題等について以下、意見交換をした。

1. 保護手袋の選択や保護具使用に関する教育に関して

保護防護手袋は、使用されている材料やその厚み、使用状況によって、防護性能、作業性、機械的強度等が異なるが、まずは対象になる化学物質の特性等を考慮して作業に適した手袋を選択する必要がある。一方で、本検討会で選択した皮膚吸収性有害物質 Group 1 (356 物質)については、事業者団体の委員から、その半数強について耐透過性のデータが確認できない状況であり、耐透過性情報の開示がなければ、各現場で正しい防護手袋の選定・使用を行うことが困難であるという現状認識が示された。本検討会では防護手袋の材質等に関する議論は対象としていないものの、一般論として、化学物質の皮膚吸収性は物質の物理化学的特性に依存するところが大きいため、耐透過性情報がない物質については、情報がないことを理由に適当な防護手袋を選択するのではなく、その物質と物性 (分子量、LogKow、官能基、粘性等)や液性 (酸・アルカリ)が近い、耐透過性情報がある物質を参照したり、それらを入力して皮膚透過量を推定するアプリケーションなどを活用すれば、適切に防護手袋を選択できるとの議論がなされた。

今後、皮膚吸収物質の一覧を明示することで、保護具メーカーが保有する。耐劣化性、耐浸透性、耐透過性のデータや各事業者で実施された透過性試験の結果を開示し、適切な保護具の選定に活用することで、経皮ばく露の防止に努めていくことが必要である。

皮膚吸収性有害物質の経皮ばく露を低減するには、適切な保護具を選定することに加えて、その使用方法や保守管理も重要である。検討会においては、事業場において、保護具の不適切な使用等が散見されるとの認識が共有された。文献でも、適正使用及び保守管理に関する教育、指導が十分ではないことが従前から指摘されており [11]、例えば、加部らが実施した事業場における化学防護手袋の選択、着用、保守管理等に関する実態調査 [12] からは、防護手袋の適正使用について、防護手袋の袖口を折り返してタレ防止をすることや、袖口をテープで取り付け化学物質の侵入を低減すること、作業開始前に保管期間の確認すること、化学防護手袋の交換基準を設定すること等について、全体として意識が低いことが指摘されて

いる。当該、実態調査は比較的大規模の事業者を対象に実施されたものであるために、中小企業における実態も把握した上で、現場管理監督者や保護具着用管理者等の職長への教育、職長から現場作業者への教育プログラムの開発が必要である。

2. 皮膚吸収性有害物質に関する教育等について

職場内における経皮ばく露による健康障害を低減するためには、皮膚吸収性有害物質の物性やその有害性の特徴について認識し、経皮ばく露についての意識を高めることが、第一歩であると考えられる。

皮膚吸収性有害物質の特徴の一つとして、その毒性学的な面から、ばく露に気付きにくいことが挙げられる。例えば、皮膚刺激・腐食性がある化学物質にばく露した場合、ばく露を受けたことを比較的短時間のうちに認識することができ、必要に応じた医学的処置、ばく露対策の強化や安全意識の向上が期待できる。一方、皮膚刺激性等がなく、皮膚に吸収される物質は、急性毒性作用がない限り、作業者がばく露に気づきにくく、ばく露が常態化してしまうおそれがある。そのような物質が、発がん性等の遅発性毒性を有していると、後々重大な健康障害につながる可能性がある。実際に、膀胱がん事例で問題となったオルトトルイジンやモカ(MOCA：4,4'-メチレンビス (2-クロロアニリン))は、皮膚刺激性等はないが、ヒトや動物に対する発がん性が認められている。

本検討会が選定した皮膚吸収性有害物質 Group 1(356 物質)は、一部物質で皮膚刺激性・腐食性も認められているが、その約 9 割で刺激性等が認められていないか、不明である。このように、経皮吸収が問題となる化学物質は、その物性面からも、ばく露が常態化してしまう要素があることを認識する必要がある。皮膚吸収性有害物質 Group 1 の物質蒸気圧と Log *Kow* の関係を示す図 4 を見ると、蒸気圧が 1mmHg 以下の領域に 6 割強の物質が存在しており、これら物質は蒸気圧が低いため、蒸発しにくく、気中濃度が低くなる傾向がある。このため、低い蒸気圧は、経皮ばく露が起きていたとしても、作業環境測定による評価では、第三管理区分になりにくく、ばく露を常態化させてしまう要因になりうる。実際に、オルトトルイジンの事例では、作業環境測定によるオルトトルイジンの気中濃度は許容濃度以下であったことが報告されている[2]。

他方、皮膚吸収性有害物質 Group 2 を構成する物質は、第 3 で記載した通り、限りなく Group 1 に近い有害性を有するものから、有害性が低いものまで、経皮毒性に大きな違いがある。このように、皮膚吸収性有害物質 Group 2 は、法令上の取り扱いは同じ努力義務であっても、実際には、主要なばく露経路や毒性学的に大きく異なる物質が混在していることを認識するべきである。

以上を踏まえ、皮膚吸収性有害物質 Group 1、Group 2 のそれぞれで留意すべき特徴や、Group 2 の中でも特に注意が必要な物質にどのような物質があるのかを、現場管理監督者や保護具着用管理者等に教育することや、効果的な教材の作成の必要性は明らかである。

3. **保護具メーカーとユーザーのリスクコミュニケーションについて**

令和 6 年 4 月 1 日から第 594 条の2が施行され、皮膚等障害化学物質の取り扱いに際して、保護具の使用が義務付けられることになる。本検討会では、皮膚等障害化学物質の中でも特に、「皮膚吸収性有害物質」について議論を進めてきたところであるが、皮膚等障害化学物質は、他に「皮膚刺激性・腐食性物質」、「皮膚感作性物質」、「眼刺激性物質」の毒性学的特徴が異なる物質から構成されている。

従って、法令が施行されたときに現場が混乱しないよう、化学物質に関して、十分な知見を持たない者に対して、各々の毒性学的特徴に対応する保護具の選択方法に加え、皮膚等障害化学物質の有害性や、保護具の必要性についての理解を促進させることが必要である。このためには、保護具メーカーとユーザーの相互理解を促進するためのリスクコミュニケーション（意見交換会)が重要になると考えられる。また、現場において、各種皮膚等障害化学物質に対応する保護具を選択ができるようにするため、保護具選択マニュアル(基準)の作成、適正な保護具装着方法、及び、使用方法について啓発するための啓発資料等の作成が必要である。

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別表１　皮膚吸収性有害物質 Group 1（356物質）

番号	CAS	化学物質名称
1	50-32-8	ベンゾ[a]ピレン
2	51-75-2	ビス（2-クロロエチル）メチルアミン（ナイトロジェンマスタード）
3	52-51-7	2 - ブロモ - 2 - ニトロプロパン - 1,3 - ジオール（別名ブロノポル）
4	53-70-3	ジベンゾ［a,h］アントラセン
5	54-11-5	３－（１－メチル－２－ピロリジニル）ピリジン　(別名：ニコチン)
6	54-64-8	エチル（２－メルカプトベンゾエート）水銀ナトリウム塩　(別名：チメロサール)
7	55-18-5	N-ニトロソジエチルアミン
8	55-38-9	チオりん酸O,O-ジメチル-O-（3-メチル-4-メチルチオフェニル）【フェンチオン】
9	55-63-0	ニトログリセリン
10	56-23-5	四塩化炭素
11	56-38-2	パラチオン
12	56-55-3	ベンゾ[a]アントラセン
13	56-72-4	O-3-クロロ-4-メチルクマリン-7-イルO,O-ジエチルホスホロチオアート【クマホス】
14	57-14-7	1,1-ジメチルヒドラジン
15	57-74-9	1, 2, 4, 5, 6, 7, 8, 8 - オクタクロロ - 2, 3, 3a, 4, 7, 7a - ヘキサヒドロ - 4, 7 - メタノ - 1H - インデン　（別名クロルデン）
16	58-89-9	1,2,3,4,5,6-ヘキサクロロシクロヘキサン (リンデン)
17	59-89-2	N-ニトロソモルホリン
18	60-34-4	メチルヒドラジン
29	60-57-1	1,2,3,4,10,10-ヘキサクロロ-6,7-エポキシー1,4,4a,5,6,7,8,8aーオクタヒドロ-エキソ-1,4-エンド-5,8-ジメタノナフタレン　（別名：ディルドリン）
20	61-82-5	3 - アミノ - 1H - 1, 2, 4 - トリアゾール　（別名アミトロール）
21	62-53-3	アニリン
22	62-73-7	ジメチル-2,2-ジクロロビニルホスフェイト（別名DDVP）
23	62-74-8	フルオロ酢酸ナトリウム
24	62-75-9	N,N-ジメチルニトロソアミン
25	63-25-2	N-メチルカルバミン酸1-ナフチル【カルバリル】
26	65-85-0	安息香酸
27	67-56-1	メタノール
28	67-66-3	クロロホルム
29	67-68-5	ジメチルスルホキシド
30	67-72-1	ヘキサクロロエタン
31	68-11-1	メルカプト酢酸
32	68-12-2	N,N-ジメチルホルムアミド
33	71-23-8	ノルマル-プロピルアルコール
34	71-36-3	1-ブタノール
35	71-43-2	ベンゼン
36	71-55-6	1,1,1-トリクロロエタン
37	72-20-8	1,2,3,4,10,10-ヘキサクロロ-6,7-エポキシ-1,4,4a,5,6,7,8,8a-オクタヒドローエンド-1,4-エンド-5,8-ジメタノナフタレン　（別名：エンドリン）
38	72-43-5	1,1,1-トリクロロ-2,2-ビス（4-メトキシフェニル）エタン【メトキシクロル】
39	74-83-9	臭化メチル
40	74-87-3	クロロメタン
41	74-88-4	沃化メチル
42	74-90-8	シアン化水素
43	74-96-4	臭化エチル
44	74-97-5	ブロモ（クロロ）メタン
45	75-04-7	エチルアミン
46	75-05-8	アセトニトリル
47	75-09-2	ジクロロメタン
48	75-12-7	ホルムアミド
49	75-15-0	二硫化炭素
50	75-21-8	エチレンオキシド
51	75-26-3	2-ブロモプロパン
52	75-27-4	ブロモジクロロメタン
53	75-31-0	イソプロピルアミン
54	75-47-8	ヨードホルム
55	75-55-8	プロピレンイミン
56	75-74-1	テトラメチル鉛
57	75-86-5	アセトンシアノヒドリン
58	75-91-2	tert-ブチル=ヒドロペルオキシド
59	76-44-8	１，４，５，６，７，８，８－ヘプタクロロー３ａ，４，７，７ａーテトラヒドロー４，７－メタノー１Ｈーインデン（別名：ヘプタクロル）
60	77-78-1	硫酸ジメチル
61	78-00-2	四エチル鉛
62	78-30-8	りん酸トリ（オルト-トリル）
63	78-34-2	1,4-ジオキサン-2,3-ジイルジチオビス（チオホスホン酸）O,O,O',O'-テトラエチル【ジオキサチオン】
64	78-89-7	2-クロロ-1-プロパノール
65	78-93-3	メチルエチルケトン
66	78-94-4	メチルビニルケトン
67	78-95-5	クロロアセトン
68	79-00-5	1,1,2-トリクロロエタン
69	79-01-6	トリクロロエチレン

70	79-04-9	クロロアセチル=クロリド
71	79-06-1	アクリルアミド
72	79-07-2	クロロアセトアミド
73	79-10-7	アクリル酸
74	79-11-8	クロロ酢酸【モノクロロ酢酸】
75	79-34-5	1,1,2,2-テトラクロロエタン (別名：四塩化アセチレン)
76	79-41-4	メタクリル酸
77	79-43-6	ジクロロ酢酸
78	79-44-7	ジメチルカルバモイル=クロリド
79	81-81-2	3-（アルファ-アセトニルベンジル）-4-ヒドロキシクマリン【ワルファリン】
80	83-79-4	ロテノン
81	85-00-7	1,1'-エチレン-2,2'-ビピリジニウム=ジブロミド (別名: ジクワット)
82	85-01-8	フェナントレン
83	85-44-9	無水フタル酸
84	86-50-0	ジチオりん酸O, O-ジメチル-S-[（4-オキソ-1, 2, 3-ベンゾトリアジン-3（4H）-イル）メチル]（アジンホスメチル）
85	86-88-4	1-ナフチルチオ尿素
86	87-59-2	2,3-ジメチルアニリン
87	87-61-6	1,2,3-トリクロロベンゼン
88	87-62-7	2,6-ジメチルアニリン
89	87-68-3	六塩化ブタジエン
90	87-86-5	ペンタクロロフェノール
91	88-12-0	N-ビニル-2-ピロリドン
92	88-72-2	２-ニトロトルエン
93	88-73-3	オルト - ニトロクロロベンゼン
94	88-89-1	ピクリン酸
95	89-72-5	オルト-セカンダリ-ブチルフェノール
96	90-04-0	o-アニシジン
97	90-12-0	1 - メチルナフタレン
98	91-08-7	2,6-トリレンジイソシアネート (別名：2,6-トルエンジイソシアネート)
99	91-20-3	ナフタレン
100	91-57-6	2-メチルナフタレン
101	91-94-1	3,3'-ジクロロベンジジン
102	92-52-4	ビフェニル
103	92-67-1	ビフェニル-4-イルアミン　（別名：4-アミノジフェニル、4-アミノビフェニル）
104	92-84-2	フェノチアジン
105	92-87-5	ベンジジン
106	92-93-3	4 - ニトロジフェニル
107	93-76-5	2,4,5-トリクロロフェノキシ酢酸
108	94-75-7	2,4-ジクロロフェノキシ酢酸
109	95-47-6	o-キシレン
110	95-48-7	o-クレゾール
111	95-50-1	o-ジクロロベンゼン
112	95-51-2	o-クロロアニリン
113	95-53-4	o-トルイジン/トルイジン塩類
114	95-64-7	3, 4-ジメチルアニリン
115	95-68-1	2,4-ジメチルアニリン
116	95-69-2	4 - クロロ - オルト - トルイジン
117	95-76-1	3, 4-ジクロロアニリン
118	95-78-3	2,5-ジメチルアニリン
119	95-80-7	2,4-トルエンジアミン (別名: 2,4-ジアミノトルエン)
120	96-05-9	アリル＝メタクリレート
121	96-09-3	フェニルオキシラン（別名：スチレンオキシド）
122	96-12-8	1,2 - ジブロモ - 3 - クロロプロパン
123	96-18-4	1,2,3-トリクロロプロパン
124	96-29-7	ブタン-2-オン=オキシム
125	96-33-3	アクリル酸メチル
126	96-34-4	クロロ酢酸メチル
127	97-56-3	２－メチル－４－（２－トリルアゾ）アニリン　(別名：２－アミノアゾトルエン)
128	98-00-0	フルフリルアルコール
129	98-01-1	フルフラール
130	98-07-7	ベンジリジン=トリクロリド
131	98-54-4	４－ターシャリーブチルフェノール
132	98-73-7	p-tert-ブチル安息香酸
133	98-95-3	ニトロベンゼン
134	99-08-1	３－ニトロトルエン
135	99-54-7	1,2-ジクロロ-4-ニトロベンゼン
136	99-65-0	m－ジニトロベンゼン
137	100-00-5	パラ-ニトロクロロベンゼン
138	100-01-6	p-ニトロアニリン
139	100-25-4	p－ジニトロベンゼン
140	100-37-8	2-（ジエチルアミノ）エタノール
141	100-41-4	エチルベンゼン

142	100-51-6	ベンジルアルコール
143	100-61-8	N-メチルアニリン
144	100-63-0	フェニルヒドラジン
145	100-74-3	N - エチルモルホリン
146	101-14-4	3,3'-ジクロロ-4,4'-ジアミノジフェニルメタン
147	101-54-2	N-フェニル-1,4-ベンゼンジアミン
148	101-68-8	メチレンビス(4,1-フェニレン)=ジイソシアネート (別名；4'4-MDI)
149	101-77-9	4,4'-メチレンジアニリン
150	101-83-7	ジシクロヘキシルアミン
151	102-81-8	2-(ジ-n-ブチルアミノ)エタノール
152	104-94-9	p-アニシジン
153	106-42-3	p-キシレン
154	106-44-5	p-クレゾール
155	106-47-8	p-クロロアニリン
156	106-49-0	p-トルイジン
157	106-87-6	4-オキシラニル-1,2-エポキシシクロヘキサン
158	106-88-7	1,2-エポキシブタン（別名： 1,2-酸化ブチレン）
159	106-89-8	２－（クロロメチル）オキシラン（別名：エピクロロヒドリン）
160	106-91-2	メタクリル酸2,3-エポキシプロピル
161	106-92-3	1-アリルオキシ-2, 3-エポキシプロパン（別名：アリルグリシジルエーテル）
162	106-93-4	1,2-ジブロモエタン【EDB】
163	106-95-6	3-ブロモ-1-プロペン
164	107-02-8	アクロレイン
165	107-05-1	塩化アリル
166	107-06-2	1,2-ジクロロエタン
167	107-07-3	エチレンクロロヒドリン
168	107-13-1	アクリロニトリル
169	107-15-3	エチレンジアミン
170	107-18-6	アリルアルコール
171	107-19-7	2-プロピン-1-オール
172	107-21-1	エチレングリコール
173	107-22-2	グリオキサール
174	107-31-3	ぎ酸メチル
175	107-49-3	テトラエチルピロホスフェイト (別名：TEPP)
176	107-66-4	りん酸ジ-ノルマル-ブチル
177	108-03-2	1-ニトロプロパン
178	108-10-1	メチルイソブチルケトン
179	108-11-2	4-メチル-2-ペンタノール
180	108-38-3	m-キシレン
181	108-39-4	m-クレゾール
182	108-42-9	クロロアニリン (3-クロロアニリン)/クロロアニリン
183	108-44-1	m-トルイジン
184	108-45-2	m-フェニレンジアミン
185	108-69-0	3,5-ジメチルアニリン
186	108-70-3	1,3,5-トリクロロベンゼン
187	108-88-3	トルエン
188	108-93-0	シクロヘキサノール
189	108-94-1	シクロヘキサノン
190	108-95-2	フェノール
191	108-98-5	チオフェノール
192	109-73-9	n-ブチルアミン
193	109-79-5	1-ブタンチオール
194	109-86-4	エチレングリコールモノメチルエーテル
195	109-89-7	ジエチルアミン
196	109-99-9	テトラヒドロフラン
197	110-49-6	エチレングリコールモノメチルエーテルアセテート
198	110-54-3	ノルマル - ヘキサン
199	110-80-5	エチレングリコールモノエチルエーテル
200	110-86-1	ピリジン
201	110-91-8	モルホリン
202	111-15-9	エチレングリコールモノエチルエーテルアセテート(別名：セロソルブアセテート)
203	111-40-0	N-（2-アミノエチル）-1,2-エタンジアミン　（別名：ジエチレントリアミン）
204	111-42-2	２，２’ーイミノジエタノール
205	111-44-4	ビス(2-クロロエチル)エーテル
206	111-69-3	アジポニトリル
207	111-76-2	エチレングリコールモノ - ノルマル - ブチルエーテル（別名ブチルセロソルブ）
208	111-96-6	ジエチレングリコールジメチルエーテル
209	112-07-2	エチレングリコールモノブチルエーテルアセタート【2-ブトキシエチルアセタート又はEGBEA】
210	115-29-7	６，７，８，９，１０，１０ーヘキサクロロー１，５，５ａ，６，９，９ａーヘキサヒドロー６，９ーメタノー２，４，３ーベンゾジオキサチエピン＝３ーオキシド(別名：エンドスルファン）
211	115-90-2	チオりん酸O,O-ジエチル-O-[4- (メチルスルフィニル) フェニル] (別名：フェンスルホチオン)
212	117-81-7	フタル酸ビス(2-エチルヘキシル)
213	118-74-1	ヘキサクロロベンゼン

214	118-96-7	２，４，６－トリニトロトルエン
215	119-12-0	チオりん酸O,O-ジエチル-O-(6-オキソ-1-フェニル-1,6-ジヒドロ-3-ピリダジニル
216	119-93-7	3,3'-ジメチルベンジジン（別名：o-トリジン）
217	120-80-9	カテコール（別名：ピロカテコール）
218	121-44-8	トリエチルアミン
219	121-69-7	N,N-ジメチルアニリン
220	121-75-5	ジチオりん酸Ｏ，Ｏ－ジメチル－Ｓ－１，２－ビス（エトキシカルボニル）エチル　（別名：マラチオン）
221	121-82-4	ヘキサヒドロ-1,3,5-トリニトロ-1,3,5-トリアジン (15質量%の水で湿性としたものに限る)
222	122-14-5	チオリン酸O,O-ジメチル-O-(3-メチル-4-ニトロフェニル) (別名：フェニトロチオン)
223	122-60-1	2,3-エポキシプロピル=フェニルエーテル (別名：フェニルグリシジルエーテル)
224	123-31-9	ヒドロキノン
225	123-39-7	Ｎ-メチルホルムアミド
226	123-54-6	アセチルアセトン【2,4-ペンタンジオン】
227	123-73-9	クロトンアルデヒド（別名：（Ｅ）－２－ブテナール）
228	123-91-1	1, 4-ジオキサン
229	126-73-8	りん酸トリ-n-ブチル
230	126-98-7	メタクリロニトリル
231	126-99-8	2-クロロ-1, 3-ブタジエン（クロロプレン）
232	127-00-4	1-クロロ-2-プロパノール
233	127-18-4	テトラクロロエチレン
234	127-19-5	N,N-ジメチルアセトアミド
235	141-66-2	りん酸ジメチル＝（E)-1-（Ｎ，Ｎ－ジメチルカルバモイル）-1-プロペン-2-イル（別名：ジクロトホス）
236	143-33-9	シアン化ナトリウム
237	143-50-0	クロルデコン
238	151-50-8	シアン化カリウム
239	151-56-4	エチレンイミン (安定剤入りのもの、別名：アジリジン)
240	156-62-7	カルシウムシアナミド
241	189-55-9	ジベンゾ［a,i］ピレン
242	189-64-0	ジベンゾ［a,h］ピレン
243	193-39-5	インデノ［1,2,3-cd］ピレン
244	205-82-3	ベンゾ［j］フルオランテン
245	205-99-2	ベンゾ[e]フルオラセン
246	207-08-9	ベンゾ［k］フルオランテン
247	218-01-9	クリセン
248	298-00-0	ジメチルーパラーニトロフェニルチオホスフェイト　（別名：メチルパラチオン）
249	298-02-2	ジチオりん酸O,O-ジエチル-S-エチルチオメチル【ホレート】
250	298-04-4	ジチオリン酸O,O-ジエチル-S-(2-エチルチオエチル) (別名：ジスルホトン)
251	300-76-5	りん酸1,2-ジブロモ-2,2-ジクロロエチル=ジメチル
252	302-01-2	ヒドラジン
253	309-00-2	1,2,3,4,10,10-ヘキサクロロ-1,4,4a,5,8,8a-ヘキサヒドロ-エキソ-1,4-エンド-5,8-ジメタノナフタレン（別名：アルドリン）
254	333-41-5	チオリン酸Ｏ，Ｏ－ジエチル－Ｏ－（２－イソプロピル－６－メチル－４－ピリミジニル）(別名：ダイアジノン)
255	335-67-1	ペルフルオロオクタン酸
256	420-04-2	シアナミド
257	431-03-8	ジアセチル
258	505-60-2	ビス（2 - クロロエチル）スルフィド　（別名：マスタードガス）
259	528-29-0	o-ジニトロベンゼン
260	534-52-1	4,6-ジニトロ-o-クレゾール
261	542-75-6	1,3-ジクロロプロペン
262	552-30-7	1,2,4-ベンゼントリカルボン酸1,2-無水物
263	556-52-5	2, 3-エポキシ-1-プロパノール
264	563-12-2	ビス（ジチオりん酸）S,S'-メチレン-O,O,O',O'-テトラエチル
265	582-25-2	安息香酸カリウム塩
266	583-60-8	2-メチルシクロヘキサノン
267	584-84-9	2,4-トリレンジイソシアネート (別名：2,4-トルエンジイソシアネート)
268	591-78-6	メチル-ノルマル-ブチルケトン
269	592-01-8	シアン化カルシウム
270	594-27-4	テトラメチルスズ
271	598-78-7	２－クロロプロピオン酸
272	615-05-4	２，４－ジアミノアニソール
273	624-83-9	イソシアン酸メチル
274	624-92-0	ジメチルジスルフィド
275	628-96-6	ニトログリコール
276	643-79-8	o-フタルアルデヒド
277	680-31-9	ヘキサメチルホスホリックトリアミド
278	684-16-2	ヘキサフルオロアセトン
279	763-69-9	エチル=3-エトキシプロパノアート
280	764-41-0	1,4-ジクロロ-2-ブテン
281	768-52-5	N-イソプロピルアニリン
282	872-50-4	N-メチル-2- ピロリドン【N-メチルピロリドン】
283	944-22-9	O-エチル-S-フェニル=エチルホスホノチオロチオナート (別名：ホノホス)
284	999-61-1	アクリル酸2-ヒドロキシプロピル
285	1024-57-3	１，４，５，６，７，８，８－ヘプタクロロー２，３－エポキシー３ａ，４，７，７ａ－テトラヒドロー４，７－メタノ－１Ｈ－インデン　(別名：ヘプタクロルエポキシド)

286	1116-54-7	N-ニトロソジエタノールアミン
287	1120-71-4	１，２－オキサチオラン＝２，２－ジオキシド (別名：1,3-プロパンスルトン)
288	1300-73-8	キシリジン
289	1319-77-3	クレゾール
290	1321-64-8	ペンタクロロナフタレン
291	1321-65-9	トリクロロナフタレン
292	1330-20-7	キシレン
293	1331-22-2	メチルシクロヘキサノン（異性体混合物）
294	1335-87-1	ヘキサクロロナフタレン
295	1336-36-3 11097-69-1 53469-21-9	ポリクロロビフェニル
296	1402-68-2	アフラトキシン
297	1477-55-0	メタ - キシリレンジアミン
298	1569-02-4	プロピレングリコールエチルエーテル (別名：1-エトキシ-2-プロパノール)
299	1763-23-1	ペルフルオロ（オクタン－１－スルホン酸）
300	1910-42-5	1,1'-ジメチル-4,4'-ビピリジニウム=ジクロリド (別名：パラコートジクロリド)
301	2074-50-2	パラコートジメチルサルフェート
302	2104-64-5	O-エチル=O-4-ニトロフェニル=フェニルホスホノチオアート (別名：EPN)
303	2234-13-1	オクタクロロナフタレン
304	2425-06-1	N-（1,1,2,2-テトラクロロエチルチオ）-1,2,3,6-テトラヒドロフタルイミド【キャプタフォル】
305	2426-08-6	ノルマル-ブチル=2,3-エポキシプロピルエーテル
306	2431-50-7	2,3,4-トリクロロ-1-ブテン
307	2528-36-1	りん酸ジ-ノルマル-ブチル=フェニル
308	2807-30-9	2-プロポキシエタノール
309	2921-88-2	チオりん酸O,O-ジエチル-O-(3,5,6-トリクロロ-2-ピリジル) (別名：クロルピリホス)
310	3333-52-6	テトラメチルコハク酸ニトリル
311	3383-96-8	テメホス
312	3689-24-5	オキシビス（チオホスホン酸）O,O,O',O'-テトラエチル【スルホテップ】
313	3766-81-2	2-s-ブチルフェニルN-メチルカーバメート
314	3811-73-2	ナトリウム＝１－オキソ－１λ（５）－ピリジン－２－チオラート
315	3825-26-1	ペンタデカフルオロオクタン酸アンモニウム
316	4170-30-3	2-ブテナール（別名:クロトンアルデヒド（(E)-2-ブテナールと(Z)-2-ブテナールの異性体混合物））
317	4685-14-7	1,1'-ジメチル-4,4'-ビピリジニウム（別名：パラコート）
318	5216-25-1	p-（トリクロロメチル）クロロベンゼン（別名p - クロロベンゾトリクロリド）
319	5392-40-5	3,7 - ジメチル - 2,6 - オクタジエナール（別名シトラール）
320	6423-43-4	二硝酸プロピレン
321	6923-22-4	りん酸ジメチル=（E）-1-メチル-2-（N-メチルカルバモイル）ビニル
322	7439-97-6	水銀
323	7440-28-0	タリウム及びその化合物
324	7440-41-7	ベリリウム
325	7440-48-4	コバルト
326	7440-61-1	ウラン
327	7664-39-3	フッ化水素酸
328	7786-34-7	りん酸ジメチル＝１－メトキシカルボニル－１－プロペン－２－イル　（別名：メビンホス）
329	8001-35-2	塩素化カンフェン（別名：トキサフェン）
330	8008-20-6	灯油
331	8022-00-2	ジメチルエチルメルカプトエチルチオホスフェイト【メチルジメトン】
332	8052-42-4	アスファルト (ストレートアスファルト)
333	8065-48-3	チオりん酸Ｏ，Ｏ－ジエチル－エチルチオエチル　（別名：ジメトン）
334	11070-44-3	テトラヒドロメチル無水フタル酸
335	11097-69-1	ポリクロロビフェニル
336	12079-65-1	シクロペンタジエニルトリカルボニルマンガン
337	12108-13-3	2-メチルシクロペンタジエニルトリカルボニルマンガン
338	13071-79-9	テルブホス
339	13463-41-7	2-ピリジンチオール-1-オキシドの亜鉛塩（別名：ジンクピリチオン）
340	14977-61-8	オキシ塩化クロム（ＶＩ）(別名：塩化クロミル)
341	16752-77-5	S-メチル-N-[（メチルカルバモイル）オキシ]チオアセトイミデート
342	17702-41-9	デカボラン
343	22224-92-6	N - イソプロピルアミノホスホン酸O - エチル - O - （3 - メチル - 4 - メチルチオフェニル）　（別名フェナミホス）
344	22781-23-3	2,2-ジメチル-1,3-ベンゾジオキソール-4-イル-N-メチルカルバマート (別名：ベンダイオカルブ)
345	25154-54-5	ジニトロベンゼン (異性体混合物)
346	25321-14-6	ジニトロトルエン (異性体混合物)
347	26471-62-5	メチル-1,3-フェニレン=ジイソシアネート
348	26530-20-1	2-n-オクチル-4-イソチアゾリン-3-オン
349	26628-22-8	アジ化ナトリウム
350	26952-21-6	イソオクタノール
351	31242-93-0	塩素化ジフェニルオキシド
352	34590-94-8	ジプロピレングリコールメチルエーテル
353	35400-43-2	ジチオりん酸O-エチル-O-（4-メチルチオフェニル）-S-n-プロピル
354	53469-21-9	ポリクロロビフェニル
355	95465-99-9	S,S-ビス（1-メチルプロピル）=O-エチル=ホスホロジチオアート（別名：カズサホス）
356	111988-49-9	チアクロプリド

別添1　皮膚吸収性有害物質 Group 1候補物質の経皮ばく露に関する評価書レビュー結果

● ACGIH　▲DFG ■NIOSH★産衛における化学物質評価書内に、経皮ばく露に関連する情報があった場合に印を付した.
ただし、複数の機関が同じ見解を示している場合は、特定の機関の情報で代表している。

CAS	物質名称	経皮ばく露に関する記述	ヒト	In vivo（動物）	In Vitro（細胞等）	モデル計算等
50-32-8	ベンゾ[a]ピレン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		
51-75-2	ビス（2-クロロエチル）メチルアミン（ナイトロジェンマスタード）	【DFG】 ・ Because of the danger of skin absorption and of sensitization the designations H and S are necessary. ・ The aqueous nitrogen mustard hydrochloride solution which is used for external treatment of skin disorders seems not to be as readily absorbed through the skin [7]. One case, however, has been reported in which the spleen and lymph nodes of a 56 year old man were enlarged and the bone marrow was hyperplastic after a nitrogen mustard hydrochloride solution (1: 5000) had been used for local treatment for two years [22].	▲			
52-51-7	2-ブロモ-2-ニトロプロパン-1,3-ジオール（別名ブロノポル）	【DFG】 ・ Absorption of BNPD through intact skin is considerable. Even higher is the absorption rate through the mucous membrane of the alimentary tract after oral administration. Absorption from aqueous metal-working fluids can be increased by solubilizers like acetone or glycols.The designation "H" is applied to BNPD because of the danger of skin absorption during occupational use of the substance. ・ 2-Bromo-2-nitro-1,3-propanediol (BNPD) is readily absorbed through the intact skin of the rat. ・ BNPD is absorbed readily and in a dose-dependent manner by intact skin [13]. Percutaneous absorption of 14C-BNPD (4 mg/ml at doses of 1 mg/kg) from aqueous or acetone solutions by rats (CFY, shaved dorsal skin, occlusive, 5 days) was low (10%-20 %). Rabbits (New Zealand White) absorbed 11 % of the BNPD from an acetone solution (conditions as for rats) in 24 hours. The use of a depilatory cream increased the absorption to 30%. The substance was distributed evenly in all tissues; enrichment was evident in the hair follicles. Excretion took place mainly in the exhaled air, the remainder being divided equally between urine and faeces [14]. ・ After topical application of a solution of BNPD in acetone to the skin of rats (> 160 mg/kg body weight as in [27]) the animals died (concentration and amount applied, number of animals, duration of application, observation period and cause of death not specified) [6]. In contrast, when BNPD was applied to the skin in an aqueous solution the LD50 was > 1600 mg/kg body weight [2, 24].		▲		▲
52-68-6	ジメチル=2,2,2-トリクロロ-1-ヒドロキシエチルホスホナート（別名トリクロルホン又はＤＥＰ）	【産衛】 ・ LD50 は，438 mg/kg(ラット，経口)，250 mg/kg, (ラット，腹腔)，579mg/kg(マウス，経口)，５００ｍｇ/ｋｇ(マウス，腹腔)，４００ｍｇ/ｋｇ(ラット，皮下)，267 mg/kg(マウス，皮下)，> 5,000 mg/kg/24h (ラット，経皮) ・ トリクロルホンを容器詰めする作業に従事する 36 人から 110 人までの様々な労働者集団であった.1977–1982 年の平均曝露濃度は，0.95–3.30 mg/m3 であったが低下傾向を示し，中毒事例も減少傾向を示した.1983–1984年の調査結果では，曝露濃度は，1 mg/m3 近辺または未満で，皮膚表面積あたりの濃度は，0.50–5.92 μg/cm3 の範囲であった.対象者において，曝露前と比較し雇用 3 ヶ月後の血中コリンエステラーゼ活性は，一様に有意に抑制された.また，1977 年から 1982 年の各年のトリクロルホンの気中濃度の中央値は，0.28 mg/m3 から 2.48 mg/m3 の間であった.0.5 mg/m3 の濃度で，血中コリンエステラーゼ活性が軽度だが明白に抑制された.呼吸器からの吸入に加え，夏の暑い時期には皮膚からの吸収も多かったものと考察している.著者らは，この結果から最大許容濃度として 0.5 mg/m3 を提案している 16)	★	★		
53-70-3	ジベンゾ［a,h］アントラセン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		
54-11-5	３－（１－メチル－２－ピロリジニル）ピリジン(別名：ニコチン)	【ACGIH】 ・ A Skin notation is based on the well-documented human experience with percutaneous absorption of nicotine and resultant systemic toxicity from handling of uncured tobacco leaves and in the manufacture and application of nicotine insecticides.	●			
54-64-8	エチル（２－メルカプトベンゾエート）水銀ナトリウム塩　(別名：チメロサール)	【ACGIH】 ・ Mercury may be absorbed via the lungs, skin, and gastrointestinal tract (Foa and Bertelli, 1986). The lungs are the major route of absorption in the workplace.	●			
55-18-5	N-ニトロソジエチルアミン	【DFG】 ・ The interpretation of the results of the animal experiment with a systemic effect of N-nitrosodiethylamine after dermal exposure seems plausible due to the calculated high dermal flux. The substance is a proven genotoxic carcinogen for which, however, no safe exposure can be estimated. Therefore, even at low percutaneously absorbed levels, it must be assumed that the carcinogenic risk is increased. N-nitrosodiethylamine is therefore marked with "H".		▲		▲
55-38-9	チオりん酸O,O-ジメチル-O-（3-メチル-4-メチルチオフェニル）【フェンチオン】	【ACGIH】 ・ A skin notation is suggested, based on the demonstration of cholinergic signs in man and red blood cell cholinesterase inhibition in rabbits following dermal exposure.	●	●		

55-63-0	ニトログリセリン	【ACGIH】 ・ Based on the weight of human data for industrial nitroglycerin exposures and by analogy with propylene glycol dintrate (see T.LV Documentation for Propylene Glycol Dinitrate). A TLV-TWA of 0.05 ppm, with a Skin notation, is recommended for nitroglycerin.	●			●
56-23-5	四塩化炭素	【ACGIH】 ・ Absorption and excretion data from volunteers exposed dermally to carbon tetrachloride support the addition of the Skin notation. ・ Carbon tetrachloride is known to be readily absorbed by ingestion, inhalation, and dermal absorption in humans. (129-132) Volunteers who immersed one thumb in carbon tetrachloride for 30 minutes had resulting carbon tetrachloride concentrations in exhaled breath ranging from 0.69 to 5.2 mg/L, which may be compared to concentrations of approximately 6 mg/L measured 25 minutes postexposure in air exhaled from volunteers exposed to carbon tetrachloride by inhalation at 10 to 11 ppm for 5 hours. ・ Dermal LD50 of 15,000 mg/kg for guinea pigs.	●	●		●
56-38-2	パラチオン	【ACGIH】 ・ HCN and, though less direct, the cyanide salts can be absorbed through the skin and produce systemic toxicity, including death. Accordingly, a Skin notation is assigned for HCN and the salts. ・ Inorganic cyanides were also reported to be rapid-acting acute poisons to humans and exhibit a dose-response relationship. The primary route of entry in the workplace is by inhalation, and for HCN, absorption through the skin. 【DFG】 ・ In an in vitro study, the permeability constant of human skin for aqueous solutions of cyanides was found to be 3.5 × 10-4 cm/hour. The permeability for an aqueous solution of HCN is almost 30 times higher, 10-2 cm/hour. A further study showed that toxic effects occur within 5 minutes after accidental exposure of a worker's hand to aqueous HCN solution. The designation “H” is therefore retained. The low dermal LD50 of HCN and cyanide salts also supports this designation.	● ▲	● ▲	▲	
56-55-3	ベンゾ[a]アントラセン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		
56-72-4	O-3-クロロ-4-メチルクマリン-7-イルO,O-ジエチルホスホロチオアート【クマホス】	【ACGIH】 ・ A Skin notation is assigned since symptoms of organophosphate poisoning were seen in rats treated dermally and delayed cholinesterase inhibition was observed following single dermal doses of 50 to 500 mg/kg or daily 100 mg/ kg doses of coumaphos to adult hens.		●		
57-14-7	1,1-ジメチルヒドラジン	【ACGIH】 ・ Systemic toxicity, including mortality and corneal opacity, following dermal application of UDMH to dogs, guinea pigs, and rabbits warrants assignment of a Skin notation.		●		
57-57-8	ベータ-プロピオラクトン	【DFG】 ・ A relevant percutaneous uptake of β-propiolactone has been substantiated by model calculations. The substance is a proven genotoxic carcinogen for which, however, no safe exposure can be estimated. Therefore, even small amounts absorbed percutaneously must be assumed to increase the carcinogenic risk. β-Propiolactone is therefore marked with "H".				▲
57-74-9	1, 2, 4, 5, 6, 7, 8, 8 - オクタクロロ - 2, 3, 3a, 4, 7, 7a - ヘキサヒドロ - 4, 7 - メタノ - 1H - インデン（別名クロルデン）	【ACGIH】 ・ A Skin notation is assigned, based on the significant toxicity, including death, from dermal exposure of animals and humans.	●	●		
58-89-9	1,2,3,4,5,6-ヘキサクロロシクロヘキサン (リンデン)	【ACGIH】 ・ Because skin absorption in humans was associated with seizures and with measurable quantities of lindane in blood, the Skin notation is appropriate.	●			
59-89-2	N-ニトロソモルホリン	【DFG】 ・ A dermal penetration was proven in vivo and the model calculations also indicate a high dermal flux. The substance is a proven genotoxic carcinogen for which, however, no safe exposure can be estimated. Therefore, even small percutaneously absorbed amounts must be assumed to increase the carcinogenic risk. N-nitrosomorpholine is therefore marked with "H".		▲		▲
60-34-4	メチルヒドラジン	【ACGIH】 ・ A Skin notation is assigned, based on the significant toxicity in dogs, rabbits, guinea pigs, hamsters, and raits following derirnail appliicatrion of methylhydrazine.		●		
60-57-1	1,2,3,4,10,10-ヘキサクロロ-6,7-エポキシー1,4,4a,5,6,7,8,8aーオクタヒドロ-エキソ-1,4-エンド-5,8-ジメタノナフタレン　（別名：ディルドリン）	【ACGIH】 ・ Dieldrin is toxic by all routes of exposure, but the greatest occupational hazard is by skin absorption (Smith, 1991). Thus, a Skin notation is recommended.	●			
61-82-5	3 - アミノ - 1H - 1, 2, 4 - トリアゾール　（別名アミトロール）	【DFG】 ・ Although dermal absorption is only about 1% of the applied dose even after several hours of application, the MAK value is very low, so that the contribution of exposure via the skin may be relevant for systemic toxicity even at this low absorption rate. From a saturated aqueous solution, at least 76 mg would be absorbed from hands and forearms (2000 cm2) after one hour of exposure, according to model calculations. This amount is significantly higher than the amount absorbed by inhalation (2 mg) at exposure levels equivalent to the MAK value. Therefore, amitrole is marked with "H".		▲		▲

62-53-3	アニリン	【ACGIH】 ・ Based on the increase in methemoglobin in blood observed at 5 ppm in animals and the skin absorption in humans, a TLV-TWA close to the structurally similar chemical, nitrobenzene, is in order. Accordingly, a TLV-TWA of 2 ppm is recommended, provided absorption through the skin by contact with liquid aniline is prevented. Based on the systemic toxicity from dermal absorption, a Skin notation is recommended. ・ Dutkiewicz　reported skin absorption from vapor exposure. He proposed 35 mg as the maximal allowable daily dose, corresponding to exposure to about 1 ppm for an 8-hour day at mild exertion. 【DFG】 ・ Single doses in the LD50/LC50 range led, after inhalation, ingestion or dermal absorption, to cyanosis, as a result of methaemoglobinaemia, and the associated signs in various species. ・ Aniline vapour was dermally absorbed by naked test persons at the same rate as after inhalation-only exposure at a respiratory volume of 418 l/h under resting conditions. The usual respiratory volume is 10 m3/8 hours (1250 l/h). If this is taken into account, absorption of aniline by inhalation is about 3 times higher than after dermal absorption. Wearing work clothes reduced absorption through the skin by 42%. ・ A comparison of the mathematically derived prediction for the amount of aniline absorbed through the skin with data from in vitro experiments in human skin yielded fluxes of 725.2 ± 213.5 µg/cm2 and hour (in vitro; Wellner et al. 2008), 677.9 µg/cm2 and hour (Fiserova-Bergerova et al. 1990), 76.6 µg/cm2 and hour (Guy and Potts 1993) and 112.8 µg/cm2 and hour (Wilschut et al. 1995).	● ▲	● ▲	▲	▲
62-73-7	ジメチル-2,2-ジクロロビニルホスフェイト（別名DDVP）	【ACGIH】 ・ A Skin notation is assigned because symptoms of organo pohospohate poisoning have been seen in humans and animals following dermal contact. ・ Dermal LD50 values were approximately 75 to 100 mg/kg in rats when dichlorvos was applied in acetone to their shaved backs. In monkeys, signs and symptoms of dichlorvos exposure included nervousness, gritting of teeth, loss of coordination, muscular fasciculations, excessive salivation, labored breathing, and miosis. These signs and symptoms typically preceded death and occurred after a single 100 mg/kg dermal dose, after 8 50 mg/kg/day doses over 10 days, and after 10 75 mg/kg doses over 12 days. The data suggested that the effects of dermal exposures might be cumulative. Serum and red blood cell (RBC) cholinesterase were significantly inhibited in one monkey that received 75 mg/kg.	●	●		
62-74-8	フルオロ酢酸ナトリウム	【ACGIH】 ・ Rapid absorption through intact and abraded or cut skin warrants a Skin notation. ・ In view of these data and the fact that death can result from gradual cardiac failure, ventricular fibrillation, or from a progressive depression of the CNS resulting in respiratory or cardiac failure, a TLV-TWA of 0.05 mg/m³ is recommended for sodium fluoroacetate. The Skin notation is based on rapid dermal absorption. (27) The TLV should minimize the risk of acute systemic toxicity when absorbed by inhalation or dermally.	●			●
62-75-9	N,N-ジメチルニトロソアミン	【ACGIH】 ・ A Skin notat ion is based on the hepatoxicity associated with workers handling DMNA and the toxicity in animals following topical application of DMNA.	●	●		
63-25-2	N-メチルカルバミン酸1-ナフチル【カルバリル】	【ACGIH】 ・ A skin notation is assigned based on a study where workers received both inhalation and dermal exposures. Based on the study by Xiia et a.I. (2005),, a Skin notaitian is assigned. ・ Following application of [14C]-carbaryl in acetone at 4 µg/cm² to the ventral forearm and after remaining unwashed and uncovered for 24 hours, some 74% of the applied dose was absorbed (as determined by urinary excretion of the label) (Feldman and Maibach, 1974). ・ Whorton et al. (1979) did not detect differences in the fertility of 49 men engaged in carbaryl production versus that of controls, but findings of abnormal sperm morphology in these men (Wyrobeck et al., 1981) remain unresolved (Baron, 1991). Examination of men participating in an infertility clinic showed an association between lower sperm motility and urinary 1-naphthol, a metabolite of carbaryl. Increased DNA damage to sperm was generally, but not consistently, related to the levels of 1-naphthol (Meeker et al., 2004a; b). Damage to sperm was reported in 16 carbaryl-exposed workers (exposures not quantified). The frequency of aneuploidy and numerical chromosomal aberrations was elevated when compared to normal individuals (Xia et al., 2005). ・ The acute oral LD50 for male rats is 850 mg/kg carbaryl and for females, 500 mg/kg. The dermal LD50 is greater than 4,000 mg/kg for both male and female rats (Gaines, 1960).	●	●		
65-85-0	安息香酸	【ACGIH】 ・ Existing data indicate significant skin uptake in humans in the range of 40% (Feldmann and Maibach, 1970 and Wester and Maibach, 1976 as cited in Federal Institute for Occupational Safety and Health (BAUA; DE) 2011; Hartwig and MAK Commission 2018; World Health Organization (WHO) 2000). Therefore, skin exposure may contribute important amounts to systemic doses received by inhalation, warranting a skin notation for these substances. 【DFG】 ・ Studies of absorption through the skin are available only for benzoic acid. As benzoic acid dissolved in aqueous media is present in equilibrium with its dissociated form (benzoate), the two compounds cannot be differentiated with regard to absorption through the skin; dermal absorption takes place via the undissociated form. Assuming a maximum absorption rate of 166 µg/cm2 and hour (Nielsen and Sørensen 2012), about 332 mg benzoic acid would be absorbed through the skin under standard conditions (2000 cm2, 1-hour exposure). The NOAEC for systemic effects after short-term inhalation exposure in rats is 250 mg/m3, so that after extrapolation to long-term exposure (1:6), extrapolation to humans (250 mg/m3 × 10 m3 respiratory volume per 8-hour exposure) and after halving the dose because the results were obtained on the basis of animal experiments, (see List of MAK and BAT Values, Section I) and correction for the increased respiratory volume at the workplace (1:2), a systemically tolerable amount of 104 mg is obtained. The possible contribution of absorption through the skin to systemic toxicity is therefore not negligible, so that both benzoic acid and alkali benzoates are designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).	●		▲	▲
67-56-1	メタノール	【ACGIH】 ・ Because methanol can be absorbed through the skin causing blindness and other visual disturbances (Rowe and Mccollister, 1982),a Skin not ation is also recommended.	●	●		

67-66-3	クロロホルム	【DFG】 ・ From the data of Bogen et al. 1992 it can be estimated that, during dermal exposure of 2000 cm2 of skin to a saturated aqueous solution of chloroform (8.1 mg/ml) for 1 hour, 2106 mg of chloroform is absorbed. The formulae of Fiserova-Bergerova et al. 1990 and Guy and Potts 1993 predict the amounts absorbed to be 2288 and 137 mg, respectively. If the MAK value is observed, the maximum amount of chloroform taken up via the respiratory tract, assuming 100 % retention, is only 25 mg in 8 hours. Therefore, under some conditions, the dermal uptake could be much higher than the uptake by inhalation. After application of chloroform to the skin of rabbits, degenerative changes were seen in the kidneys. This documents systemic toxic effects of dermally applied chloroform. Chloroform is therefore designated with an “H”.		▲		▲
67-68-5	ジメチルスルホキシド	【DFG】 ・ Generally speaking, the absorption-promoting effects of DMSO can be relevant with many substances. For this reason DMSO requires the designation "H". Liquid dimethyl sulfoxide penetrates the skin at the same rate as dimethylformamide. In addition to the amount taken up via the lung, it has to be assumed that the same amount of dimethyl sulfoxide is taken up via the skin from the gas phase as was shown with dimethylformamide in volunteers. Therefore, damage to the embryo or foetus is unlikely at the concentration of 12 l/m3 and less.		▲		▲
67-72-1	ヘキサクロロエタン	【ACGIH】 ・ A Skin notation is assigned based on data from rabbits. ・ Weeks et al. reported the oral approximate lethal dose in rabbits was greater than 1000 mg/kg; the oral LD50 for rats was 4460 mg/kg (in corn oil). When applied as a paste to the shaved skin of rabbits, the dermal LD50 for HCE was 32,000 mg/kg. 【NIOSH OSHA PEL Project Documentation 1988】 ・ Lawrence Hecker, Corporate Director of Industrial Hygiene and Toxicology for Abbott Laboratories (Ex. 3-678; Tr. p. 9-1149) stated that the skin notation should not be retained for hexachloroethane because this material is not systemically toxic via dermal absorption. However, in accordance with the Agency’s policy on skin notations (see Section VI.C.18 of this preamble), OSHA is retaining a skin notation for hexachloroethane in the final rule. OSHA is concerned, as is NIOSH (Ex. 8-47, Table N6A), about the development of tumors in hexachloroethane-exposed mice demonstrated in the NCI (1978b/Ex. 1-949) study. OSHA therefore retains its PEL of 1 ppm TWA, with a skin notation, and concludes that increasing the PEL for hexachloroethane would increase the significant risk of cancer potentially associated with exposure to this substance. 【DFG】 ・ Hexachlorobenzene can penetrate the skin and is therefore designated with an "H". ・ In animal studies the acute toxicity is low. The LD50 for the rat is of the order of 3500–10000 mg/kg body weight. The symptoms of intoxication include tremor, convulsions and ataxia. ・ Hexachlorobenzene was administered by occlusive application of a dermal dose of 10 mg/kg body weight in tetrachloroethylene to male Fischer rats. After 6 hours 1.05 % of the dose had been absorbed, after 24 hours 2.67 % and after 72 hours 9.71 % (BUA 1994).		● ▲		
68-11-1	メルカプト酢酸	【ACGIH】 ・ A Skin notation is recommended as systemic effects including death are produced in animals following low, single doses (Lewis, 1996; Fassett, 1963). ・ Significant acute toxicity follows dermal contact with an LD50 of 47 mg/kg in the mouse (Lewis, 1996) and 848 mg/kg in the rabbit (Dow Chemical, 1973). Fatalities were produced in rats following oral doses of less than 50 mg/kg and in guinea pigs following dermal administration of less than 5 ml/day (Fassett, 1963). ・ The no-observed-adverse-effect levels (NOAELs) for systemic toxicity can be estimated to be higher than 180 and 360 mg/kg body weight/day in rats and mice, respectively (OECD, 2009). ・ Thioglycolic acid, partially neutralized to pH 4, was administered dermally over a 2-day period to 3 groups of 5 male and 5 female Swiss mice at dose-levels of 0, 250, 500 and 1000 mg/kg body weight/ day for males or 0, 125, 250 and 500 mg/kg/day for females. No increase of the frequency of the micronucleated polychromatic erythrocytes was observed in the bone marrow harvested 24 hours after the last treatment. Positive and vehicle controls gave the expected results (ECHA, 2011).		●		
68-12-2	N,N-ジメチルホルムアミド	【ACGIH】 ・ Reported human dermal absorption (Lauwerys et al., 1980; Wrbitzky et al., 1996; Chang et al., 2005) and the potential contribution to systemic toxicity, including liver injury (Potter, 1973; Redlich et al., 1988, 1990; Fiorito et al., 1997) warrant the Skin notation.	●			
71-23-8	ノルマル-プロピルアルコール	【NIOSH OSHA PEL Project Documentation 1988】 ・ In the final rule, OSHA is retaining the 8-hour TWA PEL of 200 ppm and adding a STEL of 250 ppm for propyl alcohol; the skin notation is not included in the final rule because the LD(50) in rabbits is 5040 mg/kg, well above the level determined by OSHA to require a skin notation (see Section VI.C.18 for a discussion of skin notations).		■		
71-36-3	1-ブタノール	【NIOSH OSHA PEL Project Documentation 1988】 ・ A skin notation is necessary because data in beagle dogs suggest that dermal contact with n-butyl alcohol can result in a systemic dose greater than that obtained by inhalation (DiVincenzo and Hamilton 1979). ・ Systemic effects in the form of vestibular and auditory nerve injuries have been reported in workers in France and Mexico. Contact dermatitis of the hands may occur due to the defatting action of liquid n-butyl alcohol, and toxic amounts can be absorbed through the skin. Based on data describing the rate of n-butyl alcohol uptake through the skin of dogs, DiVincenzo and Hamilton (1979, as cited in Patty’s Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C, pp. 4571-78, Clayton and Clayton 1982) suggested that direct contact of human hands with n-butyl alcohol for one hour results in an absorbed dose that is four times that resulting from inhalation of 50 ppm for one hour.	■	■		■

71-43-2	ベンゼン	【ACGIH】 ・ Although dermal absorption of liquid benzene can be limited, the absorbed dose by direct dermal contact, combined with that received from body surface exposure to benzene in workplace air, may be such that a substantial fraction of the total exposure can be due to skin absorption. ・ Benzene dermal absorption was 0.05% when neat liquid benzene was applied directly to a human forearm at 4.4 mg/cm² and allowed to dry; (103) it penetrated through cultured human abdominal skin from air saturated with benzene.(104) Susten et al. (105) found that after dermal application of 5 µL ^{14}C-labeled benzene to intact skin of hairless mice, maximal skin radioactivity occurred at 1.5 minutes, and it remained "essentially unchanged for at least 2.5 hours." Based on in vitro percutaneous absorption and in vivo inhalation data, one example of calculated total benzene exposure used an adult working in ambient air containing 10 ppm benzene with 100 cm² skin surface in direct contact with gasoline containing 5% benzene. It was estimated that if the worker's entire skin surface was in contact with ambient air, the individual would absorb 7.5 µL benzene via inhalation in 1 hour, 7.0 µL from direct dermal contact with gasoline, and 1.5 µL from body surface exposure to ambient air.(105)	●	●	●	●
71-55-6	1,1,1-トリクロロエタン	【DFG】 ・ Skin absorption.1,1,1-Trichloroethane has been marked with "H" since 2001 on the basis of human data showing absorption of liquid 1,1,1-trichloroethane via the skin in toxicologically relevant amounts (2001 addendum). The marking with "H" is therefore maintained.	▲			▲
72-20-8	1,2,3,4,10,10-ヘキサクロロ-6,7-エポキシ-1,4,4a,5,6,7,8,8a-オクタヒドローエンド-1,4-エンド-5,8-ジメタノナフタレン　（別名：エンドリン）	【ACGIH】 ・ Dermal toxicity is significant but less than dieldrin; therefore, a Skin notation is recommended. ・ Dermally, endrin was less toxic; the LD50 for male and female rats was 18 and 15 mg/kg, respectively.		●		
72-43-5	1,1,1-トリクロロ-2,2-ビス（4-メトキシフェニル）エタン【メトキシクロル】	【DFG】 ・ No usable quantitative human data are available to assess the skin absorption of methoxychlor. In animal studies with goats and cows, there were indications of a penetration capacity of methoxychlor through the skin. This is of the same order of magnitude as that found in rhesus monkeys and also in humans for the structurally related compound DDT. Using a flux of 22 µg per cm2 per hour determined from data from the experiments with goats, a one-hour contact of both hands and forearms (area 2000 cm2) with a solution of methoxychlor in dichloromethane (initial concentration 200 g/l) would result in an uptake of 44 mg of methoxychlor. In contrast, exposure at the level of the TLV will result in the uptake of 10 mg. Systemic uptake of toxicologically relevant amounts of the substance is thus possible through skin absorption. Methoxychlor is therefore marked with "H".		▲		▲
74-83-9	臭化メチル	【ACGIH】 ・ Skin absorption of toxic quantities of methyl bromide among workers wearing respiratory protection indicated the need for Skin notation. ・ Watrous described nausea, vomiting, headache, skin lesions, and symptoms of mild systemic poisoning in workers (90 people) exposed for 2 weeks at concentrations generally below 35 ppm. Liquid methyl bromide has penetrated through all articles of clothing and caused superficial burns with much vesication when in contact with skin. ・ The exposure time was 40 minutes at an estimated concentration of 9000 ppm in the air. Although the ambient concentration was very high, the fact that there were high plasma bromide concentrations in the exposed workers in spite of the use of protective gear, including respiratory protection, justifies the Skin notation. 【NIOSH-OSHA PEL project 1988】 Methyl bromide is a gas and is predominantly an inhalation hazard, although there are suggestions that it can also be absorbed through the skin (Patty’s Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B, p. 3443, Clayton and Clayton 1981).	● ■			
74-87-3	クロロメタン	【ACGIH】 ・ A Skin notation is assigned, based on data indicating substantial absorpt ion of methyl chloride through human skin with resultant addition to total body burden and systemic toxicity. Because methyl chloride can be absorbed through the skin in amounts that contribute substantially to systemic intoxication, the Skin notation is considered appropriate. ・ Human Studies: While the principal route of absorption of methyl chloride is by inhalation, it can be absorbed through the skin. (20) It has been reported to cause headache, drowsiness, giddiness, ataxia, and ultimately, convulsions, coma, respiratory failure, (21-23) and death. (24)	●			
74-88-4	沃化メチル	【ACGIH】 ・ Although there are no direct studies or case reports on dermal absorption of methyl iodide and resultant systemic toxicity, the above reports (1112) imply that skin contact and absorption may have contributed to the observed toxic responses and that protective measures should be taken to prevent such exposure. Although only Indirect evidence indicates a potential for dermal absorption,(11.12) a Skin notation is recommended as an additional preventive measure.	●			
74-90-8	シアン化水素	【ACGIH】 HCN and, though less direct, the cyanide salts can be absorbed through the skin and produce systemic toxicity, including death. Accordingly, a Skin notation is assigned for HCN and the salts. ＊Inorganic cyanides were also reported to be rapid-acting acute poisons to humans and exhibit a dose-response relationship. The primary route of entry in the workplace is by inhalation, and for HCN, absorption through the skin. 【DFG】 In an in vitro study, the permeability constant of human skin for aqueous solutions of cyanides was found to be 3.5 × 10−4 cm/hour. The permeability for an aqueous solution of HCN is almost 30 times higher, 10−2 cm/hour. A further study showed that toxic effects occur within 5 minutes after accidental exposure of a worker's hand to aqueous HCN solution. The designation “H” is therefore retained. The low dermal LD50 of HCN and cyanide salts also supports this designation.	● ▲	● ▲	▲	
74-96-4	臭化エチル	【ACGIH】 ・ Animal and human data indicate the potential for dermal absorption of ethyl bromide and its contribution to systemic toxicity.	●	●		

74-97-5	ブロモ（クロロ）メタン	【DFG】 ・ The percutaneous absorption of gaseous and liquid bromochloromethane was demonstrated in experiments with animals. The permeability constants and the flux indicate marked dermal absorption. As it is a genotoxic substance, for which at present no MAK value can be given, an additional genotoxic risk must be assumed with exposure of the skin. The substance has therefore been designated with an "H". ・Gaseous bromochloromethane is absorbed well by rats after inhalation and dermal exposure, as is liquid bromochloromethane after ingestion and dermal application.		▲	▲	
75-00-3	クロロエタン	【ACGIH】 ・ Although no data were identified to document inclusion of a Skin notation for ethyl chloride, analogous chemicals such as ethyl bromide, methyl bromide, and methyl chloride carry this notation (see TLV Documentation for these chemicals). ・ Accordingly, ACGIH considers it appropriate to include the Skin notation for ethyl chloride as a safeguard against the potential contribution to overall exposure by the cutaneous route.				●
75-04-7	エチルアミン	【ACGIH】 ・ There are no human data for skin absorption; however, considering that the lethal dose to rabbits following dermal exposure was 390 mg/kg, a Skin notation for this chemical is recommended.		●		
75-05-8	アセトニトリル	【ACGIH】 ・ A Skin notation is recommended based upon the case report of child poisoning from dermal contact (52) and the reported dermal LD50 values of less than 1000 mg/kg in rodents.	●	●		
75-08-1	エタンチオール	【DFG】 ・ Experimental studies on the dermal uptake of ethanethiol are not available. Estimation of skin absorption under standard conditions using the mathematical models of Fiserova-Bergerova et al. (1990), Guy and Potts (1993), and Wilschut et al. (1995) yields substance amounts between 160 mg and 2140 mg. Similar to 1-butanethiol (see Addendum "1-Butanethiol" 2019), it is assumed that the systemically tolerable concentration should be about 1 ml/m3. Assuming complete pulmonary absorption, the inhalation uptake of ethanethiol at exposure levels equal to the TLV is 13 mg at 100% inhalation absorption and 10 m3 breathing volume per working day. Since the intake amounts estimated for dermal absorption are significantly above this value, ethanethiol is marked with "H".				▲
75-09-2	ジクロロメタン	【DFG】 ・ For the dermal absorption of dichloromethane, a study with volunteers is available which, although it confirms the absorption of dichloromethane through the skin, does not allow a quantitative assessment of the amount of the substance able to penetrate the skin. The extent of dermal penetration of dichloromethane can, however, be estimated from ex vivo investigations in human skin (Ursin et al. 1995). According to this study, the dermal exposure of both hands and forearms would result in the absorption of 4800 mg dichloromethane. Exposure for 8 hours at the MAK value would correspond to the absorption of 1800 mg dichloromethane via the airways. Even if the experiment of Ursin et al. 1995 probably overestimated dermal penetration by a factor of 3, as observed for N-methylpyrrolidone, the results indicate that, in the case of dermal exposure, observance of the MAK value would not be adequate protection against systemic toxicity. Dichloromethane is therefore designated with an “H” (for substances which are absorbed through the skin).	▲		▲	▲
75-12-7	ホルムアミド	【ACGIH】 ・ A Skin notation is recommended since formamide can produce systemic effects following, dermal exposure (Carpenter and Smyth, 1946). ・ Skin tests on rabbits showed that formamide is relatively nontoxic by skin absorption, with the LD50 reported to be 6 g/kg (Czajkowska, 1981). The approximate lethal dose in rabbits, applied dermally, is reported to be greater than 17 g/kg (Stula and Krauss, 1977). ・ Rats were treated 6 hours/day, 5 days/week for 3 months with 30 to 3000 mg formamide/kg by semi-occlusive patches to the skin (Carpenter and Smyth, 1946). The animals treated with 3000 mg/kg showed poor general health including a number of organ weight changes; those given either 300 or 1000 mg/kg developed polycythemia; no changes were seen in rats treated with either 30 or 100 mg/kg. This study demonstrated that formamide can be absorbed through the skin in quantities sufficient to produce systemic toxicity even though it is not very acutely toxic via this route and effective doses were relatively high. The NOAEL for the study was 100 mg/kg. ・ Although it had been reported previously that application of formamide to the skin of pregnant mice resulted in inhibition of fetal growth and fetal malformations (Gleich, 1974; Oettel and Frohberg, 1964), gross fetal malformations were not observed following dermal application to the rat (Stula and Krauss, 1977).		●		
75-15-0	二硫化炭素	【ACGIH】 ・ A Skin notation is warranted for carbon disulfide based on effects seen in workers following combined inhalation and dermal exposures. (55) Although few studies based on dermal contact were available, it is reasonable to assume that systemic effects follow from inhalation or dermal contact and should be controlled.	●			
75-21-8	エチレンオキシド	【ACGIH】 ・ A Skin notation is assigned, based on the skin exposure of workers to EtOH that resulted in a significant degree of nausea and vomiting. ・ According to Sexton and Henson, (16) an accidental skin exposure of three workers to a 1% EtO aqueous solution resulted in marked nausea and profuse vomiting. 【DFG 】 ・ Because absorption of the substance through the skin is potentially dangerous, ethylene oxide is given the designation "H". ・ Within a few hours after exposure of the skin to gaseous ethylene oxide, development of dermatitis bullosa with erythema and blisters was observed [2, 20]. The first signs of intoxication resulting from exclusively dermal uptake of gaseous ethylene oxide were often systemic effects such as vomiting and headaches [2]. Likewise, after exposure of a large skin area to a 1 % aqueous solution of ethylene oxide for about 2 hours followed by a latent period of up to a few hours, the first symptoms were nausea, vomiting and headaches and then, after 12–24 hours, local effects on the skin such as severe blistering [21].	● ▲			

75-26-3	2-ブロモプロパン	【産衛】 ・ 6.5 ppm 前後の 2- ブロモプロパンに曝露された女性労働者では造血機能が軽度に抑制されている可能性がある．一方，2- ブロモプロパン長期発がん試験において 67 ppmの2- ブロモプロパンへの曝露によって有意な増加が確認された外耳道腺癌はヒトにおいても稀ではあるが報告されており，LOAEL として採用可能である．ヒトにおける悪影響と関連する最低濃度 6.5 ppm，ラットの最小毒性量（LOAEL）67 ppm， 1 日の曝露時間 6 時間から1 日の労働時間 8 時間への換算，動物からヒトへの外挿の不確実性，最小毒性量から最大無毒性量（NOAEL）への外挿の不確実性を考慮し，許容濃度として 0.5 ppm（2.5 mg/m3）を提案する．2- ブロモプロパン液に両手を1 分間浸すと，1 ppm， 8 時間曝露の吸収量の約 4 倍の皮膚吸収量が予測されることから，従来どおり（皮）を付す	★			★
75-27-4	ブロモジクロロメタン	【DFG】 ・ Studies on humans exposed to bromodichloromethane as a component of chlorinated tap water, as well as in vitro experiments, show uptake of bromodichloromethane through the skin. This is also supported by calculations with theoretical models showing dermal uptake of bromodichloromethane. Since bromodichloromethane is a genotoxic carcinogen that has been proven in animal experiments and for which no MAK value can currently be specified, an additional carcinogenic risk must be assumed for the documented dermal uptake rates. Therefore, bromodichloromethane is marked with "H". The structurally analogous trihalomethane chloroform, for which a much better data situation is available, is also marked with "H". ・ This rationale is based on the compilation of data in the IARC monographs (IARC 1991, 1999) and the NTP 2006 report. Bromodichloromethane is used for the synthesis of organic chemicals and has been used for the separation of minerals and salts and as a fire extinguishing agent. According to the National Occupational Exposure Survey (1981-1983), 3266 workers, including 503 women, may have been exposed to bromodichloromethane (NTP 2002). Bromodichloromethane is formed as a byproduct of drinking water chlorination (IARC 2004; NTP 2002). Thus, segments of the population are also exposed orally, inhalationally, or dermally to bromodichloromethane (NTP 2002).	▲		▲	▲
75-31-0	イソプロピルアミン	【ACGIH】 ・ A Skin notation is recommended, as the dermal LD50 in rabbits was 380 mg/kg (Smyt h et al., 1951). ・ In rabbits, the acute skin LD50 was reported at 0.55 ml/kg (380 mg/kg) (Smyth et al., 1951), and in guinea pigs, the dermal LD50 was reported as < 5 cc/kg (< 3.4 g/kg) (Eastman Kodak, 1953). In male and female Wistar rats, the dermal LD50 for isomine was reported to be > 400 mg/kg (ECHA)		●		
75-47-8	ヨードホルム	【ACGIH】 ・ Even though iodoform may have a relatively low rate of absorption through intact skin (Gottardi, 1995), only a small increase in iodine absorption in pregnant mothers (1 00 to 150 µg per day) would be sufficient to produce toxic effects in the fetus (Miller et al. 1989). Therefore, a Skin notation is recommended, consistent with other iodine-containing compounds (see, Documentation of TLV®: Iodine and Iodides).	●			
75-55-8	プロピレンイミン	【ACGIH】 ・ Based on the low dermal rabbit LD50, a skin notation is recommended.		●		
75-74-1	テトラメチル鉛	【ACGIH】 ・ In addition to the absorption of TEL by inhalation and ingestion, systemic toxicity has been amply demonstrated following percutaneous absorption. Accordingly, a Skin notation is warranted, although TML is absorbed through the Skin at a slower rate than is tetraethyl lead.		●		
75-86-5	アセトンシアノヒドリン	【ACGIH】 ・ Animal studies reporting acute intoxication and death and clinical reports of toxicity following dermal application or accidental skin contact with acetone cyanohydrin warrant the Skin notation.		●		
75-91-2	tert-ブチル=ヒドロペルオキシド	【ACGIH】 ・ The comparatively low dermal LD50 440 mg/kg TBHP for rabbits indicates that a Skin notation is warranted		●		
76-44-8	１，４，５，６，７，８，８ーヘプタクロロー３ａ，４，７，７ａーテトラヒドロー４，７ーメタノー１Ｈーインデン（別名：ヘプタクロル）	【ACGIH】 ・ A Skin notation is recommended because the acute toxicity of heptachlor is moderate, suggesting that significant amounts of chemicals can be absorbed through the skin to produce systemic responses.		●		
77-47-4	ヘキサクロロシクロペンタジエン	【DFG】 ・ Skin absorption must be estimated for concentrations that are no longer corrosive. A saturated aqueous solution has a concentration of 0.1%, which should no longer lead to corrosive effects or significant irritant effects. Based on the physicochemical data and the two models of Fiserova-Bergerova et al. 1990 and Guy and Potts 1993, intake levels of 31 and 0.3 mg (skin surface: 2000 cm2, 1 hour), respectively, are obtained. The systemic NOAEL after inhalation is 0.56 mg/m3. This means that during an 8-hour shift, 5.6 mg would be absorbed at 100% retention. Taking the geometric mean of both models (about 3 mg), the contribution of skin absorption would be very high. Therefore, and considering the unclear in vivo data on dermal toxicity, hexachlorocyclopentadiene is marked "H".				▲
77-78-1	硫酸ジメチル	【ACGIH】 Systemic toxicity reported for workers from dermal contact with dimethyl sulfate warrants assignment of a Skin notation. 【OSHA】 OSHA proposed, and the final rule establishes, a 0.1 ppm TWA PEL, with a skin notation, for dimethyl sulfate, which is an oily, colorless liquid with a faint, onion-like odor. NIOSH (Ex./8-47, Table N6A) concurs with the selection of this limit and considers dimethyl sulfate to be a potential human carcinogen.	●			
78-00-2	四エチル鉛	【ACGIH】 ・ Because TEL can be absorbed percutaneously in amounts that cause systemic poisoning, Skin notation is considered appropriate.	●			

78-30-8	りん酸トリ（オルト-トリル）	【ACGIH】 ・ A Skin notation is assigned because cholinesterase inhibition was demonstrated in rats treated dermally and in hen studies for delayed neurotoxicity. ・ In humans, most of the information comes from clinical examination reflecting effects on the nervous system.Signs of TOCP intoxication include peripheral paresthesias, ataxia, spasticity, and flaccid paralysis (Burley, 1932; Godfrey, 1961; Sorokin, 1969). TOCF may be absorbed through intact human skin (Hodgeand Sterner, 1943) and the gastrointestinal tract. Only 0.1% to 0.4% of a topical dose appeared in urine after 3 days (Hodge and Sterner, 1943). ・ Dermal treatment of cats with 0.5 mg/kg for 90 days produced no evidence of neurologic damage, while 1 mg/kg produced ataxia (Abou-Donia et al., 1986) without microscopic evidence of response. Histopathologic damage was seen with doses of 5 mg/kg or greater, thus in the cat, as opposed to the chicken, clinical signs of damage are evident before microscopic nervous system damage can be seen.	●	●		
78-34-2	1,4-ジオキサン-2,3-ジイルジチオビス（チオホスホン酸）O,O,O',O'-テトラエチル【ジオキサチオン】	【ACGIH】 ・ A Skin notation is assigned because symptoms of organophosphate poisoning, including lethality, have been seen folllowing dermal treatmemt of rats (LD50, 63,-235 mg/kg).		●		
78-89-7	2-クロロ-1-プロパノール	【ACGIH】 ・ The Skin notation is based on acute dermal toxicity. ・ The dermal LD50 for propylene chlorohydrin (24-hour plastic-covered contact on clipped skin) was 0.48 ml/kg (530.6 mg/kg) in male New Zealand rabbits. (13) Weisbrod (16) obtained a dermal LD50 of 440 mg/kg (24-hour covered contact) in rats. No skin irritation was observed in a single New Zealand rabbit 24 hours after the uncovered topical application of 0.01 ml (10 mg) (LD50 of 528 mg/kg) neat propylene chlorohydrins to the clipped skin of the abdomen. (13)		●		
78-93-3	メチルエチルケトン	【DFG】 ・ Relevant amounts of 2-butanone can be absorbed percutaneously and the substance is therefore designated with an “H”. ・ After dermal absorption, the LD50 for the rabbit was found to be between 0.2 and 2 ml/kg body weight (corresponding to 184 and 1840 mg/kg body weight). The 2 ml/kg body weight dose was lethal in all rabbits. Narcosis was the dominant symptom of intoxication. Methaemoglobin formation was observed after 0.2 and 2 ml/kg body weight, and there was an increase in the reticulocyte count after 0.2 ml/kg body weight (no other details) (Allied 1991). In the rat, dermal application of 500 mg/kg body weight did not lead to symptoms of intoxication. No local effects on the treated areas of skin were observed (Bayer 1969).		▲		
78-94-4	メチルビニルケトン	【DFG】 ・ Methyl vinyl ketone is absorbed through the shaved, intact skin in a very short time in lethal amounts (BASF 1968b). Application of undiluted methyl vinyl ketone to various areas of skin of the shaved dorsum of rabbits led to the results described in Table 3(BASF 1968b). ・ Two animal experiments on sensitization have yielded positive results and there is onereport of sensitization in man. Therefore methyl vinyl ketone is designated with an “S”. It is also designated with an “H” because toxic amounts of the substance are readily absorbed through the skin.		▲		
78-95-5	クロロアセトン	【ACGIH】 ・ Since there is experimental animal evidence that chloroacetone is absorbed through the skin with systemic toxicity leading to death, a Skin notation is recommended.		●		
79-00-5	1,1,2-トリクロロエタン	【ACGIH】 ・ Percutaneous absorption of 1,1,2-TCE with resultant systemic toxicity, including mortality in treated animals, warrant inclusion of a Skin notation.		●		
79-01-6	トリクロロエチレン	【DFG】 ・ A comparison of the substance levels in the blood of rats exposed epicutaneously to undiluted solvents for up to 24 hours (3.1 cm2 exposed skin) revealed that trichloroethylene is absorbed as efficiently as 1,1,1-trichloroethane, but only half as readily as benzene, tetrachloroethylene, toluene and ethylbenzene. Blood trichloroethylene levels in equilibrium of about 10 mg/ml were reached after 0.5 hours exposure (Morgan et al. 1991). ・ Only 0.3% of the trichloroethylene absorbed from the gaseous phase was absorbed by volunteers via the skin, the rest via the lungs (Kezic et al. 2000). When volunteers were exposed to liquid trichloroethylene (27 cm2 skin) a flux of 430 nmol/cm2 and minute was calculated. For an exposed skin surface of 360 cm2 and eight repeated three-minute exposures, this corresponds to 3.7 mmol. In comparison, after 8-hour exposure to 50 ml/m3, 3.1 mmol is absorbed (Kezic et al. 2001). It must therefore be assumed that the absorption of liquid trichloroethylene via the skin contributes considerably to the body burden. As long as no safe limit value for trichloroethylene can be given, trichloroethylene is designated with an “H”.	▲	▲	▲	▲
79-04-9	クロロアセチル=クロリド	【ACGIH】 ・ Accidental, large skin area exposures of two or more workers that resulted in respiratory difficulties, collapse, cardiorespiratory arrest, and possible ventricular arrhythmias indicate the need for assignment of a Skin notation.	●			

79-06-1	アクリルアミド	【ACGIH】 ・ Because acrylamide is readily absorbed through the skin to produce systemic effects, and since dermal exposure accounts for most human poisonings, a Skin notation is warranted (Peterson and Sheth, 1975; Auld and Bedwell, 1967). ・ By analyzing personal air samples, surface wipe samples, and wipe samples of the exposed skin of workers, the U.S. Occupational Safety and Health Administration (OSHA) confirmed that dermal contact was the most significant route of acrylamide exposure in chemical sewer grouting operations (Cummins et al., 1992).	●			
79-07-2	クロロアセトアミド	【DFG】 ・ Experimental data on skin absorption of 2-chloroacetamide are not available. From the models, the maximum absorption is 199 mg (2.8 mg/kg bw). The rat NOAEL of 10 mg/kg bw per day from the 90-day feeding study (see above) is equivalent to 3.5 mg/kg bw for humans. In addition, since the dermal LD50 in rabbits is less than 1000 mg/kg bw, 2-chloroacetamide is marked "H".		▲	▲	▲
79-10-7	アクリル酸	【ACGIH】 ・ A Skin notation is based on the reported LD50 values of 295 to 950 mg/kg following a single, topical application of undiluted acrylic acid on rabbits.		●		
79-11-8	クロロ酢酸【モノクロロ酢酸】	【ACGIH】 ・ A skin notation is recommended because MCAA is highly toxic dermally in rabbits (LD50 = 178- 200 mg/kg) and has resulted in deaths following dermal exposure in workers.	●	●		
79-24-3	ニトロエタン	【DFG】 ・ Assuming the exposure of 2000 cm2 of skin to a saturated aqueous solution for one hour, a dermal absorption of 500 mg can be estimated for humans from a model calculation (Section 4.1). From the systemic NAEC of 31 mg/m3 extrapolated to humans, a systemically tolerable amount of 310 mg is obtained at a respiratory volume of 10 m3. Therefore, the amount absorbed through the skin is above the systemically tolerable amount, and the substance has been designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).				▲
79-34-5	1,1,2,2-テトラクロロエタン (別名：四塩化アセチレン)	【ACGIH】 ・ A Skin notation is recommended since systemic effects have been reported to occur following dermal contact, although both the acute dermal toxicity and amounts required to produce systemic effects were relatively high. The dermal LD 50 in rabbits of 6300 mg/kg suggests a low order of dermal toxicity, although narcosis can be produced following topical application.		●		
79-41-4	メタクリル酸	【NIOSH OSHA PEL Project Documentation 1988】 ・ The skin notation is necessary to prevent dermal absorption and systemic toxicity. ・ In rabbits, the skin absorption LD(50) for methacrylic acid is 0.5 to 1 g/kg (Dow Chemical Company 1977m, as cited in ACGIH 1986/Ex. 1-3, p. 362).		■		
79-43-6	ジクロロ酢酸	【ACGIH】 ・ A skin notat ion is assigned because it has been associated with lethality in rabbits following dermal application 4-day LD50 of 510 mg/kg.		●		
79-44-7	ジメチルカルバモイル=クロリド	【ACGIH】 ・ A Skin notation is recommended as repeated dermal application produced tumors in mice. The acute dermal toxicity of DMCC is low; however, the seriousness of the endpoint and the fact that very little needs to be absorbed through the skin to exceed the daily allowed inhalation dose warrants the notation (Van Duuren et al., 1972, 1974, 1987). DMCC was not a sensitizer in the guinea pig (Von Hey et al., 1974). ・ A number of experiments were conducted using dermal administration of DMCC and tumors also resulted: 50 Swiss mice were exposed to 2 mg DMCC by application to the skin by micro-pipette; and 34 mice developed a total of 92 local skin papillomas and 11 local squamous cell carcinomas as well as 2 papillary lung tumors. Another 50 Swiss mice were exposed to 5 mg DMCC by subcutaneous injection and 35 local skin sarcomas developed and 4 lung papillomas. The 88 unexposed controls did not develop any tumors (Van Duuren et al., 1972, 1974). 【DFG】 ・ Since a one-hour dermal application resulted in mortality of all test animals, the dermal penetration of this substance has been proven. It must be assumed that the carcinogenic risk is increased even with small percutaneously absorbed amounts. Therefore, the substance is marked with "H".		● ▲		
79-46-9	2−ニトロプロパン	【DFG】 ・ Based on the model calculations and the physicochemical properties, a good skin penetration can be assumed. The substance is a proven genotoxic carcinogen for which no safe exposure can be estimated. Therefore, even small percutaneously absorbed amounts must be assumed to increase the carcinogenic risk. 2-Nitropropane is therefore marked with "H". ・ Malkinson and Gehlmann 1977 assumed that 2-nitropropane is readily absorbed dermally because of its solubility in both polar and nonpolar solvents and because of its small molecular size. ・ No local or systemic symptoms were observed in rabbits after dermal application of 2000 mg 2-nitropropane/kg bw; however, rabbits appear to be more resistant to the toxicity of this substance than rodents (WHO 1992). From the data on water solubility and log KOW, the following fluxes can be calculated: Using the model of Fiserova-Bergerova et al. (1990), a flux of 0.365 mg/cm2/h and a resorption amount of 730.2 mg are obtained assuming a one-hour exposure of 2000 cm2 skin; using the model of Guy and Potts 1993, a flux of 0.040 mg/cm2/h and a corresponding resorption amount of 81.0 mg are obtained.				▲

81-81-2	3-（アルファ-アセトニルベンジル）-4-ヒドロキシクマリン【ワルファリン】	【ACGIH】 ・ A Skin notation is recommended based on evidence of animal and human skin absorption, and systemic effects associatred wiitlh skin absorptrion (Fristedt and Sterner, 1965; Green, 1955; HCN, 2004; EC, 2009). ・ Absorption of warfarin from the skin of rats was slow but measurable. Three topical applications at 50 mg/kg produced about the same pharmacologic (17) response as did three oral doses of 0.6 mg/kg. However, one dermal dose at 0.25 mg/kg was about as effective as an oral dose of 2.0 mg/kg in depressing prothrombin time in rabbits. The dermal LD50 in rats was 1400 mg/kg. 【DFG】 ・ Quantitatively assessable data on the dermal absorption of warfarin and sodium warfarin are not available. However, from animal studies with dermal application and cases of poisoning after skin contact in humans, the relevance of the dermal route of absorption can be deduced. The results of model calculations support these observations. Furthermore, since the MAK value for warfarin and sodium warfarin is very low, dermal absorption is of relatively high importance. Therefore, warfarin and sodium warfarin are marked with "H".	● ▲	● ▲		▲
83-79-4	ロテノン	【DFG】 ・ Because of the low dermal LD50 value in the rabbit, the substance is designated with an “H”. ・ Dermal LD50 values in the range from 100 to 200 mg/kg body weight have been reported for the rabbit (Ray 1991).		▲		
85-00-7	1,1'−エチレン−2,2'−ビピリジニウム=ジブロミド（別名: ジクワット）	【ACGIH】 ・ A Skin notation is recommended, based on limited dermal application studies with rabbits and rats. ・ Diquat is less toxic dermally than orally. The 24-hour percutaneous LD50 in the rabbit was greater than 400 mg cation/kg body weight, the maximal dose that could be applied. At this dose, there were no ill effects in male or female rabbits, no abnormalities upon histologic examination of the major organs, and no signs of skin irritation. ・ Dermal LD50: 433 mg/kg in rat (Fundamental and Applied Toxicology., 7(299), 1986) ・ In human volunteers, Feldman and Maibach (22) found that, although 61% of diquat injected intrave-nously was recovered in the urine, only about 0.3% was excreted in the 10 hours after dermal application.	●	●		
85-01-8	フェナントレン	【DFG】 ・ Since PAH are also known to be absorbed through the skin, pyrolysis products and other mixtures containing PAH are handled like substances designated with an “H” (DFG 2007). ・ Animal studies have demonstrated that PAH are rapidly transported from the site of administration (gastrointestinal tract, lungs or skin) to other tissues via the blood and lymph (Mitchell 1982). This was also evident from the fact that high concentrations of DNA adducts were found in the lungs after application of PAH to the rodent skin (Carmichael et al. 1990; Randerath et al. 1988; Schoket et al. 1988). Absorption of PAH through the skin of humans has been well documented. Very high dermal exposure of workers exposed to creosote was concluded from a field study since the daily excretion of 1-hydroxypyrene exceeded the daily inhalation by a factor of 50 (Elovaara et al. 1995). By means of 1-hydroxypyrene it was demonstrated in 12 coke oven workers that an average of 75% of the total absorbed amount of pyrene enters the body through the skin (Van Rooij et al. 1993 a). Wearing protective clothing reduced skin contamination among workers exposed to creosote by 35% and thus the urinary excretion of 1-hydroxypyrene as a measure of internal exposure by 50% (Van Rooij et al. 1993 b). When a coal-tar ointment was applied epicutaneously to volunteers, the urinary excretion of 1-hydroxypyrene was increased. It was estimated that about 2 µg pyrene/cm2 was systemically available (Van Rooij et al. 1993 c). After application of a coal-tar ointment to eczema patients, aromatic DNA adduct levels were increased about 2 to 4 times in monocytes, lymphocytes and granulocytes and about 20 times in skin. The urinary excretion of 3-hydroxybenzo[a]pyrene correlated with the adduct levels in the skin (Godschalk et al. 1998). After topical application of a 2% solution of crude coal tar in petrolatum, phenanthrene, anthracene, pyrene and fluoranthene were detected in the peripheral blood (Storer et al. 1984). Volunteers who had been treated with creosote (100 µl) or pyrene (500 µg, applied in a toluene solution) and psoriasis patients who used a shampoo containing coal tar excreted 1-hydroxypyrene as a conjugate in the urine. In both cases, maximum amounts were excreted 10 to 15 hours after treatment (Viau et al. 1995 a).	▲	▲		
85-44-9	無水フタル酸	【ACGIH】 ・ Skin notation is recommended based on animal studies that demonst rate phthalic anhydride can cause respiratory sensiitizaition as indicated by the development of a T helper 2 (Th2) cytokine phenotype response from dermal application		●		
86-50-0	ジチオりん酸O, O-ジメチル-S-[（4-オキソ-1, 2, 3-ベンゾトリアジン-3（4H）-イル）メチル]（アジンホスメチル）	【ACGIH】 ・ A Skin notation is assigned based on the relatively low doses applied to rabbit skin that produced lethality and the reports of cholinergic inhibition in agricultural workers dermally exposed.	●	●		
86-88-4	1-ナフチルチオ尿素	【ACGIH】 ・ Based on data from tests on workers handling thiourea prroducts tlhat demonstratied dermall absorptrion leading to effects on the thyroid, a Skin notation is assigned. ・ Tests performed on workers handling thiourea products showed ready penetration through the skin, leading to destructive changes in the thyroid glands. (11) ANTU was implicated (12) as a causative agent in occupational bladder tumors because of its content of ß-naphthylamine as an impurity in a-naphthyl-amine from which ANTU is made. 【DFG】 ・ Skin Absorption. Experimental data on dermal toxicity and skin absorption are lacking. The systemic NOAEL is unclear. Models can be used to calculate dermal uptake levels of 1.7 to 22 mg (maximum 0.3 mg/kg bw) for one-hour exposure to a saturated aqueous ANTU solution. Compared with the LOAEL of 2.5 mg/kg bw in rats (after species-specific correction for toxicokinetic differences = 0.63 mg/kg bw), the calculated dermal intake is half the LOAEL in the worst case. There is also the additional suspicion of DNA reactivity and carcinogenicity. For these reasons ANTU is marked with "H".	●			▲
87-59-2	2,3-ジメチルアニリン	【ACGIH】 ・ Based on the central nervous system effects and methemoglobin formation seen in cats that received repeated cutaneous applications of 2,4-xylidine, the Skin notation is warranted.		●		

87-61-6	1,2,3-トリクロロベンゼン	【DFG】 ・ Since all three isomers have similar solubility (insoluble in water, slightly soluble in ethanol and highly soluble in organic solvents), it can be assumed that all three isomers are similarly well absorbed when applied epicutaneously. Because of the basically comparable systemic toxicity, it can therefore be assumed that 1,2,3- and 1,3,5-trichlorobenzene can also lead to liver damage after epicutaneous application, even though no studies are available on this. The marking with "H" for 1,2,3- and 1,3,5-trichlorobenzene therefore remains. [MAK Value Documentation in German language, 1998] ・ Evidence of systemic toxicity (increased excretion of coproporphyrin) was observed in rabbits after repeated dermal application of technical grade trichlorobenzene (approximately 70 % 1,2,4-trichlorobenzene and 30 % 1,2,3-trichlorobenzene, no further details). In addition, in guinea pigs, but not in rabbits, necrotic foci were found in the liver after repeated dermal application of pure 1,2,4-trichlorobenzene (see Volume 3). A penetration rate of 0.18 mg/cm2 and hour was calculated for human skin for a saturated aqueous solution of 1,2,4-trichlorobenzene (Fiserova-Bergerova 1990). The substance has therefore been designated with an “H”.		▲		▲
87-62-7	2,6−ジメチルアニリン	【DFG】 ・ Because of the symptoms of intoxication which have been described, it must be assumed that the isomers are absorbed not only through the respiratory tract but also through the skin. Therefore the xylidines are designated with an “H”.				▲
87-68-3	六塩化ブタジエン	【ACGIH】 A Skin notation is assigned based on the dermal absorption and mortality in rabbits following topical administration of HCBD.		●		
87-86-5	ペンタクロロフェノール	【ACGIH】 ・ PCP caused chloracne in exposed workers and is readily absorbed through the skin, causing systemic toxicity and even death (Deichmann and Keplinger, 1981; Gasiewicz、1991); thus, a Skin notation is appropriate.	●			
88-12-0	N-ビニル-2-ピロリドン	【DFG】 ・ The lowest observed effect level (LOEL) which causes liver tumours is very low, and absorption through the skin after dermal exposure has been demonstrated by the occurrence of systemic effects. The calculations confirm the ready penetration of the substance through the skin. N-Vinyl-2-pyrrolidone is therefore designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts). ・From the physico-chemical data (log KOW1 0.37, determined, water solubility 52 g/l, calculated; SRC 2003), dermal absorption rates of 0.232 and 0.036 mg/cm2 and hour after exposure to a saturated aqueous solution can be calculated according to the models by Fiserova-Bergerova et al. (1990) and Guy und Potts (1993), respectively. Exposure of a 2000 cm2 area of skin (both hands and forearms) would therefore result in the absorption of 465 and 72 mg per hour, respectively.		▲		▲
88-72-2	２-ニトロトルエン	【ACGIH】 ・ A Skin notation is assigned based on the analogy of nitro-toluene to the ability of structurally similar aniline and nitrobenzene to induce cyanosis after dermal contact or topical application .	●			●
88-73-3	オルト-ニトロクロロベンゼン	【DFG】 ・ The result provides some evidence for a carcinogenic effect of o-chloronitrobenzene but requires confirmation because of the paucity of results. A MAK value cannot be established. o-Chloronitrobenzene is classified in Section III B of the List of MAK Values. For reasons of analogy o-chloronitrobenzene is designated with an "H". ・ Two early studies describe intoxications in workers employed in the separation of o-chloronitrobenzene and p-chloronitrobenzene; they are described in detail in the chapter on p-chloronitrobenzene (this volume) [3, 4]. In a comparative study of 187 cases of occupational cyanosis in the period between 1956 and 1966 which involved 13 aromatic nitro and amino compounds, o-chloronitrobenzene proved to have more severe cyanotic effects than aniline [5]. ・ o-Chloronitrobenzene, like p-chloronitrobenzene, is a powerful methaemoglobin producer in man and animals but in a chronic toxicity study in rats proved to be less effective than the p-isomer. Mutagenicity tests have yielded contradictory results but do provide evidence of a genotoxic potential which is greater than that of p -chloronitrobenzene.	▲			▲
88-89-1	ピクリン酸	【ACGIH】 ・ The Skin notation was deleted in 1990 since data available for review did not substantiate the ability of picric acid to penetrate the intact skin, and contribute to systemic toxicity. 【NIOSH OSHA PEL Project Documentation 1988】 ・ The symptoms of systemic poisoning following skin absorption include headache, vertigo, vomiting, nausea, diarrhea, and skin and conjunctival discoloration, as well as discoloration of urine and albuminuria; high-dose exposures caused destruction of erythrocytes and produced gastroenteritis, hemorrhagic nephritis, and acute hepatitis (Sunderman, Weidman, and Batson 1945/Ex. 1-383). 【DFG】 ・ After epicutaneous application, picric acid was detected in the blood. Whether intoxication is possible as a result of epicutaneous contact is unclear. As also phenol and other nitroaromatic substances are designated with an “H”, easy penetration of the skin should be expected also for picric acid, and designation with an “H” has therefore been retained.	■			▲
89-72-5	オルト-セカンダリ-ブチルフェノール	【ACGIH】 ・ Dermal absorption and resultant lethal dose 50 data warrent the Skin notation.		●		
90-04-0	o-アニシジン	【ACGIH】 ・ A Skin notation is also recommended, based on the reported dermal absorption and systemic toxicity in anisidine-exposed rodents.		●		
90-12-0	1 - メチルナフタレン	【ACGIH】 ・ A Skin notation was assigned based on lung toxicity observed in chronic dermal studies in mice and Log Kow values ranging from 3.7 to 3.9. To prevent lung toxicity following dermal exposure, a TLV ®Surface Limit (TLV ®- SL) of 3 mg/100 cm2 is recommended. This TLV ®- SL was derived using the lowest LOAEL observed (no NOAELs were determined) for lung effects in dermal studies of 29.7 mg/kg/day (Emi and Konishi, 1985). ・ Chronic skin painting with a mixture of the methylnaphthalenes (1.2% in acetone) also caused alveolar proteinosis. A dermal exposure to a mixture of 1- and 2-MN in acetone for 30 weeks (total dose was 7.14 g/kg body weight) in female mice caused the same effects as alveolar proteinosis, i.e., foamy cells, cholesterol crystals, and proteinaceous material rich with lipids in 100% of the mice.		●		●

91-08-7	2,6-トリレンジイソシアネート（別名：2,6-トルエンジイソシアネート)	【ACGIH】 ・ A Skin notation is also warranted because induction of respiratory hypersensitivity, a systemic response, occurs by this route.	●	●		
91-20-3	ナフタレン	【ACGIH】 ・ A Skin notation is recommended because powdered naphthalene has been shown to penetrate excised skin at a rapid rate that may result in moderate internal doses under extreme dermal exposure conditions (Frasch et al.. 2007; Walker et al., 1996). ・ Dermal LD50 values for mice and rats are 1 and 2.5 g/kg, respectively (U.S. NTP, 2000). ・ Dermal absorption of naphthalene powder has been measured, and the in vitro absorption rate is 7-30 µg/cm² per hour (Frasch et al., 2007). Using the U.S. EPA Interagency Testing Committee's method for determining skin absorption rates, it would take approximately 4 hours of coverage of both hands to absorb the amount that would be absorbed during an 8-hour inhalation of 5 ppm (Walker et al., 1996). ・ No histological effects on the lungs were found after 13 weeks of dermal exposure of rats to up to 1 g/kg for 6 hours per day 5 days a week (U.S. ATSDR, 2005). 【DFG】 ・ Naphthalene is designated with an “H” because of its ready penetration of the skin in vitro (see Toxicokinetics) and dermal absorption in vivo. ・ In male rats about 50 % of the dermal dose of radioactively labelled naphthalene (43 µg/13 cm2, dissolved in ethanol) was recovered within 12 hours in the urine (Turkall et al. 1994). Within 48 hours 70.3 % of the radioactivity was excreted with the urine, 3.7 % excreted with the faeces and 13.6 % exhaled. ・ A permeability constant [cm/hour] in acetone, acetone plus artificial sweat or lubricating oil of 5.12 × 10−3, 6.31 × 10−3 and 1.87 × 10−3, respectively, was determined in vitro for abdominal monkey skin (Sartorelli et al. 1998, 1999).		● ▲	● ▲	●
91-57-6	2-メチルナフタレン	【ACGIH】 ・ A Skin notation was assigned based on lung toxicity observed in chronic dermal studies in mice and Log Kow values ranging from 3.7 to 3.9. To prevent lung toxicity following dermal exposure, a TLV ®Surface Limit (TLV ®- SL) of 3 mg/100 cm2 is recommended. This TLV ®- SL was derived using the lowest LOAEL observed (no NOAELs were determined) for lung effects in dermal studies of 29.7 mg/kg/day (Emi and Konishi, 1985).		●		●
91-59-8	2-ナフチルアミン　（別名：β-ナフチルアミン）	【DFG】 ・ 2-Naphthylamine has been marked with "H" since 1966. In more recent studies, relevant penetration was demonstrated with diffusion cells after Franz on human skin (Lüersen et al. 2006; Wellner et al. 2008). No MAK value has been established for the genotoxic and carcinogenic 2-naphthylamine. Therefore, no safe exposure can be estimated, so that an increase in carcinogenic risk must be assumed even for small percutaneously ingested amounts. 2-Naphthylamine is therefore still marked with "H".			▲	
91-94-1	3,3'-ジクロロベンジジン	【ACGIH】 ・ Under some conditions, percutaneous absorption of other benzidines presents a greater hazard than inhalation of the airborne compound. Therefore, a Skin notation is assigned to DCB primarily by analogy to these similar substances that may be absorbed through the skin in amounts sufficient to induce systemic toxicity. ・ Despite the fact that Meigs et al.(5) showed that the skin is the principal portal of entry of benzidines, no acute, percutaneous toxicity tests have been performed in animals, except for an unpublished statement (4) that four of five rabbits died following application of 1 g/kg of base for 24 hours. It was considered likely that the hydrochloride salt could be absorbed percutaneously. ・ Because of benzidine's structural similarity to DCB, there is reason to suspect that occupational exposure to DCB may also represent an increased risk for human bladder carcinogenesis, despite negative but inadequate epidemiological data. Additional studies are needed to determine the clinical toxicity of DCB and its potential toxicity in the presence of other biphenyl amines. Under some conditions, percutaneous absorption of other benzidines presents a greater hazard than inhalation of airborne compound. Therefore, a Skin notation is assigned to DCB primarily by analogy to these similar substances that may be absorbed the skin in amounts sufficient to induce systemic toxicity. 【DFG】 ・ Because the substance can be absorbed through the skin in dangerous quantities, 3,3'-dichlorobenzidine must be designated with an "H". ・ 3,3'-Dichlorobenzidine is taken up mainly through the skin; dermal absorption is enhanced by increases in temperature and relative humidity. Studies of 3,3'-dichlorobenzidine, benzidine, dimethylbenzidine and dimethoxybenzidine production workers who were examined in the years between 1950 and 1953 revealed urine concentrations of benzidine derivatives (determined as the quinones and expressed as benzidine) between 0.57 and 1.48 mg/l in summer and between 0.14 and 0.43 mg/l in winter (average air concentration 0.018 mg/m3); the highest concentrations were found at the end of the shift.In control persons who were not exposed to benzidines at all or only occasionally, the urine concentrations ranged from less than 0.003 to 0.1 mg/l [1, 2]. ・ The fur was shaved from the skin of Fischer 344 rats and 24 hours later a 14C-3, 3'-dichlorobenzidine dose of 1 mg/kg in acetone was applied occlusively to the skin. 24 hours after treatment, 19.3 % of the applied radioactivity was found in the faeces, 8.4% in the urine, 5.7% in the intestine and 4.1% in the liver. The half-life of 3,3'-dichlorobenzidine on the skin was given as 24.1 hours [6]. The fur was shaved from the skin of Fischer 344 rats and 24 hours later a 14C-3, 3'-dichlorobenzidine dose of 1 mg/kg in acetone was applied occlusively to the skin. 24 hours after treatment, 19.3 % of the applied radioactivity was found in the faeces, 8.4% in the urine, 5.7% in the intestine and 4.1% in the liver. The half-life of 3,3'-dichlorobenzidine on the skin was given as 24.1 hours [6].	▲	▲		●
92-52-4	ビフェニル	【DFG】 ・ Based on the demonstrated dermal absorption in the study by Deichmann et al. 1947, biphenyl is labeled "H". ・ Dermal absorption following repeated epicutaneous application to rabbits was demonstrated qualitatively in the experiments of Deichmann et al. 1947 (see justification 1979). From calculations using the formulas of Fiserova-Bergerova et al. 1990 and Guy and Potts 1993, a one-hour epicutaneous exposure of 2000 cm2 (area of hands and forearms) to a saturated aqueous solution of biphenyl results in an uptake of 151 and 2.5 mg, respectively. ・ LD50 Rabbit dermal 2500 mg/kg Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984., p. V7 788 (1979) ・ Subchronic or Prechronic Exposure/ Repeated application of a 25% solution in olive oil to rabbit skin at 0.5 g/kg/day, 5 days/week, caused no local irritation, but these treatments did result in the death of one rabbit after 8 applications and weight loss in three others after 20 applications.		▲		▲

92-67-1	ビフェニル-4-イルアミン　（別名：4-アミノジフェニル、4-アミノビフェニル）	【ACGIH】 ・ A Skin notation is recommended as an additional precaution for undue exposure. Available data associate 4-aminodiphenyl with a high incidence of bladder cancer in humans and bladder and liver tumors in experimental animals. The compound appears to be one of the most potent known bladder carcinogens. A Skin notation is recommended as a further precaution. 【DFG 】 ・ To date, it has not been labeled "H," although good dermal penetration can be assumed (Henschler and Lehnert 1989). An animal study described below clearly demonstrates good dermal penetration and the occurrence of DNA adducts after epicutaneous exposure: female mice received 50 nmol of 4-aminobiphenyl applied epicutaneously twice a week for 21 weeks. At 21 weeks after the onset of exposure, maximum "relative adduct labeling" of 55, 82, and 58x109, respectively, were detected in liver, bladder, and skin with 32P postlabelling. 4-Aminobiphenyl is therefore labeled with ,,H" because of its demonstrated dermal accessibility.		▲		● ▲
92-84-2	フェノチアジン	【ACGIH】 ・ Dermal absorption with a contribution to systemic toxicity has been adequately demonstrated; thus, a Skin notation is considered appropriate.	●			
92-87-5	ベンジジン	【ACGIH】 ・ A Skin notation is recommended, based on the skin being a significant route of entry into the body leading to systemic toxicity, including cancer.	●			
92-93-3	4 - ニトロジフェニル	【ACGIH】 ・ Based on studies with rabbits that indicate that 4-aminodiphenyl can be absorbed through the skin in amountls sufficienit to cause systemic toxiciity, a Skin notation is assigned.		●		
93-76-5	2,4,5-トリクロロフェノキシ酢酸	【DFG】 ・ As 2,4,5-T is readily absorbed through the human skin the “H” designation has been retained. ・ 2,4,5-T is absorbed readily by man and animals both orally and dermally. In analogy to 2,4-dichlorophenoxyacetic acid (2,4-D, this volume) it can be assumed that the acid is formed from the salts and esters both in the stomach and in the skin, and is then rapidly absorbed. ・ With LD50 values of over 5000 mg/kg body weight, 2,4,5-T, the dimethylamine salt and the amyl ester, mixed butyl ester and 2-ethylhexyl ester were found to be of low toxicity after dermal application (DFG 1982). ・ Dermal LD50: 1535 mg/kg in rat. Fundamental and Applied Toxicology., 7(299), 1986 ・ The most probable route of exposure to 2,4,5-T would be inhalation and dermal exposure of workers involved in the manufacture, handling or application of 2,4,5-T, related ester compounds or certain tetradifon formulations which contain 2,4,5-T.	▲	▲		
94-75-7	2,4-ジクロロフェノキシ酢酸	【DFG】 ・ In the earlier MAK documentation the amine compounds and esters of 2,4-D were designated with an “H” due to their dermal absorbability and the observed systemic effects. Recent investigations indicate that the acid and the sodium salt are also absorbed; therefore all 2,4-D compounds are now designated with an “H”. ・ The good dermal absorption of the DMA salt and the ester of 2,4-D has already been described in the earlier MAK documentation (see Volume 4 of the present series). Dermal absorption has been shown to be dependent on the compound, the vehicle, the species and the site of application. In man and animals the proportion of a dermal dose which is absorbed usually ranges between 5 % and 20 % . For the DMA salt up to 60 % absorption has been described in man. ・ Recent studies also indicate that 2,4-D and its sodium salt are absorbed dermally to about the same extent as is the DMA salt. Harris and Solomon 1992 applied 10 mg 2,4-D (in acetone) or the 2,4-D DMA salt (in aqueous solution) to the skin of 5 volunteers and found absorption of 4.6 % and 1.8 % of the dose, respectively. In rats, after dermal application of 2.6 mg/kg body weight of a sodium salt herbicide and 1.9 mg/kg body weight of a DMA salt herbicide in aqueous solutions, absorption of 10 % and 15 % of the dose was found (Knopp and Schiller 1992). ・ Several cases of intoxication were attributed to cutaneous absorption of 2,4-D or commercially available derivatives. These cases are summarized in the earlier MAK documentation. Persons exposed to 2,4-D esters showed neurological symptoms such as flaccid paresis and disorders in the sensitivity to pain, pressure and temperature. Peripheral neuropathy was described after exposure to the 2,4-D DMA salt. Stiff muscles and muscle tremor occurred in one worker after exposure to a preparation containing 2,4-D. In the earlier MAK documentation, 3 cases are reported of persons who developed peripheral neuropathy and polyneuritic symptoms after the use of an undefined 2,4-D ester, probably as a result of percutaneous absorption of the liquid product.	▲	▲		
95-14-7	1,2,3-ベンゾトリアゾール	【DFG】 ・ Skin contact is expected to contribute significantly to systemic toxicity. Therefore, benzotriazole is designated with an “H”. Limited data show no sensitization. ・ Model calculations for dermal absorption give dermal intakes of 120-1340 mg for a saturated aqueous solution or 30-335 mg for 0.5% benzotriazole in a cooling lubricant preparation. The systemic NOAEL for rats in an OECD Test Guideline 421 study with daily oral administration is 12.5 mg/kg bw. For humans at the workplace, this dose corresponds to a concentration of 3.8 mg/m3 (see above) and, assuming 100% inhalation absorption and a respiratory volume of 10 m3, to a systemically tolerable amount of 38 mg. The calculated dermal uptake is considerably above this value for both saturated solutions and cooling lubricant preparations, so that benzotriazole is marked with "H".				▲
95-47-6	o−キシレン	【DFG】 ・ As described in Section 2, dermal exposure to liquid xylene can contribute considerably to the body burden and the toxic effects. Xylene is therefore designated with an “H”.As a result of a lack of data, xylene is at present not designated with an “S” (for sub-stances with sensitization potential). ・ In an acute toxicity study, male and female rabbits (2/sex/group, strain not reported) were given single dermal exposures on abraded skin to o-xylene at dose levels of 200 and 3,160 mg/kg. The animals were observed for 14 days following exposure. None of the animals died during the study.	▲	▲		▲
95-48-7	o-クレゾール	【ACGIH】 ・ A Skin notation is warranted because dermal LD50 values, along with evidence from accidental human exposure, show that systemic toxicity can resu lt from skin exposure (Larcan et al., 1974; Green, 1975).	●	●		

95-50-1	o-ジクロロベンゼン	【DFG】 ・ As a result of the systemic and even lethal effects observed without accompanying skin changes in animal experiments after dermal application of the substance, and because the log Pow is 3.4, designation with an “H” has been retained. ・ Quantitative studies of skin penetration after dermal application of 1,2-dichlorobenzene are not available. The models of Fiserova-Bergerova et al. 1990 and Guy and Potts 1993 predict absorption of 592 and 15 mg, respectively, after exposure of the hands and forearms (2000 cm2) to a saturated aqueous solution of 1,2-dichlorobenzene for one hour. ・ In a study already described in the documentation from 1988, rats showed signs of severe generalized toxicity after non-occlusive dermal application of the substance to the shaved abdomen twice a day for 5 days. The same treatment over 9 days was lethal for one animal; gross pathological examination revealed a pale spotted liver and alterations in the kidneys. The treated area of skin, however, was not found to have any changes. The authors attributed the systemic effects to absorption of the substance through the skin; they tried to minimize inhalation exposure as a result of the non-occlusive application by keeping the animals in the open (Riedel 1941). Also the high log Pow of 3.4 suggests absorption through the skin.		▲		▲
95-51-2	o-クロロアニリン	【DFG】 ・ The dermal toxicity of o-chloroaniline demonstrated in animal studies requires the designation "H". ・ The LD50 value for o-chloroaniline after intragastric administration to mice was 256 mg/kg, after dermal application to cats 222 mg/kg . ・ Cyanosis, dilation of the pupils, increased respiration rate and unsteady gait were seen in cats after subcutaneous injection or dermal application of o-chloroaniline in an early study. The animals did not survive a subcutaneous dose of 310 mg/kg body weight. Applied dermally, a dose of 3–6 g o-chloroaniline was lethal. Autopsy revealed discoloured brown lungs; methaemoglobin (metHb) was not always detectable. ・ After administration of lethal doses of o-chloroaniline to mice by the intragastric route or to cats by dermal application, the animals died within 3 days with blood metHb levels of 60 to 80 %. o-Chloroaniline proved to be more toxic than aniline. ・ There are no reports available of intoxications with o-chloroaniline. In a study of 187 cases of occupational cyanosis in the period between 1956 and 1966 the most severe cyanosis-inducing effects among 13 amino and nitro compounds were ascribed to the three chloroanilines.	▲	▲		
95-53-4	o-トルイジン/トルイジン塩類	【ACGIH】 ・ Based on the reports of percutaneous absorption, the Skin notation is considered appropriate. ・ The LD50 for rabbits by skin application was 3.25 ml/kg (3250 mg/kg) body weight. A single intravenous injection of 27 mg/kg. ・ Clinical signs of intoxication with o-toluidine in humans have included methemoglobinemia, hematuria, marked renal and bladder irritation, and physiological and psychological disturbances. o-Toluidine has been absorbed via the respiratory tract and skin. (3,52) Exposure at 40 ppm o-toluidine in air for 60 minutes produced severe intoxication. (53) ・ The U.S. EPA (66) calculated a permeability coefficient for o-toluidine through human skin of 0.0037 cm/hour.	●	●		●
95-64-7	3, 4-ジメチルアニリン	【ACGIH】 ・ Based on the central nervous system effects and methemoglobin formation seen in cats that received repeated cutaneous applications of 2,4-xylidine, the Skin notation is warranted.		●		
95-68-1	2,4-ジメチルアニリン	【DFG】 ・ Because of the symptoms of intoxication which have been described, it must be assumed that the isomers are absorbed not only through the respiratory tract but also through the skin. Therefore the xylidines are designated with an “H”. In rabbits treated dermally with technical grade 2,4-xylidine (composition unknown) in doses of 3300 mg/kg body weight, lethal cyanosis developed without local skin reactions (Treon et al. 1949). ・ The dermal LD50 for a mixture of 2,4-xylidine with other isomers (40–60 % 2,4-xylidine, 10–20 % 2,5-xylidine and other isomers) was 1500 mg/kg body weight for the rabbit, 2000 for the rat and 1670 mg/kg body weight for the mouse. The lowest dose of the mixture of isomers producing toxic effects when 5 % of the body surface area was exposed was 500 mg/kg body weight for all three species (Egorov et al. 1976).		▲		▲
95-69-2	4 - クロロ - オルト - トルイジン	【DFG】 ・ Because the substance can be absorbed through the skin in dangerous quantities, 4-chloro-o-toluidine must be designated with an "H". ・ After dermal application of 4 g 4-chloro-o-toluidine (in 4 g fat) to the shaved skin of a cat, daily for 5 days, there were liver changes (ochre discoloration, fatty degeneration in the acinocentral regions), multiple haemorrhage on the bladder mucosa and a plum sized dark brown coagulum in the bladder [28]. ・ In 1982, cases of bleeding in the bladder as a result of 4-chloro-o-toluidine exposure were reported again [14, 15]. There were 22 cases of intoxication which developed in workers in 4-chloro-o-toluidine production after accidental exposure of the skin or by inhalation; 15 of the cases occurred during the years 1952 to 1970. The symptoms included haematuria, dysuria and pollakiuria and sometimes abdominal pain. The haematuria appeared after a latent period of several hours to two days after the exposure (this delay in the appearance of haematuria was also observed in early studies [11]). In 20 of the 22 cases, cystoscopy revealed haemorrhagic cystitis which can thus be considered to be the characteristic symptom of this intoxication. Cyanosis, sometimes confirmed by detection of metHb, developed in more than half of the cases; in about one quarter, reduced haemoglobin levels were demonstrated [15].	▲	▲		
95-76-1	3, 4-ジクロロアニリン	【DFG】 ・ There are no studies available of the dermal penetration of 3,4-dichloroaniline. The dermal LD50 in the cat was below 1000 mg/kg body weight. Dermal application of 3,4-dichloroaniline doses of 60 mg/kg body weight for 14 days led in rabbits to systemic effects. 3,4-Dichloroaniline is therefore designated with an „H”.		▲		

95-78-3	2,5-ジメチルアニリン	【DFG】 ・ Because of the symptoms of intoxication which have been described, it must be assumed that the isomers are absorbed not only through the respiratory tract but also through the skin. Therefore the xylidines are designated with an “H”. ・ The dermal LD50 for a mixture of 2,4-xylidine with other isomers (40–60 % 2,4-xylidine, 10–20 % 2,5-xylidine and other isomers) was 1500 mg/kg body weight for the rabbit, 2000 for the rat and 1670 mg/kg body weight for the mouse. The lowest dose of the mixture of isomers producing toxic effects when 5 % of the body surface area was exposed was 500 mg/kg body weight for all three species (Egorov et al. 1976).		▲		
95-80-7	2,4-トルエンジアミン (別名: 2,4-ジアミノトルエン)	【DFG】 ・ The substance is a proven genotoxic carcinogen, for which no safe exposure level can be assessed. As a result of the skin absorption properties that were demonstrated in humans, it must be assumed that the carcinogenic risk is increased by dermal exposure. Toluene-2,4-diamine is designated with “H”.	▲			▲
96-05-9	アリル＝メタクリレート	【ACGIH】 ・ A Skin notation is recommended based on a dermal LD50 of 500 mg/kg (Lewis, 1996) and unexplained deaths of white rabbits dermally treated at 50 mg/ kg/day in a 28-day subchronic dermal toxicity study (Siddiqui et al., 1982).		●		
96-09-3	フェニルオキシラン（別名：スチレンオキシド）	【ACGIH】 ・ A Skin notation is recommended because of the dermal LD50 of 930 mg/kg reported in rats and rabbits (Smyth et al., 1954) and analogy to ethylene oxide.		●		●
96-12-8	1,2 - ジブロモ - 3 - クロロプロパン	【DFG】 ・ Because of the low dermal LD50 (500 mg/kg bw, 10% diluted in propylene glycol), where an irritant effect does not seem to play a role, 1,2-dibromo-3-chloropropane is marked "H".		▲		
96-18-4	1,2,3-トリクロロプロパン	【DFG】 ・ The symptoms of intoxication observed after acute oral, intraperitoneal and dermal administration of 1,2,3-trichloropropane included dyspnoea, lethargy, ataxia, ptosis, polyuria, discoloration of the urine, cyanosis, diarrhoea, piloerection, lacrimation, salivation, discharge from the eyes and nose, dilation or contraction of the pupils, clouding of the cornea and liver and kidney damage (Albert 1982, Bio/dynamics Inc. 1985a, 1985b, Clark 1977, Låg et al. 1991). The oral and dermal LD50 values ranged between 99 and 2460 mg/kg body weight (Table 2).		▲		
96-24-2	3-クロロ-1, 2-プロパンジオール	【DFG】 ・ No experimental data are available on dermal uptake or toxicity following dermal application of 3-chloro-1,2-propanediol. The dermal uptake levels resulting from model calculations (5, 9, and 27 mg/kg bw) are well above the systemic NOAEL for spermatotoxicity of 0.05 mg/kg bw per day. Therefore, 3-chloro-1,2-propanediol is marked with "H".				▲
96-29-7	ブタン-2-オン=オキシム	【DFG】 ・ The data for the acute toxicity of butanone oxime in rabbits indicate percutaneous absorption. The substance is therefore designated with an „H”.		▲		
96-33-3	アクリル酸メチル	【ACGIH】 ・ The Skin notation is also recommended (despite its acute irritant properties) due to significant, acute percutaneous absorption of the compound found in animal studies. ・ Percutaneous absorption through rabbit skin resulted in an LD50 of 1.3 ml/kg		●		
96-34-4	クロロ酢酸メチル	【DFG】 ・ Because there have been lethal intoxications after dermal contact with chloroacetic acid (Christofano et al. 1970; Kusch et al. 1990; Millischer et al. 1988), chloroacetic acid methyl ester has been given the “H” designation.		▲		
96-48-0	ガンマ-ブチロラクトン	【DFG】 ・ The intake level calculated from an in vitro human skin test for a one-hour dermal exposure of 2000 cm2 skin is 2.9 mg/kg bw, which is about one-fifth of the systemic LOAEL of 15 mg/kg bw at which anesthesia occurs in humans. Since no NOAEL is known for the anesthetic effect, and preanesthetic effects cannot be excluded even at 2.9 mg/kg bw, γ-butyrolactone is marked "H".			▲	
97-56-3	２－メチル－４－（２－トリルアゾ）アニリン (別名：２－アミノアゾトルエン)	【DFG】 ・ No data for absorption through the skin are available. Since 2-aminoazotoluene led to liver tumours in several studies with epicutaneous application after only a few months and the substance is a highly potent genotoxic carcinogen, an additional carcinogenic risk is assumed even if only small amounts are absorbed through the skin, and the substance is designated with an “H”.		▲		
98-00-0	フルフリルアルコール	【ACGIH】 ・ A Skin notation is supported by the dose-dependent mortality observed when neat furfuryl alcohol (31 mg/kg) was applied topically to rabbits (Woods and Seevers, 1954 as cited in U.S. NIOSH, 1979).		●		
98-01-1	フルフラール	【ACGIH】 ・ A Skin notation is supported by the dermal LD50 of 192 mg/kg for rats (Joseph, 2003).		●		
98-07-7	ベンジリジン=トリクロリド	【ACGIH】 ・ A Skin notation is warnantred, based on skin-paiting experiments that produced lung and thymic tumors in mice.		●		

98-54-4	4 ーターシャリーブチルフェノール	【DFG】 ・ Because very large amounts of p-tert-butyl phenol can be absorbed through the skin, designation with an “H” is necessary. Avoidance of skin contact is of utmost importance for occupational safety. ・ In addition to disturbances in the formation of pigment in the skin, p-tert-butyl phenol can induce systemic damage in the liver and thyroid gland. Degenerative destruction of hormone-forming thyroid cells, which can be detected by the formation of auto-antibodies, results in diffuse goitre. ・ Cases of contact dermatitis with subsequent skin depigmentation are also known (see Table 1) (Calnan and Cooke 1974, Malten 1975, Wozniak and Hamm 1977) in which the leukoderma was not found in the area affected by the eczema but was systemic. This indicates percutaneous absorption and systemic distribution of p-tert-butyl phenol (Wozniak and Hamm 1977). ・ 23 of 52 workers with different functions in the factory (2 chemists, 2 machine operators, 3 labourers and cleaning staff, 5 mechanics, 11 technicians/skilled personnel) had the characteristic vitiligo-like skin changes, in some cases as little as one year after the beginning of production; the changes appeared first on the exposed parts of the body such as hands and feet, head and neck, but then also spread to non-exposed areas such as back, breast, armpits, abdomen, genital region and anal groove. The affected persons complained of headaches, drowsiness, profuse sweating, in particular an increase in sweating on the palms of the hands and soles of the feet, hoarseness, throat irritation, thirst, weight gain, loss of libido and other neurological and otolaryngological disorders. ・ Ikeda et al. 1978 also came to this conclusion and suggested a p-tert-butyl phenol concentration of 2 µ g/ml urine for biological monitoring to exclude leukodermogenic effects (2 µ g p-tert-butyl phenol per ml urine was also the detection limit). Because of the danger of skin penetration they advised the monitoring of exposed persons by urinalysis.	▲	▲		
98-73-7	p-tert-ブチル安息香酸	【ACGIH】 ・ A Skin notation is recommended because male and female Fischer 344 rats exposed for 5 days/ week to aqueous solutions of 0.0, 17.5, 35.0, 70.0, or 140.0 mg/kg bw TBBA on shaved skin over 13 weeks resulted in dose-related increases in relative hepatic and renal weights and decreased testis weight in male rats.		●		
98-82-8	クメン	【DFG】 ・ No data from studies of the absorption of isopropyl benzene through the skin are available. For this reason, the absorption of the substance through the skin was estimated using mathematical models (Wilschut et al. 1995; Guy and Potts 1993; Fiserova-Bergerova et al. 1990). Model calculations yielded flux values of up to 0.42 mg/cm2 and hour. As the results for other aromatic alkyls obtained using the model of Fiserova-Bergerova et al. (1990) coincide better with the in vivo data available for these substances, this model is used to assess the dermal absorption of this group of substances. Assuming a penetration rate of 0.42 mg/cm2 and hour, the dermal absorption of about 830 mg has been estimated after exposure of both hands and forearms (2000 cm2) to a saturated aqueous solution of isopropyl benzene for one hour. Assuming 60% absorption by inhalation, as is the case for ethylbenzene (supplement “Ethylbenzene” 2012), an inhalation absorption of 300 mg is estimated after 8-hour exposure at the level of the MAK value of 10 ml/m3 (respiratory volume of 10 m3). Thus, the contribution of dermal absorption to systemic exposure is toxicologically relevant and isopropyl benzene remains designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).				▲
98-87-3	ベンジリデン=ジクロリド	【DFG】 ・ Model calculations indicate a significant dermal absorption. α,α-Dichlorotoluene is a proven genotoxic carcinogen for which, however, no safe exposure can be estimated. Therefore, even small amounts absorbed percutaneously must be assumed to increase the carcinogenic risk. α,α-Dichlorotoluene is therefore marked with "H".				▲
98-95-3	ニトロベンゼン	【ACGIH】 ・ Human skin absorption was reported by Piotrowski, but the U.S. Agency for Toxic Substances and Disease Registry concluded that there is no clear evidence that dermal exposure to nitrobenzene at commonly encountered levels can cause methemoglobinemia in humans. Accordingly, a TLV-TWA of 1 ppm is recommended for nitrobenz ene. The Skin notation is based on the reports of acute and chronic systemic toxicity of topical nitrobenzene and on the estimate that, at 1 ppm nitrobenzene in air, 8 mg are absorbed through the skin over an 8-hour workday and 20% of that is eliminated in the urine. 【DFG】After the exposure of volunteers at rest to nitrobenzene in exposure chambers, two thirds of the total uptake was absorbed from the gas phase via the lungs, and one third through the skin (documentation “Nitrobenzene” 2003). Therefore, the internal exposure to nitrobenzene via absorption through the skin may be increased by more than 25%, so that the designation of nitrobenzene with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts) has been retained. ・ Nitrobenzene is taken up through the skin. When nitrobenzene (dose not specified) was applied one or three times to about one tenth of the surface of the unshaved or shaved skin of mice, the animals died within 2 to 3 days as a result of reduction of the respiration rate to zero. The main symptoms of intoxication were cyanosis, restlessness, narcosis. Histological examination revealed necrosis in the liver, and swelling of the glomerulus and tubule epithelium in the kidneys. No changes were found in the spleen, lungs or testes. When nitrobenzene was applied in doses of 0.25 ml per animal to the shaved skin of rats, one dog, guinea pigs, rabbits or cats (about 1.0, 0.025, 1.0, 0.1 or 0.075 ml/kg body weight, respectively) or administered by subcutaneous injection, the treatment caused dyspnoea and weakness within 6 to 12 hours. Cyanosis was seen in the cats, rats, rabbits and the dog. All animals died within one day (BUA 1991). ・ In experimental animals, nitrobenzene is acutely toxic. For the rat the oral LD50 is 640 mg/kg body weight and the dermal LD50 2100 mg/kg body weight. High doses cause neurological symptoms. In rats exposed by inhalation for 90 days to nitrobenzene concentrations of 5 ml/m3 or more, dose-dependent methaemoglobin formation was seen.	● ▲	● ▲		
99-08-1	3 ーニトロトルエン	【ACGIH】 ・ A Skin notation is assigned based on the analogy of nitro-toluene to the ability of structurally similar aniline and nitrobenzene to induce cyanosis after dermal contact or topical application .	●			●
99-54-7	1,2-ジクロロ-4-ニトロベンゼン	【DFG】 ・ An epidemiological study in humans suggests dermal uptake of the substance, but this is not substantiated due to concurrent inhalation exposure. ・ The dermal LD50 in the cat, which is more suitable as an experimental model than the rat because of its higher sensitivity to methemoglobin formers, was less than 1000 mg/kg bw. Therefore, 1,2-dichloro-4-nitrobenzene is labeled "H." This is also consistent with the labeling of the structurally related chloronitroaromatics 1-chloro-2-nitrobenzene, 1-chloro-3-nitrobenzene, and 1-chloro-4-nitrobenzene with ", which has already been done.	▲	▲		▲

99-65-0	mージニトロベンゼン	【ACGIH】 ・ A Skin notation is assigned, based on the ready absorption of dinitrobenzene through the skin and its established contribution to systemic toxicity. Ready absorption of DNB　through the skin is a well-emphasized factor in the toxicity and hazard of this substance. (3.5)	●			
99-99-0	4ーニトロトルエン	【ACGIH】 ・ A Skin notation is assigned based on the analogy of nitro-toluene to the ability of structurally similar aniline and nitrobenzene to induce cyanosis after dermal contact or topical application . ・ Although no quantitative data on nitrotoluene percutaneous absorption were located, the Skin notation appears warranted by structural analogy to the well-known ability of aniline and nitrobenzene to induce cyanosis after skin contact.				●
100-00-5	パラ-ニトロクロロベンゼン	【ACGIH】 ・ In humans, dermal absorption of PNCB contributed to the development of methemoglobinemia, thus, a Skin notation is assigned. ・ The dermal LD50 in rabbits was greater than 3040 mg/kg. While the chemical did not produce irritation when applied to the skin or eyes of rabbits, (2) it was absorbed through the skin producing methemoglobinemia. Heinz bodies (granules containing oxidized hemoglobin) were formed, and clinical symptoms (e.g., anemia, hematuria, and hemoglobinuria) were also noted. 【DFG】 ・ Because of the possibility of intoxication as a result of absorption of the substance through the skin, p-chloronitrobenzene is designated with an “H”. ・ Three to four days exposure of workers to p-chloronitrobenzene in an English factory resulted in four cases of intoxication. In these four workers, the skin was discoloured grey, particularly the lips, conjunctiva and finger nails appeared cyanotic and the pulse was almost imperceptible. They also suffered from severe pains in the head and neck and from nausea and vomiting. Three of the affected persons collapsed; their haemoglobin levels were reduced for several days [4]. ・ In a comparative study of 187 cases of occupational cyanosis in the period between 1956 and 1966, cases which involved 13 aromatic nitro and amino compounds, p-chloronitrobenzene proved to have more severe cyanotic effects than aniline [5]. ・ LD50 values for dermal exposure: rat (female), 16,000 mg/kg and rabbit (n.s.) 3040 mg/kg. ・ After dermal application of various doses (< 16 g/kg, no other details) the rats lost weight for some time and had not regained their initial weights at the end of the 2-week post-exposure observation period [11]. ・ The maximum metHb levels in individual rats after intraperitoneal (55–1400 mg/ kg), intragastric (120–2100 mg/kg) and dermal (up to 16000 mg/kg) administration were between 10 and 70%. The proportion of cells with Heinz bodies 24 hours after dermal application of p-chloronitrobenzene was 10–30%, after intraperitoneal and intragastric administration, 40–60%. ・ Parenchymatous degeneration was also seen in the kidneys; it was most severe after dermal treatment and accompanied by necrosis of single epithelial cells [11].	● ▲	● ▲		
100-01-6	p-ニトロアニリン	【ACGIH】 ・ A Skin notation is designated based on the systemic toxicity elicited from absorption of p-nitroaniline through skin contact. ・ Human Studies p-Nitroaniline is a potent methemoglobin inducing agent and given sufficiently high or prolonged exposures, hemolysis can occur. Prolonged exposure may also result in liver damage. It is readily absorbed through the skin.(1) 【DFG】 ・ A large number of intoxication cases are described, in which methaemoglobinaemia occurred after ingestion as well as after absorption of 4-nitroaniline through the skin. Headache, dizziness, breathing difficulties, generalized muscle weakness, sleepiness and cyanosis are described as symptoms (BUA 1987) ・ 4-Nitroaniline is readily absorbed orally, dermally and by inhalation. Twenty-four hours after application of 4-nitroaniline in acetone at 4 µg/cm2 to isolated human skin in vitro or to the shaved abdominal skin of monkeys in vivo, 34.5% was absorbed in vitro and 100% in vivo – taking the evaporated amount into account. Maximum absorption was within the first two hours in each case (Bronaugh and Maibach 1985).	● ▲	▲	▲	
100-25-4	pージニトロベンゼン	【ACGIH】 ・ A Skin notation is assigned, based on the ready absorption of dinitrobenzene through the skin and its established contribution to systemic toxicity. ・ Ready absorption of DNB through the skin is a well-emphasized factor in the toxicity and hazard of this substance. (3,5) Unfortunately, no reference to the degree of exposure that produced these symptoms was found in the historical reviews. 【DFG】 ・ Because of the danger of uptake of toxic amounts of the substances through the skin the dinitrobenzenes are designated with an H. ・ Therefore the gloves which had been worn were examined and it was shown that m-DNB had accumulated on the damp inner surface and so could be absorbed through the skin It was concluded that the workers had been poisoned by skin absorption of m-DNB. ・ Studies of the penetration of animal skin by DNB are only known in older literature and do not meet modern requirements (see Table 3). In general the DNB (probably technical!) applied is not specified in detail and the description of procedures and animals are incomplete. Nonetheless the studies demonstrate clearly that DNB readily penetrates intact skin and can cause systemic toxicity and death. No skin irritation was observed.	● ▲	● ▲		
100-37-8	2-（ジエチルアミノ）エタノール	【ACGIH】 ・ By analogy with the other ethanolamines, and by applying the dermal LD50 data reported for rabbits, a Skin notation is recommended. 【DFG】 ・ On the basis of the physico-chemical properties of a saturated aqueous 2-diethylaminoethanol solution, a rate of penetration of human skin of 3.44 mg/cm2 and hour was estimated and thus that the body burden resulting from exposure for 8 hours to 10 ml/m3 can be increased at least three-fold by additional dermal absorption (Fiserova-Bergerova et al. 1990). ・ With dermal application the LD50 was 1260 mg/kg body weight for rabbits and 885 mg/kg body weight for guinea pigs. Application-related skin damage was not mentioned (ACGIH 1996, ECB 1995, Torén 1994).		● ▲		● ▲

100-41-4	エチルベンゼン	【DFG】 ・ As animal studies show, absorption of the substance through the skin must be expected after skin contact with ethylbenzene. Also, the data available for the homologous substance toluene suggests that ethylbenzene is likely to be absorbed. Taking the flux values of 2.2 and 2.8 mg/cm2 and hour determined in animal studies as the basis, the amount absorbed after contact with the substance for one hour of both hands and forearms (skin area 2000 cm2) would be up to 5.6 g ethylbenzene, corresponding to 80 mg/kg body weight. ・ For the homologous compound toluene, the animal studies used to calculate the amount of ethylbenzene absorbed yielded flux values which are about six times higher than the penetration rates from corresponding studies in humans. Assuming a comparable overestimation of the penetration for ethylbenzene in animal studies, absorption would be reduced by a factor of 6 to produce 13 mg/kg body weight. ・ As exposure at the level of the MAK value for 8 hours (respiratory volume 10 m3, 6% absorption) yields an absorbed amount of 8 mg/kg body weight, dermal absorption of ethylbenzene must be assumed to make a relevant contribution to systemic toxicity, even taking into account the possible overestimation of dermal absorption as a result of the data taken from animal studies. The designation of ethylbenzene with an “H” has therefore been retained.		▲		▲
100-42-5	スチレン	【産衛】 職業的にスチレンを取り扱う労働者の主たる侵入経路 は蒸気の吸入に伴う経気道侵入であって曝露実験によれ ば65~93%，が吸収される.経皮からの吸収は1.9~5 %と報告されている.スチレンの物理化学的特性は皮膚からの吸収も重要であることを示している. 予想浸透率は 0.52mg/cm²/h (log = 2.95),液体もしくは濃縮溶液の皮膚接触がスチレンの生物学的レベルを上げるだろうと予測された.しかし, Sedivec et al39) は肺からの吸収と比較して皮膚からの吸収はほんの僅かであると報告した. この見解は Berode et al.40) によって追試され、9人の男性ボランティアの一方の手に液体スチレンを10分から30分間浸漬させ,0.5~1μg/cm²/min という吸収率を算出した.このようにスチレン蒸気の経皮吸収については,体表面での濃縮が起こらない限り, 吸入曝露単独ほど有意に生物学的レベルが増加しないと思われる. ACGIH TLV もドイツ MAKもスチレンの皮膚マークに対する表記はない。	★			★
100-51-6	ベンジルアルコール	【DFG】 ・ Absorption through the skin. From the available in vitro studies of the penetration of benzyl alcohol through the human skin, flux values of 29 to 275 µg/cm2 and hour were obtained when using physiological receptor media. In vivo, a considerably lower flux of 0.1 µg/cm2 and hour was found in monkeys, in this case, however, only a very small absolute amount of substance was applied (4 µg). Assuming the worst case, with a maximum flux of 275 µg/cm2 and hour, the amount dermally absorbed (one-hour exposure of both hands and forearms with a penetration area of about 2000 cm2) would be 550 mg. The dermal uptake of benzyl alcohol estimated from this is more than 25% of the tolerable dose; the possible contribution of dermal absorption to systemic toxicity is therefore not considered to be negligible. Benzyl alcohol is therefore designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).		▲	▲	▲
100-61-8	N-メチルアニリン	【ACGIH】 ・ N-Methylaniline is readily absorbed through the skin in amounts that can contribute substantially to systemic poisoning; therefore, a Skin notation is appropriate. ・ N-Methyl-aniline also readily caused poisoning by percutaneous absorption. The application of 2~3 g/kg body weight upon the intact skin of a rabbit for 1 hour or more always produced death		●		
100-63-0	フェニルヒドラジン	【ACGIH】 ・ Hemolytic anemia as a result of occupational exposure by both dermal and inhalation routes is also considered a potential toxic effect. ・ The observed significant reduction in body weight of rodents following topical application of phenylhydrazine warrants designation of the Skin notation.	●	●		
100-74-3	N - エチルモルホリン	【ACGIH】 ・ A Skin notation is assigned by analogy with morpholine, which is reported to produce systemic toxicity in animals and humans following dermal applications (see TLV Documentation for Morpholine). 【NIOSH OSHA PEL Project Documentation 1988】 ・ N-ethylmorpholine is also readily absorbed through the skin (Smyth, Carpenter, Weil, and Pozzani 1954/Ex. 1-440).	■	■		●
100-75-4	N-ニトロソピペリジン	【DFG】 ・ N-nitrosopiperidine is genotoxic (Andersson et al. 2003).There are no studies on the percutaneous absorption of N-nitrosopiperidine, neither in animals nor in humans.Based on experimentally determined physicochemical data (water solubility 77 g/l, log KOW 0.36; SRC 2004), the dermal flux is 0.32 mg/cm2 and hour using the model of Fiserova-Bergerova et al. 1990 and 0.05 mg/cm2 hour using the model of Guy and Potts 1993. This would correspond to a total intake of 641 mg and 101 mg, respectively, for a one-hour exposure of both hands and forearms (approximately 2000 cm2). ・ No quantitative data on the percutaneous uptake of N-nitrosopiperidine can be found in the literature. ・ In analogy to other nitroso compounds (N-nitrosodiethylamine, N-nitrosodimethylamine and N-nitrosomorpholine; see corresponding justifications 2004), the substance must be evaluated as skin-resorptive. The calculation of dermal absorption also suggests this. The substance is a proven genotoxic carcinogen for which, however, no safe exposure can be estimated. Therefore, even small amounts absorbed percutaneously must be assumed to increase the carcinogenic risk. N-nitrosopiperidine is therefore marked with "H".				▲
101-14-4	3,3'-ジクロロ-4,4'-ジアミノジフェニルメタン	【ACGIH】 ・ In humans, skin absorption from direct contact is concluded to be the major source of absorption.<92·97·98>Evidence that humans have been exposed is provided by analyzing urine for MBOCA (see BEi® Documentation for 4,4'-Methylene bis(2-chloroaniline).	●			

101-54-2	N-フェニル-1,4-ベンゼンジアミン	【DFG】 ・ The detection of 4-aminodiphenylamine in the urine of a worker after accidental skin contact, as well as results from animal and in vitro studies, indicate systemic availability of 4-aminodiphenylamine after dermal exposure. Model calculations provide uptake levels of up to 161.4 mg (2.31 mg/kg bw) for a one-hour exposure of both hands and forearms to a saturated aqueous solution of 4-aminodiphenylamine. ・ Assuming the NAEL at 20 mg/kg bw for the rat and taking into account the toxicokinetic differences between the rat and humans (1:4), the corresponding dose for humans would be 5 mg/kg bw. Thus, about half of the systemic NAEL would be exhausted by the calculated dermal intake. Since 4-aminodiphenylamine also has a structural analogy to other monocyclic aromatic amines for which genotoxic and carcinogenic potential is generally suspected and which are also marked with "H", 4-aminodiphenylamine is also marked with "H".	▲	▲		▲
101-68-8	メチレンビス(4,1-フェニレン)=ジイソシアネート (別名；4'4-MDI)	【DFG】 ・ The available studies indicate that, after dermal exposure, MDI and PMDI mainly react with molecular components of the skin, and thus only very small quantities are absorbed systemically in unchanged form. In humans, intensive skin contact with MDI can, however, play a role in the induction of specific hyperreactivity of the airways. As technical-grade PMDI contains a considerable amount of monomeric MDI, similar effects are to be assumed. As the prevention of respiratory sensitization was one of the decisive criteria for establishing the MAK value, and this critical effect can also be caused by skin contact, both MDI and PMDI are designated with an “H” (for substances which can be absorbed through the skin).	▲			
101-77-9	4,4'-メチレンジアニリン	【ACGIH】 ・ Dermal contact with MDA, with subsequent percutaneous absorption, has been the primary route of occupational exposure; this contribution ta systemic toxicity serves as the basis for Skin notation. From the McGill and Moto study, percutaneous absorption was clearly a major route of MDA exposure for the mill helpers who experienced MDA poisonililg. ・ Hepatic degeneration was produced in rabbits following oral or dermal treatment with floor-pan sweepings containing MDA. These data suggest that MDA can be absorbed through the skin of rabbits.	●	●		
101-83-7	ジシクロヘキシルアミン	【DFG】 ・ The compound is corrosive, but in the dermal LD50 tests, the documentation (Younger Laboratories 1977) shows no evidence of corrosivity as a cause of death. Only systemic reactions and effects are described in the list of intoxication signs and autopsy results. Therefore, dicyclohexylamine remains marked with "H".		▲		
101-90-6	1,3-ビス[（2,3-エポキシプロピル）オキシ]ベンゼン	【DFG】 ・ The diglycidyl resorcinol ether is sensitizing in humans. This proves that the substance can be absorbed through the skin.By analogy, we can refer to phenylglycidyl ether, which is also classified in category 2 for carcinogenic substances, and is marked with both "Sh" and "H". The substance is a proven genotoxic carcinogen for which no safe exposure can be estimated. Therefore, even small amounts absorbed percutaneously must be expected to increase the carcinogenic risk. Diglycidyl resorcinol ether is therefore marked with "H".				▲
102-81-8	2-(ジ-n-ブチルアミノ)エタノール	【ACGIH】 ・ The Skin notation is recommended because the dermal LD 50 in rabbits was reported at 1.44g/kg.		●		
103-71-9	フェニルイソシアネート	【ACGIH】 ・ The acute toxicity following dermal application is low with an LD50 of 7130 mg/kg in rabbits (Engel and Hansen, 1993).		●		
104-51-8	ノルマル−ブチルベンゼン	【DFG】 ・ No studies are available on dermal absorption. For a saturated aqueous solution, the models of Fiserova-Bergerova et al. 1990, Guy and Potts 1993, and Wilschut et al. 1995 calculate fluxes of 337; 4.2 and 1.2 µg/cm2 and hour, respectively. Assuming a one-hour exposure of 2000 cm2 skin surface, this would correspond to uptake levels of 674; 8.4 and 2.4 mg, respectively. ・ Thus, the dermal uptake calculated with the Fiserova-Bergerova model is more than 25% of the systemically tolerable amount, and n-butylbenzene is marked "H". ・ According to skin absorption models, percutaneous absorption can contribute significantly to systemic toxicity and n-butylbenzene is designated with an “H” notation.				▲
104-94-9	p-アニシジン	【ACGIH】 ・ A Skin notation is also recommended, based on the reported dermal absorption and systemic toxicity in anisidine-exposed rodents.		●		
106-42-3	p-キシレン	【DFG】 ・ As described in Section 2, dermal exposure to liquid xylene can contribute consider-ably to the body burden and the toxic effects. Xylene is therefore designated with an “H”.As a result of a lack of data, xylene is at present not designated with an “S” (for substances with sensitization potential).	▲	▲		▲
106-44-5	p-クレゾール	【ACGIH】 ・ A Skin notation is warranted because dermal LD50 values, along with evidence from accidental human exposure, show that systemic toxicity can resu lt from skin exposure (Larcan et al., 1974; Green, 1975).	●	●		
106-46-7	p-ジクロロベンゼン	【DFG】 ・ The isomeric substance 1,2-dichlorobenzene is designated with an “H” (see documentation from 1988 and 2001 in Volume 1 of the present series and in the present volume); 1,4-dichlorobenzene and 1,2-dichlorobenzene have similar physical chemical properties and therefore similar skin penetration; for reasons of analogy 1,4-dichlorobenzene is also designated with an “H”. ・ There are no data for skin penetration of dermally applied 1,4-dichlorobenzene. The models of Fiserova-Bergerova et al. 1990 and Guy and Potts 1993 yield calculated absorbed doses of 318 mg and 8 mg, respectively, for a one-hour exposure of the hands and forearms (2000 cm2) to a saturated aqueous solution of 1,4-dichlorobenzene. ・ Absorption through the skin. From the NAEL of 5 mg/kg body weight and day obtained in the 52-week oral study with dogs, after toxicokinetic correction (1:1.4) and extrapolation of the data from an animal study to humans (1:2), a tolerable daily uptake of 201 mg is calculated when the oral absorption of 90%, the absorption by inhalation of 56% and the body weight of 70 kg are taken into account. The model calculations for dermal absorption yield values of 5.5 mg, 10.4 mg or 430 mg, so that the contribution of absorption through the skin to the total amount absorbed is not negligible and 1,4-dichlorobenzene remains designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).				▲

106-47-8	p-クロロアニリン	【DFG】 ・ The designation "H" is necessary because of the danger of absorption through the skin. ・ Intoxication with p-chloroaniline dust is described in another report. A 34 year old worker in a paint factory had to determine the powder quality of p-chloroaniline which was packed in sacks. He wore protective gloves but because of the heat he had rolled his shirt sleeves up high and his arms became covered in the dust. After 3 hours work he became cyanotic (metHb 70%) and complained of weakness, exhaustion, headache, vertigo, buzzing in his ears and retrosternal pains. Later investigation of the working conditions suggested that the p-chloroaniline uptake through the skin had been promoted by excessive perspiration. It is, however, very likely that the man had also inhaled and swallowed the dust because he had eaten a meal in the factory room. A follow-up examination 3 months later revealed no abnormal findings [19]. ・ The only available study investigated the ability of human abdominal skin fragments (from surgical procedures) to absorb p-chloroaniline in vitro. Radioactively labelled p-chloroaniline was dissolved in various carriers and applied to the intact or scarified skin. 24 hours later the amount absorbed was determined as 1.7 ng/cm2 for 26.5 µg p-chloroaniline/g carrier 1 (polyethylene glycol (PEG) 400) applied to intact skin and 148 ng/cm2 for scarified skin. With 26.5 µg p-chloroaniline/g carrier 2 (vaseline and PEG 400), 16.4 ng/cm2 was absorbed by intact skin and 43.1 ng/cm2 by scarified skin. The amount absorbed after application of 19.8 µg p-chloroaniline/g carrier 3 (PEG 400 and liquid soap) to the intact skin was 14.3 ng/cm2 and to the scarified skin 56.2 ng/cm2 [23].	▲		▲	
106-49-0	p-トルイジン	【ACGIH】 ・ Reported significant percutaneous absorption of p-toluidine and its systemic health effects warrant assigning the Skin notation. The results of mutagenicity tests presented a conflicting picture. The U.S. Environmental Protection Agency calculated a permeability coefficient for o-toluidine through intact human skin of 0.0037 cm/ hr. Therefore, by analogy with o-toluidine and aniline, and indirectly nitrobenzene, a TLV- TWAof 2 ppm, with a Skin notation, is recommended. ・ The oral LD50 of p-toluidine was 656 mg/kg body (5) weight in rats and 794 mg/kg body weight in mice; the hydrochloride has an oral LD50 of 1285 mg/kg body weight in rats. (5) The LD50 for rabbits by topical application was 890 mg/kg body weight. (5) ・ Clinical signs of p-toluidine intoxication in humans have included methemoglobinemia and hematuria. p-Toluidine is absorbed via the respiratory tract and skin. 【DFG】 ・ Although the toxicological profile of p-toluidine is very like that of o-toluidine, the database for p-toluidine is much smaller and so inadequate that a final assessment is not possible. The substance is therefore classified in Section III B in the List of MAK Values. A MAK value cannot be established. The toxicity demonstrated in rabbits after application to the skin and the analogy with other arylamines makes it necessary to warn users with the designation "H".		● ▲		● ▲
106-50-3	p-フェニレンジアミン	【ACGIH】 ・ Sufficient data were not available to recommend Skin or SEN notations or a TLV-STEL. 【NIOSH】 ・ A critical review of available data has resulted in the following SK assignment for PPD: SK: DIR (IRR)-SEN.				
106-87-6	4-オキシラニル-1,2-エポキシシクロヘキサン	【ACGIH】 ・ Because of the demonstrated toxicity to the rodent reproductive tract, the potent carcinogenicity at sites distant from initial contact when the VCD is applied to the skin and by analogy to the TLV for the parent VCD. TLV- TWA of 0.1 ppm, with a Skin notation, and the A3, Confirmed Animal Carcinogen with Unknown Relevance to Humans, notation are recommended for VCD.		●		●
106-88-7	1,2-エポキシブタン（別名： 1,2-酸化ブチレン）	【DFG】 ・ 1,2-Butylene oxide is therefore classified in Section III A 2) in the "List of MAK and BAT Values". A MAK value cannot be established. Because of the danger associated with uptake through the skin, the designation "H" is necessary. ・ The LD50 after epicutaneous application to rabbit skin was 2.10 (1.5 − 2.95) ml/kg.		▲		
106-89-8	２－（クロロメチル）オキシラン（別名：エピクロロヒドリン）	【ACGIH】 ・ Systemic toxicity and a rabbit dermal LD50 of 755 mg/kg of body weight warrant a Skin notation.		●		
106-91-2	メタクリル酸2,3-エポキシプロピル	【産衛】 ウサギでの経皮曝露のLD50は低く，経皮吸収はGMAの重要な曝露経路のひとつである．また，GMA の皮膚透過係数は，分子量と log Pow から 3.3×10－7 cm/sec と推計される50)．この値は皮膚の角質細胞層の透過閾値とされる 1.0×10－9 cm/sec51)よりも十分に大きく，皮膚に付着すると皮膚を透過して体内に吸収されると考えられる．従って，皮膚マーク「皮」を付す．		★		★
106-92-3	1-アリルオキシ-2, 3-エポキシプロパン（別名：アリルグリシジルエーテル）	【NIOSH】 ・ No estimates of percent absorption of AGE following dermal exposure were identified. However, a mathematical model predicts that the chemical is poorly absorbed through the skin. Acute dermal toxicity data demonstrate that AGE has low systemic toxicity. AGE is assigned a composite skin notation of SK: DIR (IRR)-SEN. 【DFG】 ・ In addition, the lowest dermal lethal dose is given as 500 mg/kg body weight. The absorption of relevant amounts by the skin has therefore been demonstrated. The substance is a known genotoxic carcinogen, for which no tolerable level of exposure can be deduced. It must be assumed, therefore, that even after the percutaneous absorption of small amounts the carcinogenic risk is increased. The substance is therefore designated with an “H”.		▲		▲
106-93-4	1,2-ジブロモエタン【EDB】	【ACGIH】 ・ A Skin notation is assigned based on the reported CNS depressron and moriality in rabbits, followig dermal application of EDB.		●		

106-94-5	1-ブロモプロパン【臭化プロピル】	【DFG】 ・ No experimental studies are available. Data for the homologous compound bromoethane as well as model calculations suggest a dermal penetration of 1-bromopropane. According to the calculations, a one-hour exposure of 2000 cm2 skin surface results in an uptake of 44 to 48 mg of 1-bromopropane. Since no MAK value can currently be specified for the carcinogenic 1-bromopropane, a carcinogenic risk cannot be ruled out for the calculated quantities absorbed. In addition, there is a structural analogy to bromoethane marked with "H". 1-Bromopropane is therefore marked with "H".				▲
106-95-6	3-ブロモ-1-プロペン	【ACGIH】 ・ A Skin notation is recommended based on analogy with allyl chloride and the positive findings of a nontraditional dermal absorption study in mice (Rabotnikova and Sarycheva, 1970).		●		●
107-02-8	アクロレイン	【ACGIH】 ・ A Skin notation is assiigned, based on the rabbit dermal absorption study for which an ILD50 of 560 mg/kg was reported.		●		
107-05-1	塩化アリル	【ACGIH】 ・ A Skin notation is recommended based on industry reports of dermal exposure of workers (Torkelson et al., 1959; Dow, 2008) and by analogy with allyl bromide, which showed positive findings in a non-traditional dermal absorption study in mice (Rabotnikova and Sarycheva, 1970). ・ In range finding tests, Smyth and Carpenter (1948) found the rat oral LD50 = 700 mg/kg, the rabbit dermal LD50 = 2.2 ml/kg (2066 mg/kg) and the rat four-hour inhalation LC50 = 2000 ppm. ・ Van Duuren et al. (1979) tested allyl chloride for carcinogenicity by chronic administration in Ha:ICR Swiss mice. Allyl chloride was active as a skin tumor initiator in the two-stage carcinogenesis assays; phorbol myristate acetate was used as a promoter.	●	●		●
107-06-2	1,2-ジクロロエタン	【DFG】 ・ Animal experiments showed 1,2-dichloroethane to have a high level of dermal penetration compared to other substances designated with an „H” in the List of MAK and BAT Values (benzene, ethylbenzene, toluene). The substance is a known genotoxic carcinogen, for which no tolerable level of exposure can be deduced. It must be assumed, therefore, that even after the percutaneous absorption of small amounts the carcinogenic risk is increased. The substance is therefore designated with an „H”.		▲		▲
107-07-3	エチレンクロロヒドリン	【ACGIH】 ・ LD50 values reported for dermal application of ethylene chlorohydrin in a variety of animals warrant the Skin notation. ・ Two-year dermal bioassay studies with rats and mice produced no evidence of carcinogenicity,		●		
107-13-1	アクリロニトリル	【ACGIH】 ・ Since systemic toxicity and lethality have been reported following dermal exposure to acrylonitrile (IARC, 1979), a Skin notation is warranted for acrylonitrile. ・ Acrylonitrile applied to the skin of rats at doses of 14 or 28 mg/kg for 2 months or at 0.11, 0.56, or 2.8 mg/kg for 4.5 months had a general toxic effect; the dominant changes were in the blood vessels (congestive plethora and hemorrhages) (IARC, 1979). 【DFG】 ・ Human: Some accidental poisonings with acrylonitrile have been described; most of these were caused by inhalation of high concentrations or prolonged skin contact. Deaths were also observed sporadically (Brieger et al. 1952). ・ The dermal LD50 values were determined to be in a range of 148–693 mg/kg body weight for rats, guinea pigs and rabbits. The LC50 values were in a concentration range of 300–990 mg/m3. A decrease of glutathione down to 30–60% was measured in the liver, blood, lungs and brain. The glucose level increased in the blood (BUA 1995; WHO 1983). All of 15 rabbits died after dermal application of 200 mg/kg body weight. ・ In vitro skin penetration rates of 0.033 and 0.066 mg/cm2 and minute were determined for 30- and 60-minute applications, respectively (Bakker et al. 1991).	● ▲	● ▲	▲	
107-15-3	エチレンジアミン	【ACGIH】 ・ The dermal LD50 reported for rabbits treated with EDA and a worker fatality following dermal and inhalation exposures warrant a Skin notation. ・ Range-finding studies on EDA showed low acute oral toxicity, with an LD50 in rats of 1160 mg/kg, and moderate percutaneous absorption toxicity, with a dermal LD50 of 657 mg/kg in rabbits. ・ A fatal poisoning is reported to have occurred when a worker was splashed by a gust of EDA and exposed both dermally and by inhalation. Clinical signs accompanied by changes in blood chemistry and hematologic values led the authors to conclude that exposure produced lysis of red cells, which induced tubulonephritis with anuria and lethal hyperkalemia. Death occurred from cardiac collapse 55 hours after the accident.	●	●		
107-18-6	アリルアルコール	【ACGIH】 ・ Overt signs of systemic toxicity following dermal contact, including periportal necrosis, congestion of the liver, hematuria, nephritis, mortality in animals, and nausea and vomiting in humans warrant a Skin notation. ・ Smyth and Carpenter (12) listed the rabbit dermal LD50 as 45 mg/kg (0.053 ml/kg). ・ Given the relatively small amount required to produce systemic poisoning and death after percutaneous uptake in rabbits(¹2) and the reports of human nausea and vomiting after combined skin and respiratory contact with allyl alcohol,(8) the Skin notation is justified. 【DFG】 ・ The LD50 for rabbits after dermal absorption (24 hours, occlusive) was 45 mg/kg body weight (Smyth and Carpenter 1948). ・ Skin contact with the substance resulted in corrosion and pain in deeper-lying muscles (Clayton and Clayton 1982) and to effects on the liver and kidneys (ACGIH 1991). ・ Because of the high toxicity of allyl alcohol after dermal contact, the designation with an “H” has been retained. There are no data available for sensitizing effects of allyl alcohol.	● ▲	● ▲		
107-19-7	2-プロピン-1-オール	【ACGIH】 ・ The Skin notation is recommended because of its rapid skin absorption and toxicity to rabbits and also by analogy to allyl alcohol. ・ The single percutaneous LD50 for propargyl alcohol in rabbits was 88 mg/kg.)		●		●

107-20-0	クロロアセトアルデヒド	【DFG】 ・ The calculated flux values suggest that a significant amount of chloroacetaldehydemay be taken up through the skin; therefore the substance is designated with an “H”.				▲
107-21-1	エチレングリコール	【DFG】 ・ Because the substance can be absorbed through the skin in toxic amounts, the designation "H" is necessary. The few available reports of sensitization with ethylene glycol do not provide enough evidence for the designation of the substance with an "S". ・ The daily intake of the substance through the skin was calculated by the authors to be 3550 mg/kg in the highest dose group (0.1 ml 100% ethylene glycol). There were no signs of maternal toxicity but the body weights of the progeny were slightly reduced and there was a slight increase in skeletal variations.		▲		
107-22-2	グリオキサール	【DFG】 ・ Both models predict a relatively good dermal penetration, and skinsensitization is also an indication of systemic availability after dermal exposure.Dermal penetration is thus plausible. The substance is genotoxic, and no exposure level can be assessed as harmless the substance is therefore designated with an“H”. ・ After dermal application of 40% glyoxal, the LD50 values were greater than 2000 mg/kg body weight in the rat, 12 700 mg/kg body weight in rabbits and great-er than 5000 mg/kg body weight in guinea pigs (BG Chemie 1997).	▲	▲		▲
107-31-3	ぎ酸メチル	【ACGIH】 ・ A Skin notation is warranted due to the ability of methyl formate to be absorbed through skin, resulting in toxic effects as noted in a case report of a. 19-mantlh-old child (Gettler, 1940) and a rat dermal study (BASF AG, 1979).	●	●		
107-49-3	テトラエチルピロホスフェイト (別名：TEPP)	【ACGIH】 ・ A Skin notation is assigned due to the high level of toxicity seen in animals following both single and repeated exposures. ・ The dermal LD50 was 2.4 mg/kg in male rats (4) and 1.2 mg/kg in rabbits. Following an acute dose (1 mg/kg), rats, showing minimal cholinergic signs, had brain, red blood cell (RBC), and plasma cholinesterase activity depressed 26%, 67%, and 81%, respectively. ・ LD 50 values in mice were reported as follows: 3 mg/kg oral, 8 mg/kg dermal.		●		
107-66-4	りん酸ジ-ノルマル-ブチル	【ACGIH】 ・ A report that a delayed neuropathy was induced in chickens as a result of a 90-day dermal exposure to 100 mg/kg/day (Abaui-Doniia,, 1981) warrants the additdon of a Skin notation.		●		
108-03-2	1-ニトロプロパン	【DFG】 ・ Skin contact is expected to contribute significantly to systemic toxicity and 1-nitropropane is designated with an “H”. 1-Nitropropane is not genotoxic and data for carcinogenicity are lacking. Sensitization is not expected from the limited data.		▲		
108-10-1	メチルイソブチルケトン	【DFG】 ・ It can be deduced from toxicokinetic data that the internal exposure resulting from exposure at the level of the MAK value can be considerably increased by dermal absorption. Hexone is therefore designated with an “H”. ・ In the same study 1 ml undiluted hexone was applied occlusively to 3.14 cm2 of the shaved dorsal skin of guinea pigs. The maximum average values for blood concentration (26.7 µmol/l) and percutaneous rate of absorption (1.1 µmol/cm2 and minute corresponding to 6.6 mg/cm2 and hour) were reached 10 to 45 minutes after the beginning of exposure. Assuming the dermal rate of absorption in man to be only a tenth of the value for guinea pigs, the authors estimated that when a hand is dipped into liquid hexone the same amount of substance is taken up per unit time as during exposure to a hexone concentration of 25 ml/m3 (Wigaeus Hjelm et al. 1991).		▲		▲
108-11-2	4-メチル-2-ペンタノール	【NIOSH OSHA PEL Project Documentation 1988】 ・ In rabbits, a 24-hour skin application of 3.56 ml/kg (2.9 g/kg) was lethal to half the animals (Smyth, Carpenter, and Weil 1951/Ex. 1-439). Rats exposed by inhalation to 2000 ppm of methyl isobutyl carbinol vapor died, and the same authors report that the oral LD(50) for rats is 2.6 g/kg (Smyth, Carpenter, and Weil 1951/Ex. 1-439).		■		
108-18-9	ジイソプロピルアミン	【ACGIH】 ・ The Skin notation is justified by analogy with diethylamine, diethyleneamine, ethylamine, n-butylamine, and other related amines.				●
108-38-3	m-キシレン	【DFG】 ・ As described in Section 2, dermal exposure to liquid xylene can contribute consider-ably to the body burden and the toxic effects. Xylene is therefore designated with an “H”.As a result of a lack of data, xylene is at present not designated with an “S” (for sub-stances with sensitization potential).	▲	▲		▲
108-39-4	m-クレゾール	【ACGIH】 ・ A Skin notation is warranted because dermal LD50 values, along with evidence from accidental human exposure, show that systemic toxicity can resu lt from skin exposure (Larcan et al., 1974; Green, 1975).	●	●		
108-42-9	クロロアニリン (3-クロロアニリン)/クロロアニリン	【DFG】 ・ The demonstrated dermal toxicity of m-chloroaniline requires the designation "H". ・ In an early study cyanosis, dilation of the pupils, increased respiration rate and unsteady gait were seen in cats after subcutaneous injection or dermal application of m-chloroaniline. The animals did not survive a subcutaneous dose of 310 mg/kg. Applied dermally, a dose of 3–6 g m-chloroaniline was lethal. Autopsy revealed discoloured brown lungs; metHb was not always detectable . ・ After intragastric administration of m-chloroaniline to mice or dermal application of lethal doses to cats the animals died within 3 days with blood metHb levels of 60–80% .	▲	▲	▲	
108-44-1	m-トルイジン	【ACGIH】 ・ As for ortho-toluidine, m-toluidine is reporrtred to be absorbed percurtaneollsly in amounts that may contribute to systemic toxicity and a Skin notation is considered appropriate. By analogy with the toxicologiy of aniline and the o- and p-toluidine TLVs, a TLV-TWA of 2 ppm, with a Skin notation, is recommended.	●			●

108-45-2	m-フェニレンジアミン	【DFG】 ・ Because of the lack of information as to the effects of m-phenylenediamine in man and particularly as to the sensitizing potential of the substance, a MAK value cannot be established. m-Phenylenediamine produced metHb in experimental animals. After metabolic activation, it is genotoxic in most short-term tests; on the other hand, in most carcinogenicity studies m-phenylenediamine yielded negative results. A weak carcinogenic effect was seen after subcutaneous injection of the substance. Because of the clearly genotoxic properties of the substance, m-phenylenediamine is to be classified in Section III B in the "List of MAK and BAT Values" until the inconsistencies in the in vivo studies have been clarified. m-Phenylenediamine must be designated with an "H". ・ In an early study of the local effects of the phenylenediamines, m-phenylenediamine was found to have no effect when the solid was rubbed into a 1 to 5 cm2 area of human skin (no other details). However, a 10 % alcoholic solution applied to the skin non-occlusively caused slight burning and itching [4]. ・ m-Phenylenediamine was applied directly to a 25 cm2 area of shaved and cleansed rabbit skin (no other details) and left uncovered. No effects were observed. However, application of a 10 % alcoholic solution resulted in slight erythema [4].		▲	▲	▲
108-69-0	3,5-ジメチルアニリン	【ACGIH】 ・ Based on the central nervous system effects and methemoglobin formation seen in cats that received repeated cutaneous applications of 2,4-xylidine, the Skin notation is warranted.		●		●
108-70-3	1,3,5-トリクロロベンゼン	【DFG】 ・ Since all three isomers have similar solubility (insoluble in water, slightly soluble in ethanol and highly soluble in organic solvents), it can be assumed that all three isomers are similarly well absorbed when applied epicutaneously. Because of the basically comparable systemic toxicity, it can therefore be assumed that 1,2,3- and 1,3,5-trichlorobenzene can also lead to liver damage after epicutaneous application, even though no studies are available on this. The marking with "H" for 1,2,3- and 1,3,5-trichlorobenzene therefore remains. [MAK Value Documentation in German language, 1998] 【DFG】 ・ Evidence of systemic toxicity (increased excretion of coproporphyrin) was observed in rabbits after repeated dermal application of technical grade trichlorobenzene (approximately 70 % 1,2,4-trichlorobenzene and 30 % 1,2,3-trichlorobenzene, no further details). In addition, in guinea pigs, but not in rabbits, necrotic foci were found in the liver after repeated dermal application of pure 1,2,4-trichlorobenzene (see Volume 3). A penetration rate of 0.18 mg/cm2 and hour was calculated for human skin for a saturated aqueous solution of 1,2,4-trichlorobenzene (Fiserova-Bergerova 1990). The substance has therefore been designated with an “H”.		▲		▲
108-88-3	トルエン	【DFG】 ・ Percutaneous penetration of gaseous toluene leads to relatively low internal toluene exposures compared to inhalation (at air exposures at the level of the TLV). However, the flux determined by Monster et al. 1993 for skin contact to liquid toluene in one hour over both hands and forearms (approx. 2000 cm2) results in an intake of 1000 mg toluene. In comparison, 1100 mg of toluene are absorbed during an 8-hour, purely inhalation exposure at the level of the TLV (190 mg toluene/m3, 10 m3 air volume, 60% absorption). The percutaneous penetration is thus so high that compliance with the established TLV alone does not provide sufficient protection. Therefore, the marking "H" is assigned for toluene.	▲			▲
108-93-0	シクロヘキサノール	【ACGIH】 ・ A Skin notation is assigned based on the studies with rabbits in which narcosis, tremors, hypothermia, and death ensued following dermal application of cyclohexanol.		●		
108-94-1	シクロヘキサノン	【ACGIH】 ・ A Skin notation is assigned, based on the dermal LD50 data. ・ The dermal LD50 in rabbits was 950 mg/kg, indicating significant absorption through the skin.		●		
108-95-2	フェノール	【ACGIH】 ・ Because phenol, as a vapor, liquid, or solid, can penetrate the intact skin causing systemic effects, the Skin notation is considered appropriate. ・ Human Study: Numerous investigators (18-25) have reported the clinical and pathological findings in cases of acute phenol poisoning, usually as a result of skin absorption, in industry and in the home. Death was a common outcome. Skin absorption represents the primary route of entry for vapor, (28) liquid,(18-22) and solid phenol. Phenol vapor readily penetrates the skin with an absorption efficiency approximately equal to that by inhalation.(28) Skin absorption occurs at low vapor pressures and apparently without discomfort. (28,30) Damage to the lungs and CNS(31-35) have been described following both lethal and nonlethal percutaneous absorption of phenol.	●	●		
108-98-5	チオフェノール	【ACGIH】 ・ A skin absorption study with guinea pigs that indicated the designation of a Skin notation would be appropriate. A skin notation was assigned, based upon the low dermal LD50.		●		
109-59-1	エチレングリコールモノイソプロピルエーテル	【ACGIH】 ・ By analogy with the glycol ether 2-butoxyethanol, for which systemic toxicity was reported following topical application to rabbit skin, a Skin notation is assigned. 【DFG 2017】 ・ The amount absorbed through the skin is thus less than 25% of the systemically tolerable amount. 2-Phenoxyethanol is therefore no longer designated with an “H” 【DFG 2018】 ・ In an in vitro penetration study with human skin, a dermal flux of 240 µg/(cm2 × h) was calculated for 2-isopropoxyethanol (pure substance). This is equivalent to the total absorption of 480 mg 2-isopropoxyethanol after 1-hour exposure of both hands and forearms (about 2000 cm2). Taking into consideration the higher respiratory volume of humans at the workplace in comparison with test animals at rest (1:2), a concentration of 15 ml/m3 (66 mg/m3) is calculated from the NOAEC of 30 ml/m3 for haemolytic effects established from a 28-day inhalation study in Wistar rats. Assuming complete absorption and a respiratory volume of 10 m3, 660 mg 2-isopropoxyethanol is absorbed after exposure by inhalation. Even after taking into account that humans are much less sensitive to haemolytic effects than are rats, the substance is absorbed through the skin so readily that observation of the MAK value is not sufficient to prevent systemic effects after contact with the skin. As absorption through the skin is a very important route of absorption at the workplace, 2-isopropoxyethanol retains its “H” designation (for substances which can be absorbed through the skin in toxicologically relevant amounts).			▲	● ▲

109-73-9	n-ブチルアミン	【ACGIH】 ・ A Skin notation is assigned, based on the dermal LD50 of 0.5 ml/kg for guinea pigs.		●		
109-79-5	1−ブタンチオール	【DFG】 ・ In various studies butanethiol is described as not irritative to slightly irritative to the skin (no other details; Farr and Kirwin 1994). Various alkyl mercaptans, including butanethiol, were tested in the rabbit and found to cause weak to moderate mucosal irritation (Fairchild and Stokinger 1958). In another study, impairment of the iris within the first 24 hours and moderate to slight conjunctival irritation up to 72 hours after the application were observed (no other details; Farr and Kirwin 1994). Mucosal irritation was likewise observed in rats and mice after inhalation exposure to high concentrations of butanethiol (Fairchild and Stokinger 1958). ・ The dermal LD50 value for 1-butanethiol is higher than 2000 mg/kg bw, as is that of ethanethiol, 1-propanethiol and 2-methyl-2-propanethiol. For 1-butanethiol and ethanethiol, the values are for the rat, and for the last two, for the rabbit. Apart from skin reactions, no effects were observed (OECD 2010). ・ Calculations based on physicochemical data and mathematical models result in a dermal intake of between 20 mg and 540 mg of 1-butanethiol under standard conditions. From the systemic NOAEC derived for the workplace of 1.1 ml/m3 (4.2 mg/m3) (Table 3, before application of the preferred value approach), a tolerable amount of about 42 mg is calculated for an inhalation intake assuming complete pulmonary absorption and a respiratory volume of 10 m3. The dermal uptake may therefore be more than 25% of the systemically tolerable amount, so that 1-butanethiol is marked with "H".		▲		▲
109-86-4	エチレングリコールモノメチルエーテル	【ACGIH】 ・ Given that EGME is readily absorbed through the skin in amounts sufficient to elicit systemic toxicity, the Skin notation is appropriate. Because skin absorption is likely to be a primary route of exposure in most occupational settings, biological monitoring, and application of the ACGIH BEI are recommended and are likely to provide more reliable estimates of exposure than air monitoring alone ・ A dermal LD50 of 8100 mg/kg (9 mL/kg) was reported in rabbits. No skin irritation was observed; however, marked CNS depression was reported and deaths occurred within 48 hours (Boatman, 2001). ・ The rate of pure PGEE penetration in vitro through human skin was determined to be approximately 1400 ± 400 µg/cm²/hour and increased by around 50% to around 2100 ± 100 µg/cm²/hour when applied as a 50% aqueous solution (Korinth et al., 2012). Therefore, the amount that could be absorbed over the course of an 8-hour work shift through 100 cm² of exposed skin could be as much as 1680 mg. This approximates the dose of 2125 mg associated with 8 hours of exposure at the TLV -TWA of 50 ppm (assuming 100% absorption). 【DFG】 ・ Several research groups have observed a complex of neurological and psychiatric symptoms in persons exposed dermally or by inhalation to 2-methoxyethanol [6-11]. ・ According to unpublished results obtained at BASF [15], symptoms of toxicity are also to be expected in the rabbit after dermal intake of the substance (dermal LD50 2 g/kg). ・ Clear teratogenic and embryotoxic effects were also seen in rats after dermal application of single doses of diluted and undiluted 2-methoxyethanol under non-occlusive conditions [35, 36].	●	●	●	●
109-89-7	ジエチルアミン	【ACGIH】 ・ Even though there are no human data for skin absorption, considering the lethal dose of diethylamine to rabbits following dermal exposure was 820 mg/kg (Smyth et al., 1951), a Skin notation for this chemical is recommended.		●		
109-94-4	ぎ酸エチル	【DFG】 ・ Data for the dermal absorption of formic acid ethyl ester are not available. In analogy to formic acid methyl ester, formic acid ethyl ester is also designated with an “H”. ＊As dermal absorption of toxicologically relevant amounts must be expected, formic acid methyl ester is designated with an „H”.				▲
109-99-9	テトラヒドロフラン	【ACGIH】 ・ Because THF is absorbed through the skin of animals in amounts surficiernt to elicit systemic toxicity, a Skin notation is assigned. A Skin notation is recommended because THF has the potential for significant contribution to the overall ,exposure. Up to 6% of the total body burden in humans was related to the dermal route of entry by a dermal exposure to the vapor alone of 150 ppm THF. THF was rapidly absorbed through the skin of rabbits and was rapidly fatal to rats when 10% of the body surface was exposed to the liquid.		●		●
110-00-9	フラン	【DFG】 ・ Based on the theoretical models of Fiserova-Bergerova et al. (1990) and Guy and Potts (1993), it must be assumed that furan is readily absorbed through the skin. Because of its very high vapour pressure, this theoretical ability to penetrate the skin will probably not be completely exhausted in practice. As furan was carcinogenic in animal studies and genotoxic effects cannot be ruled out, an additional carcinogenic risk has to be assumed for dermal exposure and the estimated amounts absorbed. Furan has therefore been designated with an “H” (for substances which can be absorbed through the skin in relevant amounts).				▲
110-49-6	エチレングリコールモノメチルエーテルアセテート	【ACGIH】 ・ Given that EGME is readily absorbed through the skin in amounts sufficient to elicit systemic toxicity, the Skin notation is appropriate. Because skin absorption is likely to be a primary route of exposure in most occupational settings, biological monitoring, and application of the ACGIH BEI are recommended and are likely to provide more reliable estimates of exposure than air monitoring alone. ・ Anemia has been associated with human inhalational exposures of 35.7 ppm EGME that were accompanied by dermal exposure. When airborne exposures were lowered to 0.55 ppm and dermal exposures were reduced, the anemias resolved. ・ Adermal LD50 of 5.6 g/kg EGMEA in rabbits has been observed. 【DFG】 ・ Toxic amounts of the substance can be absorbed through the skin [2, 3].	●	●		
110-54-3	ノルマル - ヘキサン	【ACGIH】 ・ Based on the human peripheral neuropathy after skin contact with n-hexane and by analogy to methyl n-butyletone (the proximate neurotoxic metabolite of n-hexane which carries a Skin designation), the Skin notation is assigned.	●			●

110-65-6	2-ブチン-1,4-ジオール	【DFG】 ・ With regard to dermal toxicity and penetration, pure butynediol appears to behave differently from aqueous solutions and pastes. According to the studies of Jedrychowski et al. 1992a, the dermal toxicity of dissolved butindiol is likely to be many times greater than that of the solid. Consequently, a quantitative assessment of the dermal penetration of butindiol is not possible from the experiments of the NIEHS study (NIEHS 2002), in which drying of the initially dissolved substance took place. Consequently, theoretical models must be used for a quantitative estimate of penetration. Based on an air exposure of 25 mg/m3 , a total uptake of 250 mg butynediol is calculated for pure inhalative uptake in the case of an 8-hour exposure (respiratory volume 10 m3) and complete absorption. According to the model calculations, 19 or 151% of this inhalatively absorbable amount would be absorbed via the skin in the dermal scenario. Consequently, toxicologically relevant amounts of butynediol may be absorbed through the skin. This conclusion is supported by the comparably low LD50 values for the oral and dermal routes. Therefore, butindiol is marked with "H".				▲
110-80-5	エチレングリコールモノエチルエーテル	【ACGIH】 ・ Rabbit mortality, LD50 of 3.4 g/kg of body weight, following dermal application and absorption of 2-ethoxyethanol warrants the Skin notation. 【DFG】 ・ Teratogenic effects were also seen after dermal application of 2-ethoxyethanol [32]. Rats were treated 4 times daily from day 7 to day 16 of gestation with 0.25 or 0.5 ml of the undiluted substance applied to the skin with an automatic pipette. Evaporation from the skin produced concentrations of about 37–68 ml/m3 in the air inhaled by the animals.		●		
110-86-1	ピリジン	【DFG】 ・ Studies on dermal absorption are not available. The acute dermal LD50 for rabbits is about the same as the oral LD50 for rats and slightly lower than the oral LD50 for mice. This is indicative of good skin penetration. The model calculations give very high intake levels of 48 and 85 mg/kg bw at 70 kg bw, respectively. This dose is well above the oral LOAEL for rats. Therefore, dermal exposure may result in systemic toxicity and pyridine is marked "H".		▲		▲
110-91-8	モルホリン	【ACGIH】 ・ A Skin notation is assigned based on a report of human dermal penetration and a dermal LD50 for 24-hour skin contact of 0.5 ml/ kg in rats. ・ Concentrated morpholine readily permeates the skin. The undiluted compound was very irritating to the eyes and is moderately irritating to the skin. (20) 【NIOSH】 ・ The evaluation method compares an estimated dose accumulated in the body from skin absorption and an estimated dose from respiratory absorp- tion associated with a reference occupational exposure limit. On the basis of this algorithm, a ratio of the skin dose to the inhalation dose (SI ratio) of 1.76 was calculated for morpholine. An SI ratio of ≥0.1 indicates that skin absorp- tion may significantly contribute to the overall body burden of a substance [NIOSH 2009]; therefore, morpholine has the potential to be absorbed through the skin and to become avail- able systemically following dermal exposure. ・ No epidemiological studies or human case reports or repeated-dose, subchronic, or chronic dermal toxicity studies in animals were identified. ・ Although no toxicokinetic data were identified to evaluate the potential of morpholine to be absorbed through the skin, data from an acute dermal toxicity study in rabbits [Smyth et al. 1954] and from a short-term dermal toxicity study in guinea pigs and rabbits [Shea 1939] are sufficient to suggest that morpholine can be absorbed by the skin, become systemically available, and be toxic, with the potential to cause liver, kidney, and spleen effects following repeated exposure. Therefore, on the basis of the data for this assessment, morpholine is assigned the SK: SYS notation.	●	● ■		■
111-15-9	エチレングリコールモノエチルエーテルアセテート(別名：セロソルブアセテート)	【ACGIH】 ・ Although the rabbit dermal LD 50 for 2-ethoxyethyl acetate is large, 10.3 g/kg body weight compared to 3.4 g/kg for the parent alcohol (2-ethoxyethanol), a Skin notation is still recommended. ・ Based upon the reported testicular effects and by analogy to the TLV for 2-ethoxyethanol (see TLV Documentation for 2-Ethoxyethanol), a TLV-TWA of 5 ppm, with a Skin notation, is recommended for 2-ethoxyethyl acetate 【NIOSH】 ・ Toxicokinetic studies were identified for 2-EEA, but percent absorption estimates were not available. In vitro evaluation of the skin permeability of 2-EEA [Dugard et al. 1984; Barber et al. 1992] indicates the chemical is readily absorbed. No epidemiological or occupational exposure studies were identified that evaluated the potential of 2-EEA to cause systemic effects following dermal exposure. 2-EEA is not acutely toxic following dermal exposure; however, repeat-dose developmental toxicity studies identified in animals that employed high dermal doses resulted in maternal and developmental effects [Hardin et al. 1984]. The weight of evidence from standard irritation tests indicates that 2-EEA is not likely to be a skin irritant under typical workplace scenarios. Limited data from a predictive test (GPMT) indicate that 2-EEA is not a skin sensitizer. Therefore, on the basis of these assessments, 2-EEA is assigned a composite skin notation of SK: SYS. 【DFG】 ・ Cardiovascular and skeletal malformations were also observed in rats after dermal administration of 2-ethoxyethyl acetate doses of 5900 mg/kg and day [11].		● ■ ▲	■	● ■
111-40-0	N-（2-アミノエチル）-1,2-エタンジアミン　（別名：ジエチレントリアミン）	【ACGIH】 ・ A Skin notation is recommended, based on the LD50 values for guinea pigs and rabbits following dermal application of DETA.		●		
111-42-2	２，２’ーイミノジエタノール	【ACGIH】 ・ The 2 mg/kg dose, assuming 100% absorption, would be equivalent to an inhalation dose of 14 mg/m3 or 3.2 ppm. Integrating this calculated dose with the no-effect inhalation exposure demonstrated in multi-species suggests that exposure of 0.2 ppm (1 mg/m3) should be sufficient to protect nearly all workers from the unwanted effects of DEA. A skin notation is recommended since relatively low dermal doses in animals can produce systemic effects.		●		●
111-44-4	ビス(2-クロロエチル)エーテル	【ACGIH】 ・ The dermal guinea pig LD so of 300 mg/kg body weight provides the basis for recommending a Skin notation.		●		
111-69-3	アジポニトリル	【ACGIH】 ・ A Skin notation is recommended, based on the significant systemic toxicity in rabbits, guinea pigs, and rats treated dermally with adiponitrile.		●		

111-76-2	エチレングリコールモノ - ノルマル - ブチルエーテル（別名ブチルセロソルブ）	【ACGIH】 ・ A skin notation is not recommended, based on estimates from physiologically based pharmacokinetic models which indicate that, even in worst-case dermal-exposure scenarios, 2-butoxyethanol is not absorbed in amounts sufficient to cause red blood cell hemolysis in humans. 【NIOSH】 ・ Sufficient information was available from human and animal dermal toxicokinetic studies in vivo and in vitro [Bartnik et al. 1987; Sabourin et al. 1992, 1993; Jakasa et al. 2004] and from dermal toxicity stud- ies [Carpenter et al. 1956; Duprat and Gradiski 1979] to demonstrate that BE is absorbed through the skin, is systemically available, and can elicit systemic effects such as hemoglobinuria (and other blood effects and changes in body weight). 【DFG】 ・ The data from the workplace studies do not contradict – as a result of the great influence of dermal exposure to liquid 2-butoxyethanol – the relationships between the concentration of 2-butoxyethanol in the air and butoxyacetic acid in the blood derived using the PBPK model, as these were determined in volunteers under the exclusion of direct skin contact. ・ In the male rat, both after inhalation and after dermal or oral exposure (via gavage and drinking water), butoxyacetic acid was eliminated with the urine as the main metabolite in amounts of 60% to 75% of the absorbed dose of 2-butoxyethanol (supplement “2 - Butoxyethanol” 2010).	■ ▲	■ ▲	■	■ ▲
111-96-6	ジエチレングリコールジメチルエーテル	【DFG】 ・ Because of the possible absorption of toxic amounts via the skin, the substance is marked with "H". ＊DEGDME is rapidly absorbed by the gastrointestinal tract, metabolized and excreted mainly with the urine. It is to be expected that, like methoxyethanol, DEGDME is readily absorbed through the skin. ＊The MAK value was therefore established, in analogy to that for 2-methoxyethanol, at 5 ml/m3 (27 mg/m3). Diethylene glycol dimethyl ether has teratogenic effects. Observance of the MAK value cannot guarantee that the unborn child will not be damaged. The substance is therefore classified in pregnancy risk group B.In analogy to 2-methoxyethanol, diethylene glycol dimethyl ether is classified in category II,1 for the limitation of exposure peaks because it is a substance with systemic effects. As it is possible to absorb toxic amounts through the skin, diethylene glycol dimethyl ether is designated with an H.		▲		▲
112-07-2	エチレングリコールモノブチルエーテルアセタート【2-ブトキシエチルアセタート又はEGBEA】	【DFG】 ・ Because it is possible to absorb toxic amounts of the substance through the skin, 2-butoxyethyl acetate is designated with an "H". ・ Dermal LD50 (rabbit) 1500 mg/kg (approx.)		▲		
115-29-7	６，７，８，９，１０，１０－ヘキサクロロ－１，５，５ａ，６，９，９ａ－ヘキサヒドロ－６，９－メタノ－２，４，３－ベンゾジオキサチエピン＝３－オキシド　（別名：エンドスルファン）	【ACGIH】 ・ A skin notation is recommended since lethality is produced in animals following the application of relatively low doses to the skin (the LD50 in male and female rats was 130 and 78 mg/kg, respectively) (Smith, 1991).		●		
115-90-2	チオりん酸O,O-ジエチル-O-[4- (メチルスルフィニル) フェニル] (別名：フェンスルホチオン)	【ACGIH】 ・ A skin notation is assigned because symptoms of organophosphate poisoning have been seen following dermal contact in human and the derrived lettlhall dose in animals is extremely low.	●	●		
117-81-7	フタル酸ビス(2-エチルヘキシル)	【ACGIH】 ・ A skin notation is recommended since lethality is produced in animals following the application of relatively low doses to the skin (the LD50 in male and female rats was 130 and 78 mg/kg, respect ively) (Smit h, 1991).		●		
118-74-1	ヘキサクロロベンゼン	【ACGIH】 ・ A Skin notation is based on the reported dermal absorption of HCB in rats, reflected by increased concentriaitions in the liver, fait, and blood. HCB is believed to be able to penetrate the intact skin in significant quantities, based on the work reported by Kiozumi et al., therefore, a Skin notation is also recommended for this substance.	●	●		
118-96-7	２，４，６－トリニトロトルエン	【ACGIH】 ・ Percutaneous absorption of sufficient quantities of TNT to induce systemic toxicity, including the possible development of cataracts, is reported for exposed workers; accordingly, a Skin notation is assigned to TNT. ・ The combined effects of vasomotor changes and methemoglobinemia contribute to the signs and symptoms characteristic of TNT intoxication after exposure to ambient air concentrations well in excess of 1.5 mg/m³. (15) Exposure to TNT may cause sneezing, sore throat, or skin irritation. (16) TNT is also absorbed through intact skin. In one instance, combined respiratory and percutaneous absorption resulted in 43% methemoglobinemia within 24 hours.(17) Ten percent of workers exposed by skin contact (hands) became ill.(16) However,the details of TNT exposure leading to these adverse effects are not available. ・ Considerably higher amounts of urinary metabolites were observed than were anticipated from the results of static air monitoring, leading the authors to conclude that skin absorption is the major route of occupational exposure to TNT.	●			
119-12-0	チオりん酸O,O-ジエチル-O-(6-オキソ-1-フェニル-1,6-ジヒドロ-3-ピリダジニル	【産衛】 ラットの急性経口 LD50 は 667mg/kg (雄) 660 mg/kg (雌) , 急性経皮 LD50 は 2,300mg/kg (雄) 2,100mg/kg (雌), マウスの急性経口 LD50 は 290 mg/kg (雄) 340mg/kg (雌), 急性経皮 LD50 は 660 mg/kg (雄) 1,100mg/kg (雌) である.		★		

119-93-7	3,3'-ジメチルベンジジン（別名：o-トリジン）	【ACGIH】 ・ Under some conditions, percutaneous absorption of o-tolidine presents a greater hazard (6,7) than inhalation of airborne compound. ・ Because o-tolidine is absorbed through the skin in amounts sufficient to induce systemic toxicity, Skin notation is considered apprapriate ・ o-Tolidine is rapidly absorbed through intact human skin (A Study of Exposure to Benzidine and Substituted Benzidines in a Chemical Plant: Arch. Ind. Hyg. Occup. Med. 4:533-540 (1951), Penetration by Diamines of the Benzidine Group. Arch. Ind. Hyg. Occup. Med. 9:122-132 (1954). 【DFG】 ・ 3,3'-Dimethylbenzidine has teratogenic potential and can induce tumours after transplacental exposure. The substance is classified in Section III A 2) of the "List of MAK and BAT Values". Because it can be absorbed through the skin in dangerous quantities, 3,3'-dimethylbenzidine is designated with an "H". ・ 3,3'-Dimethylbenzidine enters the organism mainly through the skin. Increases in temperature and in relative humidity promote dermal absorption [4]. Incorporated 3,3'-dimethylbenzidine is rapidly metabolized and excreted in urine and faeces. After application of 130 mg 3,3'-dimethylbenzidine to the hand of a volunteer under an occlusive patch for 8 hours, 0.082 mg benzidine-derivatives (determined as the quinones and expressed as benzidine) was found in the 24-hour urine, whereas before the study and on the second day the amount found in the urine was less than 0.020 mg [5].	● ▲	●	●	
120-80-9	カテコール（別名：ピロカテコール）	【ACGIH】 ・ A Skin notation is assigned based on dermal studies with mice and data from dermally exposed workers who exhibited symptoms of illness resembling those of phenol as well or central nervous system effects.	●	●		
121-44-8	トリエチルアミン	【ACGIH】 ・ There were no human data for skin absorption. However, the LD50 dose to rabbits following dermal exposure was 420 mg/ kg; herefore, a Skin notation is recommended.		●		
121-69-7	N,N-ジメチルアニリン	【ACGIH】 ・ The rapid and significant dermal absorption of dimethylaniline and contribution to systemic toxicity warrant the Skin notation. ・ The oral LD 50 in rats was reported as 1410 mg dimethylaniline/kg body weight, while the dermal LD50 for rabbits was reported as 1770 mg/kg. 【DFG】 ・ In a study to determine the LD50, N,N-dimethylaniline was applied occlusively for 24 hours to the shaved skin of groups of 4 male rabbits (New Zealand White); an LD50 of 1692 mg/kg (see Table 3) was determined [25]. ・ Another study investigated the absorption of N,N-dimethylaniline through the intact tail skin of 8 rats during 10 days (exact experimental protocol not described). N,N-Dimethylaniline was taken up through the skin and was lethal for most animals. Body weight loss, marked methaemoglobinaemia, erythropenia and reticulocytosis were observed in the survivors [21].		● ▲		
121-75-5	ジチオりん酸Ｏ，Ｏ－ジメチル－Ｓ－１，２－ビス（エトキシカルボニル）エチル　（別名：マラチオン）	【ACGIH】 ・ Dermal absorption of malathion in humans appears to be about 9% or less and experimental studies have not shown toxicity following dermal exposure. However, early reports of cholinergic toxicity in children treated with malathion for head lice suggest that a Skin notation is warranted.	●			
121-82-4	ヘキサヒドロ-1,3,5-トリニトロ-1,3,5-トリアジン (15質量%の水で湿性としたものに限る)	【ACGIH】 ・ A Skin notation is assigned based on a report that skin absorption was a possible route of entry that led to CNS effects in cyclonite-exposed munitions workers. Results of human intoxication from cyclonite reported by Kaplan et al. (37) refer to the possible contribution of skin absorption as a mode of exposure and resultant systemic toxicity.	●			
121-92-6	mーニトロ安息香酸	【DFG】 ・ From an in vitro study with human skin, a dermal uptake of 120 mg is obtained under standard conditions. The systemic NOAEL converted to humans is at most 500 mg, since 1930 mg (see above 193 mg/m3, 10 m3 respiratory volume) is a LOAEL and this still has to be extrapolated to humans. Thus, the dermal intake is at least about 25% of the systemic NOAEL, and 3-nitrobenzoic acid is marked "H".			▲	▲
122-14-5	チオリン酸O,O-ジメチル-O-(3-メチル-4-ニトロフェニル) (別名：フェニトロチオン)	【産衛】 ラットの急性経口 LD50 は 215mg/kg (雄) 245mg/kg (雌) [190~315mg/kg], 急性経皮LD50 は330 mg/kg(雄, 雌) [53,330~500mg/kg], マウスの急性経口 LD50 は 227mg/kg (雄) 225mg/kg (雌)である.		★		
122-39-4	ジフェニルアミン	【DFG】 ・ No studies on skin absorption are available. Acute dermal toxicity is low. The dermal bioavailability is approximately 28%. From the mathematical models, the worst-case intake is 137 mg per day, which is higher than the inhalation intake in compliance with the MAK value (at 10 m3 breathing volume 50 mg/day). In addition, good skin absorption is generally to be expected with aromatic amines. Diphenylamine is therefore marked with "H".				▲
122-60-1	2,3-エポキシプロピル=フェニルエーテル (別名：フェニルグリシジルエーテル)	【ACGIH】 ・ Because acute dermal treatment of rats and rabbits with PGE demonstrated the substance was rapidly absorbed through the skin and that topical application caused hematopoietic toxicity) and lethality, the Skin notation is recommended.		●		
123-31-9	ヒドロキノン	【DFG】 ・ The absorption of relevant amounts of hydroquinone by the skin has been demonstrated in rats and mice. The substance is a known genotoxic carcinogen, for which no tolerable level of exposure can be deduced. It must be assumed, therefore, that even after the percutaneous absorption of small amounts the carcinogenic risk is increased. The substance is therefore designated with an „H”.		▲		▲
123-39-7	N-メチルホルムアミド	【ACGIH】 ・ The Skin notation is based on studies demonstrating that dermal application of NMF to pregnant rats caused fetotoxicity and teratogeniciity		●		

123-42-2	ジアセトンアルコール	【DFG】 ・ The dermal LD50 in rabbits is 13630 mg/kg bw (Smyth and Carpenter 1948; Union Carbide 1946 a). Skin erythema occurred (Union Carbide 1946 a). ・ Model calculations for skin absorption suggest an intake of 530-2900 mg (7.5-41 mg/kg bw at 70 kg bw) under the assumed conditions. The systemic NOEL from the oral study is 100 mg/kg bw and the LOEL from the inhalation study is about 125 mg/kg bw. Thus, dermal exposure could significantly increase internal exposure and contribute to toxic effects. The amphiphilicity of the substance is also an indication of good dermal exposure. Therefore, the substance is marked with "H".		▲		▲
123-54-6	アセチルアセトン【2,4-ペンタンジオン】	【ACGIH】 ・ Dermal absorption of PD liquid and vapor can contribute to systemic doses (Ballantyne, 2001), so a skin notation is recommended. ・ High dermal doses of PD were lethal to rabbits and produced slight skin irritation. Ballantyne et al. (1986) applied 0.5 ml of the undiluted chemical to the shaved back of New Zealand white rabbits and covered the sites with impervious sheeting for four hours. Dermal LD50s were determined to be 1375 and 790 mg/kg for male and female rabbits, respectively. Times to death ranged from 45 minutes to 24 hours, with the fatalities occurring sooner at the higher dosages. Clinical signs in victims included dilated pupils and blood-stained saliva.		●		
123-73-9	クロトンアルデヒド（別名：（Ｅ）－２－ブテナール）	【ACGIH】 ・ A Skin notation is assigned based on the dermal LD50 of 26 mg/kg of body weight for crotonaldehyde-treated guinea pigs.		●		
123-75-1	ピロリジン	【DFG】 ・ N-nitrosopyrrolidine No quantitative data on the percutaneous uptake of N-nitrosopyrrolidine can be found in the literature. ・ In analogy to other nitroso compounds (N-nitrosodiethylamine, N-nitrosodimethylamine and N-nitrosomorpholine; see corresponding justifications), the substance must be evaluated as skin-resorptive. Calculation of dermal absorption also suggests this. ・ N-nitrosopyrrolidine is a proven genotoxic carcinogen for which, however, no safe exposure can be estimated. Therefore, even small amounts absorbed percutaneously must be assumed to increase carcinogenic risk. N-nitrosopyrrolidine is therefore marked with "H".				▲
123-91-1	1, 4-ジオキサン	【ACGIH】 ・ The rapid absorption of dioxane following application to the skin of rabbits and guinea pigs led to signs of incoordination and narcosis, which, together with the systemic toxicity seen in workers following dermal exposure, warrants a Skin notation.	●	●		
126-73-8	りん酸トリ-n-ブチル	【DFG】 ・ Despite the low acute dermal toxicity of tributyl phosphate, as the substance has been shown to penetrate the skin and because of its carcinogenic effects, it has been designated with an “H”. ・ In man a dermal penetration rate of 0.18 µg/cm2 and minute (10.8 µg/cm2 and hour) in vitro and in vivo was reported (Marzulli et al. 1965). Dermal penetration rates of 0.155 mg/cm2 and hour (Guy and Potts 1993) and of 0.1947 mg/cm2 and hour have been calculated (Fiserova-Bergerova et al. 1990). ・ The carcinogenic potential of tributyl phosphate was investigated in long-term studies with Sprague-Dawley rats and CD-1 mice. In both female and male rats, damage to the bladder epithelium, and benign and malignant tumours of the bladder epithelium were found. An increase in the incidence of both hyperplasia and papillomas was detected from the middle dose, and of bladder carcinomas from the high dose; sex-specific differences were found. In the high dose group, the incidence of bladder tumours in the male animals (61 %) was higher than that in the females (27 %). ・ The dermal toxicity of tributyl phosphate is low. The LD50 for rabbits is above 3100, 4640 and 10000 mg/kg body weight (FMC Corp 1975e, Johannsen et al. 1977, Stauffer Chem Co 1973) and in guinea pigs between 9700 and 19400 mg/kg body weight (Eastman Kodak 1986).	▲	▲		
126-98-7	メタクリロニトリル	【ACGIH】 ・ The rapid dermal absorption of methylacrylonitrile through intact animal skin with subsequent toxicity, including death (Hartung, 1982; Pozzani et al., 1968; Smyth et al., 1962; McOmie, 1949), warrants the Skin notation.		●		
126-99-8	2-クロロ-1, 3-ブタジエン（クロロプレン）	【ACGIH】 ・ A Skin notation is recommended based on rodent studies showing that chloroprerne can be absorlbed through the skin in amounts sufficient to elicit acute toxicity (von Oettingen et al., 1936; Clary et al., 1978).		●		
127-00-4	1-クロロ-2-プロパノール	【ACGIH】 ・ The Skin notation is based on acute dermal toxicity. ・ The dermal LD50 for propylene chlorohydrin (24-hour plastic-covered contact on clipped skin) was 0.48 ml/kg (530.6 mg/kg) in male New Zealand rabbits. Weisbrod obtained a dermal LD50 of 440 mg/kg (24-hour covered contact) in rats. No skin irritation was observed in a single New Zealand rabbit 24 hours after the uncovered topical application of 0.01 ml (10 mg) (LD50 of 528 mg/kg) neat propylene chlorohydrins to the clipped skin of the abdomen.		●		

127-18-4	テトラクロロエチレン	【DFG】 ・ The body burden resulting from dermal exposure of both hands and forearms for 1 hour corresponds to an external concentration of up to 150 ml/m3 (Section 4.1.1), which is higher than that after 8-hour exposure by inhalation at the level of the MAK value. Tetrachloroethylene is thus designated with “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts). ・ Dermal absorption of tetrachloroethylene from contaminated soil material was investigated in rats and humans. Permeability coefficients of about 0.1 cm/hour in rats were calculated by analysing tetrachloroethylene in the exhaled air and by means of physiologically based pharmacokinetic (PBPK) modelling. Lower values averaging 0.0009 cm/hour were determined for humans. Immersion of a hand in a mass containing a tetrachloroethylene dose of 30 g/kg led to a total amount absorbed of 20.2 ± 7.77 mg in 3 volunteers within 2 hours (Poet et al. 2002). Other animal studies confirmed the absorption of tetrachloroethylene through the skin (Bogen et al. 1992; Jakobson et al. 1982; Morgan et al. 1991; Tsuruta 1975). ・ After the immersion of one thumb (about 20 cm2) in tetrachloroethylene for 30 minutes, a concentration of 0.31 ml/m3 was determined in the exhaled air. This corresponds to the uptake by inhalation after exposure to 2 to 5 times the concentration in the air over the same period (Stewart and Dodd 1964). For the area of 2000 cm2 assumed under standard conditions, this would result in a concentration 100 times as high as in the exhaled air, namely 31 ml/m3. Therefore, the corresponding concentration in the air for absorption by inhalation only would be 60 to 150 ml/m3. ・ The penetration of liquid tetrachloroethylene through the skin led to similar results in an in vitro model with human skin and hairless guinea pig skin (permeability coefficients: 0.14 to 0.19 cm/hour) (Frasch and Barbero 2009). A permeability coefficient of 0.018 cm/hour was determined in another in vitro study in human skin (Nakai et al. 1999). In addition, a dermal penetration rate of 0.554 nmol/cm2 and minute (5.5 µg/cm2 and hour) was reported for tetrachloroethylene in an in vitro study in rat skin (Tsuruta 1977).	▲	▲	▲	▲
127-19-5	N,N-ジメチルアセトアミド	【ACGIH】 ・ Dermal exposure contributes significantly to the overall toxicity of this compound in animals (Stula and Krauss, 1977) and workers (Johnson, 1961); therefore, a Skin notation is assigned. 【DFG】 ・ In humans, the dermal absorption of N,N-dimethylacetamide in vapour form is about 40% (Nomiyama et al. 2000).	● ▲	●		
127-91-3	ベータ-ピネン	Turpentine 8006-64-2が該当する (ACGIH表より) 【DFG】 ・ The dermally absorbed quantities of α-pinene and β-pinene calculated from in vitro penetration experiments with human epidermis and whole skin diverge greatly from 78 mg to 266 g and 43 mg to 81 g, respectively, assuming one-hour exposure to turpentine oil of 2000 cm2 of skin. It is unclear which of the two experiments is more relevant for the in vivo situation. An 8-hour exposure to the substance at the level of the MAK value (28 mg/m3) would result in the uptake of 280 mg turpentine oil, assuming complete absorption at a respiratory volume of 10 m3. Even taking the lower of the two values obtained for dermal absorption as a basis, the uptake of α-pinene and β-pinene through the skin is in sum more than 25% of the systemically tolerable amount, so that turpentine oil is designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).			▲	▲
137-17-7	2,4,5-トリメチルアニリン	【DFG】 ・ A dermal absorption is plausible from the calculated data and from the structural analogy to other amino aromatics. The substance is a proven genotoxic carcinogen for which, however, no safe exposure can be estimated. Therefore, even small percutaneously absorbed amounts must be assumed to increase the carcinogenic risk. 2,4,5-Trimethylaniline is therefore marked with "H".				▲
140-88-5	アクリル酸エチル	【DFG】 ・ Based on model calculations, dermal uptake is estimated to range from 232 to 2608 mg after 1-hour exposure of both hands and forearms to 3% ethyl acrylate solution. Data from the 2-year oral ethyl acrylate administration experiment (Justification 1986) in rats indicate a systemic chronic NOAEL of 200 mg/kg bw. Based on this value, a toxicokinetic transfer (1:4) from rat to human results in a dose of 50 mg/kg bw. Since this value is derived from an animal experiment (1:2), it results in a tolerable dose for systemic effects in humans of 25 mg/kg bw, which corresponds to a total exposure of 1750 mg ethyl acrylate at a body weight of 70 kg. The results of the model calculations indicate that this tolerable dose cannot be safely met due to dermal uptake. Accordingly, ethyl acrylate is marked with "H".				▲
141-66-2	りん酸ジメチル＝（E)-1-（Ｎ，Ｎ－ジメチルカルバモイル）-1-プロペン-2-イル（別名：ジクロトホス）	【ACGIH】 ・ A Skin notation is assigned since symptoms of organophosphate poisoning have been seen following dermal contact with low doses of dicrotaphos in animals.		●		
141-79-7	酸化メシチル　(別名：メシチルオキシド)	【DFG】 ・ Due to the lack of human studies and the low validity of the present animal study, an evaluation of the dermal uptake of 4-methyl-3-penten-2-one is limited to model calculations. These result in a dermal absorption with uptake amounts of 2905, 247 and 312 mg 4-methyl-3-penten-2-one in one hour, respectively. At a MAK value of 5 ml/m3, about 200 mg (10 m3 breathing volume) are absorbed per day. Thus, dermal uptake results in higher exposure than inhalation. Comparable aliphatic ketones such as methyl ethyl ketone, methyl butyl ketone and methyl isobutyl ketone, which is structurally related to 4-methyl-3-penten-2-one, also exhibit relevant skin penetration and are marked with "H". Experience with these agents indicates that such ketones are generally readily absorbed through the skin. On the basis of the model calculations and due to analogy conclusions, 4-methyl-3-penten-2-one is marked with "H".				▲

143-33-9	シアン化ナトリウム	【ACGIH】 ・ HCN and, though less direct, the cyanide salts can be absorbed through the skin and produce systemic toxicity, including death. Accordingly, a Skin notation is assigned for HCN and the salts. ・ Inorganic cyanides were also reported to be rapid-acting acute poisons to humans and exhibit a dose-response relationship. The primary route of entry in the workplace is by inhalation, and for HCN, absorption through the skin. 【DFG】 ・ In an in vitro study, the permeability constant of human skin for aqueous solutions of cyanides was found to be 3.5 × 10−4 cm/hour. The permeability for an aqueous solution of HCN is almost 30 times higher, 10−2 cm/hour. A further study showed that toxic effects occur within 5 minutes after accidental exposure of a worker's hand to aqueous HCN solution. The designation “H” is therefore retained. The low dermal LD50 of HCN and cyanide salts also supports this designation.	● ▲	● ▲	▲	
143-50-0	クロルデコン	【DFG】 ・ To evaluate the toxicological relevance of skin absorption, data are available from experiments with rats showing penetration of chlordecone through the skin. Based on these data, a flux of 0.140 µg/cm2 and hour can be calculated. Assuming a one-hour exposure of both hands and forearms (area 2000 cm2), this would result in an uptake of 280 µg chlordecone under the conditions given in the animal study. In comparison with a limit value derived from rat data (see above) of 0.05 mg/m3, i.e. an intake of 500 µg at 10 m3 respiratory volume, a relevant contribution of skin absorption to the systemic toxicity of chlordecone can be assumed. The compound is therefore marked with "H".		▲		▲
151-50-8	シアン化カリウム	【ACGIH】 HCN and, though less direct, the cyanide salts can be absorbed through the skin and produce systemic toxicity, including death. Accordingly, a Skin notation is assigned for HCN and the salts. ＊Inorganic cyanides were also reported to be rapid-acting acute poisons to humans and exhibit a dose-response relationship. The primary route of entry in the workplace is by inhalation, and for HCN, absorption through the skin. 【DFG】 In an in vitro study, the permeability constant of human skin for aqueous solutions of cyanides was found to be 3.5 × 10−4 cm/hour. The permeability for an aqueous solution of HCN is almost 30 times higher, 10−2 cm/hour. A further study showed that toxic effects occur within 5 minutes after accidental exposure of a worker's hand to aqueous HCN solution. The designation “H” is therefore retained. The low dermal LD50 of HCN and cyanide salts also supports this designation.	● ▲	● ▲	▲	
151-56-4	エチレンイミン (安定剤入りのもの、別名：アジリジン)	【ACGIH】 ・ Based on the systemic effects resulting from dermal exposure in humans (Reinhardt and Brittelli, 1981), a skin notation is also recommended.	●			
156-62-7	カルシウムシアナミド	【DFG】 ・ Because the substance is readily absorbed through the skin, the designation “H” has been retained. Since studies in humans did not provide evidence of sensitization, the substance is not designated with “Sa” or “Sh” ・ The LD50 for rabbits after dermal application of calcium cyanamide and Perlka were higher than 2000 mg/kg body weight. ・ After 6-hour dermal application of the same dose (20 mg) to 32 cm2, an average of 2.3 mg cyanamide was available for absorption (remainder in the patch and rinse water). 7.7% of this was excreted as acetylcyanamide (= 0.16 mg cyanamide) in the urine of the volunteers. Thus, 0.8% of the total amount administered was recovered (Mertschenk et al. 1991a).	▲	▲		
189-55-9	ジベンゾ［a,i］ピレン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		
189-64-0	ジベンゾ［a,h］ピレン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		
193-39-5	インデノ［1,2,3-cd］ピレン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		
205-82-3	ベンゾ［j］フルオランテン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		
205-99-2	ベンゾ[e]フルオラセン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		
207-08-9	ベンゾ［k］フルオランテン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		
218-01-9	クリセン	【DFG】 ・ The ready skin penetration of individual PAH has been demonstrated in humans and animal studies. There is no reason to assume that there is any substantial difference in the penetration behaviour of PAH. Since absorption via the skin at the workplace is the main contributor to the body burden, PAH are designated with an “H”.	▲	▲		

298-00-0	ジメチルーパラーニトロフェニルチオホスフェイト（別名：メチルパラチオン）	【ACGIH】 ・ The dermal LD50 is 67 mg/kg (Gaines,. 1960) and inhibition of cholinesterase following 10 or 100 mg/kg dermal applications to rabbits (EPA, 1998) suggests the need for a skin notation.		●		
298-02-2	ジチオりん酸O,O-ジエチル-S-エチルチオメチル【ホレート】	【ACGIH】 ・ A skin notation is assigned because symptoms of organophosphate poisoning have been seen following dermal contact with relatively low doses of phorate in animals.		●		
298-04-4	ジチオリン酸O,O-ジエチル-S-(2-エチルチオエチル)(別名：ジスルホトン)	【ACGIH】 ・ A Skin notation is recommended because disulfoton was highly toxic by the dermal route in animals and has produced organophosphate poisoning in workers.	●	●		
300-76-5	りん酸1,2-ジブロモ-2,2-ジクロロエチル=ジメチル	【ACGIH】 ・ A Skin notation is assigned because symptoms of organophosphate poisoning have been seen following dermal contact in animals (lethal concentration in rodents is in the 400 to 800 mg/kg range).		●		
302-01-2	ヒドラジン	【ACGIH】 ・ A Skin notation is recommended, based on the reported rapid and significant absorption and significant systemic toxicity following dermal application of hydrazine to test animals.		●		
309-00-2	1,2,3,4,10,10-ヘキサクロロ-1,4,4a,5,8,8a-ヘキサヒドロ-エキソ-1,4-エンド-5,8-ジメタノナフタレン（別名：アルドリン）	【ACGIH】 ・ A Skin notation is recommended, based on the effects of aldrin in rabbits following relatively low dermal doses.		●		
333-41-5	チオリン酸Ｏ，Ｏ－ジエチル－Ｏ－（２－イソプロピル－６－メチル－４－ピリミジニル）（別名：ダイアジノン）	【ACGIH】 ・ A skin notation was assigned because symptoms of organophosphate poisoning have been seen in humans following dermal contact.	●			
335-67-1	ペルフルオロオクタン酸	【DFG】 ・ No dermal toxicity studies are available for PFOS. In a toxicokinetic study in rabbits, a PFOS concentration of 130 mg/l serum was measured 28 days after a single dermal application of 5000 mg/kg body weight. This is about 10 times higher than the systemic NOAEL in monkeys. Accumulation and increased serum levels of PFOS have to be expected after repeated exposure because of its long half-life. Since absorption through the skin is relatively important for the body burden as compared with inhalation because of the very low MAK value, PFOS and its salts have been labelled with “H”.		▲		▲
420-04-2	シアナミド	【DFG】 ・ On account of the relatively low dermal LD50 via the skin, cyanamide is designated with “H”. ・ According to a publication of SKW from 1973, the dermal LD50 in rabbits is between 2120 and 3200 mg/kg body weight. Apathy, paralysis and dilation of the pupils were observed as signs of systemic intoxication. The gross-pathological examination of rabbits that died yielded swollen liver and haemorrhagic erosions in the stomach. Enlarged periportal hepatocytes, atrophy of the white splenic pulp, haemorrhagic erosions in the stomach, acanthosis and hyper- and parakeratosis were obtained as histopathological findings in the organs; further changes that occurred on the skin are described in Section 6.3 (SKW 1973c). An LD50 of 901 mg cyanamide/kg body weight for males and of 742 mg cyanamide/kg body weight for females was obtained in a repeat study. The animals died within 24 hours after application of the substance. Signs of toxicity included diarrhoea, tremor, ataxia, anorexia and weakness. The application of 1325 mg cyanamide/kg body weight to the rabbit skin caused intensely red lungs and additionally pallor of the kidneys in one animal of the group receiving 2120 mg cyanamide/kg body weight; some of the animals that died intercurrently were not examined by gross pathology (SKW 1988a).		▲		
431-03-8	ジアセチル	【DFG】 ・ In rabbits, the dermal LD50 value was found to be > 5000 mg diacetyl/kg bodyweight (no other details; Opdyke 1979). There are no studies available for the toxicity of diacetyl after repeated epicutaneous application. The acute dermal toxicity is low with an LD50> 5000 mg/kg body weight. The models of Fiserova-Bergerova et al.(1990), Guy and Potts (1993) and Wilschut et al. (1995) yield calculated absorbeddoses of 303, 24 and 70 mg, respectively.After conversion according to the species-specific correction value (1:4), the oralNOAEL of 90 mg/kg body weight and day in rats in the 13-week gavage studywould correspond to 22.5 mg/kg body weight, and after extrapolation to the long-term exposure of persons, 6 mg/kg body weight. For a body weight of 70 kg, theamount of diacetyl absorbed would thus be 420 mg. As the calculated maximumamount dermally absorbed is 303 mg, absorption through the skin could contributeto systemic toxicity. Diacetyl is therefore designated with an“H”(for substanceswhich can be absorbed through the skin).		▲		▲
479-45-8	テトリル	【DFG】 ・ Because of the structural similarity to trinitrotoluene which can be absorbed through the skin, it can be assumed that N-methyl- N,2,4,6-tetranitroaniline is also readily absorbed through the skin. The “S” and “H” designations for substances with sensitizing potential and those absorbed by the skin have therefore been retained.				▲
492-80-8	オーラミン	【DFG】 ・ The data situation is insufficient, but the structural relationship with other aromatic amines suggests a relevant dermal uptake of the substance. The substances are proven genotoxic carcinogens for which, however, no safe exposure can be estimated. Therefore, even small percutaneously absorbed amounts must be assumed to increase the carcinogenic risk. The substances are therefore marked with "H".				▲
505-60-2	ビス（2 - クロロエチル）スルフィド　（別名：マスタードガス）	【DFG】 ・ Because of the danger associated with absorption of bis(β-chloroethyl)sulfide through the skin, the substance is designated with an "H". ・ The substance penetrates the skin readily and produces symptoms of systemic poisoning after a latent period of a few hours. Bis(β-chloroethyl)sulfide is cytotoxic and a capillary poison. It causes brain cell degeneration, bone marrow aplasia, breakdown of blood constituents, reduction in blood pressure and cardiac output, toxic internal haemorrhage, ulcerous inflammation of the mucous membranes of the digestive tract and necrosis in the renal epithelia. The effects are a result of damage to essential enzymes.	▲	▲		

509-14-8	テトラニトロメタン	【DFG】 ・ There are no studies on the dermal route of uptake. Model calculations support a dermal uptake. Tetranitromethane is a genotoxic carcinogen proven in animal studies, for which no safe exposure can be estimated. Therefore, an additional carcinogenic risk must be assumed for dermal exposure at the absorption levels calculated here. Tetranitromethane is therefore marked with "H".				▲
512-56-1	トリメチルホスフェート	【DFG】 ・ Due to the inconclusive carcinogenesis findings and the mutagenic efficacy, which is usually described as weak, TMP is provisionally classified in Group III B of the carcinogenic agents; a MAK value cannot be established. Because of the risk of skin penetration, the substance is given the label "H".				▲
528-29-0	o-ジニトロベンゼン	【ACGIH】 ・ A Skin notation is assigned, based on the ready absorption of dinitrobenzene through the skin and its established contribution to systemic toxicity. Ready absorption of DNB through the skin is a well-emphasized factor in the toxicity and hazard of this substance. (3.5)	●			
534-52-1	4,6-ジニトロ-o-クレゾール	【ACGIH】 ・ The Skin notation is recommended since lethal doses can be absorbed through the skin. 【NIOSH】 ・ Several studies were identified that showed that dinitro-o-cresol is absorbed through the skin following dermal exposure. Dermal acute toxicity studies [Spencer 1948; Dow Chemi- cal Company 1992]* demonstrated that the substance is systemically available and acute- ly toxic. This is supported by case reports of exposure to dinitro-o-cresol [Bidstrup and Payne 1951; Steer 1951; Buchinksii 1974; Jastroch et al. 1978] that resulted in increased sweating, headache, nausea, discoloration of the skin, increased body temperature followed by death in some cases. While it is unclear how much inhalation contributed to dinitro- o-cresol exposure in many of these case re- ports [Bidstrup and Payne 1951; Steer 1951; Jastroch et al. 1978], there was no inhalation exposure in a fatality [Buchinksii 1974] and the health effects were similar to the other case reports identified. Therefore, on the basis of the data for this assessment, dinitro-o-cre- sol is assigned the SK: SYS notation. ・ On the basis of this algorithm, a ratio of the skin dose to the inhalation dose (SI ratio) of 1.08 was calculated for dinitro-o-cresol. An SI ratio of ≥0.1 indicates that a chemical is capable of producing systemic toxicity from skin exposure [NIOSH 2009]; therefore dinitro-o-cresol is considered to be absorbed through the skin following dermal exposure.	● ■	■		■
540-73-8	1,2-ジメチルヒドラジン	【DFG】 ・ 1,2-dimethylhydrazine: There is no practical need for a MAK value for SDMH. Reference is made to the strong carcinogenic effect in animal experiments. ・ 1,1-dimethylhydrazine: Since field experience in humans under analytically controlled exposure conditions is not known, animal experimental findings must be used. They state that 5 ppm still induce anemia, albeit slight, in the anemia-sensitive dog. A maximum tolerated dose has not yet been determined in animal experiments; it can therefore not be ruled out that the currently valid MAK of 0.5 ppm will still cause damage. For this reason, and also taking into account the acute tests in which UDMH is more toxic than hydrazine, the MAK value for UDMH is set at 0.1 ppm. ・ The suffix "H" is necessary because of the rapid absorption through the skin. The marking "S" is to be regarded as a precautionary measure.				▲
542-75-6	1,3-ジクロロプロペン	【ACGIH】 ・ The mortality of rabbits following 24-hour dermal application of 125 and 250 mg/kg DCP as a 10% solution in corn oil provided the basis for the Skin notation.		●		
552-30-7	1,2,4-ベンゼントリカルボン酸1,2-無水物	【ACGIH】 ・ Animal studies indicate that dermal contact may cause or exacerbate respiratory sensitization, providing a justification for a Skin notation.		●		
556-52-5	2, 3-エポキシ-1-プロパノール	【DFG】 ・ Glycidol is genotoxic in vitro and in vivo. After oral administration glycidol was found to be carcinogenic in various organs of the rat and mouse. With regard to its carcinogenic effects, glycidol, a simple aliphatic epoxy compound, therefore joins ranks with a series of analogous substances, which are classified either in Carcinogen category 3 (butyl glycidyl ether, diglycidyl ether, isopropyl glycidyl ether, bisphenol A diglycidyl ether) or in Carcinogen category 2 (glycidyl trimethylammonium chloride, phenyl glycidyl ether). Glycidol has been classified in Carcinogen category 2 in Section III of the List of MAK and BAT Values. The MAK value which was valid until 1999 has therefore been withdrawn. ・ The determination of the acute dermal toxicity of glycidol showed that the substance can be absorbed by the skin and lead to toxic effects. Glycidol is therefore designated with an “H”.		▲		
563-12-2	ビス（ジチオりん酸）S,S'-メチレン-O,O,O',O'-テトラエチル	【ACGIH】 ・ A Skin notation is assigned because symptoms of organophosphate poisoning, irnduding lethality, have been seen following dermal testing in rats (LD50, 62- 245 mg/kg).		●		
582-25-2	安息香酸カリウム塩	【ACGIH】 ・ Existing data indicate significant skin uptake in humans in the range of 40% (Feldmann and Maibach, 1970 and Wester and Maibach, 1976 as cited in Federal Institute for Occupational Safety and Health (BAUA; DE) 2011; Hartwig and MAK Commission 2018; World Health Organization (WHO) 2000). Therefore, skin exposure may contribute important amounts to systemic doses received by inhalation, warranting a skin notation for these substances.	●			
583-60-8	2-メチルシクロヘキサノン	【ACGIH】 ・ The toxicity, including narcosis and death, reported in rabbits following cutaneous application of o-methylcyclohexanone serves as the basis for designation of the Skin notation.		●		

584-84-9	2,4-トリレンジイソシアネート (別名：2,4-トルエンジイソシアネート)	【ACGIH】 ・ A Skin notation is also warranted because induction of respiratory hypersensitivity, a systemic response, occurs by this route. ・ Using the weight of evidence from a series of that in mice, TDI (and has the ability to cause studies, it was concluded other tested isocyanates) respiratory hypersensitivity following dermal exposure (Selgrade et al., 2006). ・ TDI is a recognized sensitizer following its dermal absorption and/or inhalation in the workplace (White et al., 1980; Tarlo et al., 1997; Conner, 2002; Tarlo and Liss, 2002). Workers who have become sensitized to TDI may report dry cough, chest tightness, exertional dyspnea, rhinitis, and wheezing (Weill et al., 1981; Sari-Minodier et al., 1999; Conner, 2002), which are common symptoms in other patients with asthma that is not chemically related.	●	●		
591-78-6	メチル-ノルマル-ブチルケトン	【ACGIH】 ・ A Skin notations assigned, based on data reporting absorption of MnBK through the skin of humans that contributed substantially to the tatal body burden.	●			
594-27-4	テトラメチルスズ	【DFG】 ・ Because of the high acute dermal toxicity of trimethyltin compounds demonstrated in animal experiments (Cincinnati Milacron Chemicals Inc 1971 d, 1974 a) and because of their tenfold higher systemic toxicity compared to dimethyltin compounds, these methyltin species are marked "H". For the same reason (Nalco Chemical Company 1979 b), tetramethyltin is also marked "H".		▲		
598-78-7	２－クロロプロピオン酸	【ACGIH】 ・ A skin absorption study with guinea pigs that indicated the designation of a Skin notation would be appropriate. ・ 2-chloropropionic acid). 2-Chloro-propionic acid was corrosive to the skin and eyes (3,5) and possessed some potential for absorption through the skin in acutely toxic amounts; the dermal LD50 was 0.1 to 1 ml/kg (126 to 1258 mg/kg) for guinea pigs.(3)		●		
615-05-4	２，４－ジアミノアニソール	【DFG】 ・ A relevant dermal uptake of 2,4-diaminoanisole has been documented. The substance is a proven genotoxic carcinogen for which, however, no safe exposure can be estimated. Therefore, it must be assumed that the carcinogenic risk is increased even in the case of small percutaneously absorbed quantities. The substance is therefore marked with "H". ＊A flux of 1.58 µg/cm2 was calculated for 40 min dermal application of dissolved diaminosanisol dihydrochloride to rats (Tsomi and Kalopissis 1982). Animal experiments (Hofer and Hruby 1983 s. [4] in Reason 1985; Marzulli et al. 1981 s. [14] in Justification 1985) and on the basis of studies in humans (Marzulli et al. 1979 s. [15] in Justification 1985; Marzulli et al. 1981 s. [14] in Reason 1985), dermal penetration of 2,4-diaminoanisole could be clearly demonstrated (absorption rates up to 4.7%). Under practical conditions of use as a component of hair dye solutions, the absorption rates were much lower (Maibach and Wolfram 1981; Wolfram and Maibach 1985).	▲	▲		▲
621-64-7	ニトロソジプロピルアミン	【DFG】 ・ N-nitrosodi-n-propylamine is a genotoxic carcinogen proven in animal studies for which no safe exposure level can be estimated. Therefore, additional carcinogenic risk from dermal exposure must be assumed at the resorption levels calculated here. Therefore, N-nitrosodi-n-propylamine is marked with "H". ・ No data are available on the acute dermal toxicity and penetration of N-nitrosodi-n-propylamine. Based on a saturated aqueous solution, a dermal flux of 0.382 mg/cm2/h is calculated for N-nitrosodi-n-propylamine using the model of Fiserova-Bergerova et al. (1990) and 0.035 mg/cm2/h using the model of Guy and Potts 1993. This would correspond to a total intake of 765 mg and 70 mg, respectively, for a one-hour exposure of both hands and forearms (approximately 2000 cm2).				▲
624-83-9	イソシアン酸メチル	【ACGIH】 ・ A Skin notation is recommended based on the mortality seen in rabbits following relatively low dermal doses (Mellon Institute, 1963b). ・ The oral LD50 of MIC in rats is 71 mg/kg (Mellon Institute, 1963b). The LD50 was 210 mg/kg when applied dermally to rabbits.		●		
624-92-0	ジメチルジスルフィド	【ACGIH】 ・ Dermal application of DMDS resulted in the rapid onset of CNS and other systtemic effects in rabbits, therefore, a Skin notation was assigned. ・ Application of undiluted DMDS to the intact skin of rabbits resulted in the rapid onset of CNS and other systemic effects. Loss of righting reflex, spontaneous spasms, lethargy, excessive salivation, nasal discharge, and flared nostrils were noted within 5 minutes of the DMDS application and persisted for approximately 4 hours. (15-17) ・ DMDS (10.6-1063 mg/kg) was repeatedly applied to the intact skin of rabbits for a period up to 28 days. (24) These exposures resulted in severe skin irritation and necrosis. Like the acute studies, there was also evidence of CNS and other systemic effects (e.g., cardiovascular, hemopoietic). The NOEL for systemic effects was 10.6 mg/kg/day (assuming a 70-kg human), which is equivalent to inhalation of approximately 70 mg/m³ (= 20 ppm) over an 8-hour work shift. Based on the acute and subchronic dermal studies, skin absorption can clearly contribute to the overall DMDS exposure.		●		
625-45-6	メトキシ酢酸	【DFG】 ・ At present, no data are available on the skin absorbability of methoxyacetic acid. Model calculations according to Guy and Potts 1993 and Wilschut et al. 1995 give a total absorption of between 396 mg and 902 mg for a one-hour exposure of the hands and forearms (approx. 2000 cm2) to undiluted methoxyacetic acid. However, due to the strong corrosivity and associated protective measures in the workplace, even short-term exposures to undiluted methoxyacetic acid are unlikely. Therefore, a concentration of 2.5% by volume is used as a basis for estimating dermal uptake. This assumption is based on EEC Directive 67/548/EEC (GESTIS 2008), according to which methoxyacetic acid concentrations below 5% are no longer classified as irritating to the skin. For the resulting methoxyacetic acid concentration of 25 g/l, the two model calculations provide a absorption of between 8 mg and 19 mg. In contrast, about 37.4 mg would be absorbed by inhalation under MAK value conditions (c=3.74 mg/m3, respiratory volume approx. 10 m3/shift, 100% retention). According to the model calculations, the contribution of a dermal absorption corresponds to between 21% and 51% of the inhalation absorption. Therefore, the methoxyacetic acid with "H".				▲

628-96-6	ニトログリコール	【ACGIH】 ・ A Skin notation is assigned based on the ability of EGDN to be readily absorbed through intact skin and cause vasodilation as evidenced by headaches among workers dermally exposed to EGDN (Crandall et al., 1931). 【DFG】 ・ In animal studies, absorption through the skin may easily lead to ethylene glycol dinitrate poisoning. Compared with nitroglycerin, ethylene glycol dinitrate is absorbed much more rapidly through the skin of test animals and quickly reaches fatal doses. ・ Based on a study in vivo (Section 4.1), dermal absorption of 800 mg has been estimated for humans after exposure to ethylene glycol dinitrate, assuming the exposure of 2000 cm2 of skin for 1 hour. The systemically tolerable dose calculated from the MAK value at a respiratory volume of 10 m3 is 0.6 mg. Absorption through the skin is therefore markedly higher than the systemically tolerable dose and the substance retains its “H” designation.	● ▲	● ▲		▲
643-79-8	o-フタルアルデヒド	【ACGIH】 ・ A Skin notation is assigned based on evidence of systemic sensitization occurring via skin contact in topically treated mice (Anderson et al., 2010).		●		
646-06-0	1,3-ジオキソラン	【DFG】 ・ There are no human experimental studies available that can be used to evaluate skin absorption. The high dermal LD50 indicates low acute systemic toxicity following dermal application. An 8-hour exposure at a TLV of 100 ml/m3 would result in an inhalation intake of about 3000 mg 1,3-dioxolane (assumption: 10 m3 breathing volume). In comparison, based on the model of Wilschut et al. 1995, a dermal intake of 1626 mg is calculated. Due to the expected dermal absorption, it can be assumed that the internal load is relevantly increased by dermal exposure. Therefore, it is marked with "H".				
650-51-1	ナトリウム=2,2,2-トリクロロアセタート	【DFG】 ・ For sodium trichloroacetate, but not for trichloroacetic acid, skin contact may contribute significantly to systemic toxicity; sodium trichloroacetate is designated with an “H” notation. ・ For humans, a dermal uptake of 6 mg trichloroacetate can be estimated from an in vitro study (Xu et al. 2002) for exposure to a 0.5% non-irritant solution of trichloroacetic acid, assuming a 1-hour exposure of 2000 cm2 skin surface. The oral chronic NOAEL from a feeding study with rats of 32.5 mg/kg bw, converted to an air concentration for humans (see MAK value derivation for systemic toxicity) gives a systemically tolerable level of 225 mg (45 mg/m3 / 2 (animal-human transfer) × 10 m3). Thus, dermal uptake is less than 25% of the systemically tolerable amount, and trichloroacetic acid is not labeled "H." ・If an uptake of 6 mg for 0.5% trichloroacetic acid is used as calculated above, an uptake of 120 mg would be expected for a 10% sodium trichloroacetate solution that is no longer an irritant, using linear extrapolation. For trichloroacetate, the same tolerable amount of 225 mg derived above applies. Thus, dermal uptake is more than 25% of the systemically tolerable amount, and sodium trichloroacetate is marked "H".				▲
680-31-9	ヘキサメチルホスホリックトリアミド	【ACGIH】 ・ A Skin notation is assigned, based on the rabbit dermal application study with HMPA where systemic toxicity and deaths were reported. ・ The acute toxicity of HMPA has been rated as low to moderate with oral LD50 values of 2650 mg/kg in male rats and 3360 mg/kg in female rats. A dermal LD50 of 2600 mg/kg has been reported in rabbits. (4) Clinical signs of systemic toxicity preceding death included alterations of nervous, gastrointestinal, and respiratory systems. ・ Repeated application of HMPA for 3 weeks at 100 to 500 mg/kg to the skin of rabbits caused dose-related weight loss, altered gastrointestinal function, apparent nervous system dysfunction, and mortality.		●		
684-16-2	ヘキサフルオロアセトン	【ACGIH】 ・ A Skin notation is warranted, based on the systemic response seen in rats following denrmal applications and on the possible developmental toxicity seen in rats. ・ HFA (as the sesquihydrate) was applied to the skin of pregnant rats at various dosages on days 6 through 16 of gestation. Maternal toxicity was observed at 90 mg/kg/day. The number of resorptions and live fetuses per litter suggested fetal toxicity at 25 mg/kg with fetal size being reduced at the 5 and 25 mg/kg doses (but not at 1 mg/kg). A small increase in soft tissue and external abnormalities was seen, but a definite teratogenic response could not be concluded.		●		
763-69-9	エチル=3-エトキシプロパノアート	【DFG】 ・ In an acute dermal toxicity study, an LD50 greater than 20 ml ethyl 3-ethoxypropionate/kg bw (approximately 19 000 mg/kg bw) was determined in guinea pigs (n.d.; Eastman Kodak Co 1984 a). ・ Regarding the dermal penetration rate of ethyl 3-ethoxypropionate, there is an in vitro study on human skin in which a resorption rate of 0.73 mg/cm2 and hour was calculated. Based on the usual assumptions (2000 cm2 exposed skin surface, one hour exposure, 70 kg body weight), this would correspond to an intake of about 21 mg/kg bw. If the MAK value is adhered to, 87 mg/kg bw (10 m3 breathing volume/8 h, 70 kg bw) will be absorbed by inhalation. The contribution of dermal exposure to systemic toxicity under the assumed conditions is therefore relevant and the substance is marked "H".		▲	▲	▲
764-41-0	1,4-ジクロロ-2-ブテン	【ACGIH】 ・ The dermal LD50 of 0.62 ml/kg in rabbits justifies a Skin notation.		●		
768-52-5	N-イソプロピルアニリン	【ACGIH】 ・ Some aromatic amino compounds such as N-isopropylaniline, aniline, and N,N-dimethylaniline are known to cause methemoglobinemia in humans following oral, dermal, or inhalation exposure. (4) Following addition of alkyl groups to benzene derivatives, the toxicological properties are usually modified to some degree but remain basically similar to those of the parent compound. Based on analogy with the toxicology of aniline and N,N-dimethylaniline, a TLV-TWA of 2 ppm, with a Skin notation, is currently recommended for N-isopropylaniline. ・ The oral LD50 of N-isopropylaniline be about the same as that of aniline. The oral LD50 for rats is 560 mg/kg. The dermal LD50 for rabbits is 3550 mg/kg.		●		●

838-88-0	4,4'-ジアミノ-3,3'-ジメチルジフェニルメタン (別名：4,4'-メチレンジ-o-トルイジン、4,4'-メチレンビス（2-メチルアニリン))	【DFG】 ・ Data on skin absorption are missing. However, the structure suggests good skin penetration. The structurally analogous 4,4'-diaminodiphenylmethane is marked with "H". 3,3'-Dimethyl-4,4'-diaminodiphenylmethane is a potent genotoxic carcinogen for which, however, no safe exposure can be estimated. Therefore, even small amounts absorbed percutaneously must be expected to increase carcinogenic risk, and the substance is labeled "H" to minimize dermal exposure.				▲
872-50-4	N-メチル-2- ピロリドン【N-メチルピロリドン】	【DFG 1998】 ・ Because of the danger associated with absorption of N-methyl-2-pyrrolidone through the skin, the designation “H” is necessary. ・ Taken as a whole, the results of the reproductive toxicity studies with N-methyl-2-pyrrolidone administered to rats and rabbits orally, dermally and especially by inhalation indicate that the substance, with its new MAK value of 80 mg/m3 (20 ml/m3), is to be classified in Pregnancy risk group C; the possibility of dermal absorption must, however, be ruled out. It is important to remember that the tendency of gaseous N-methyl-2-pyrrolidone to form aerosols and to condense onto skin is affected by the concentration, humidity and temperature. N-Methyl-2-pyrrolidone is readily absorbed through the skin. 【DFG 2010】 ・ As N-methyl-2-pyrrolidone is readily absorbed through the skin, designation with an “H” is still necessary.		▲		
924-16-3	N-ニトロソジ-n-ブチルアミン	【DFG】 ・ Since N-nitrosodi-n-butylamine is a genotoxic carcinogen that has been proven in animal experiments and for which no MAK value can currently be stated, an additional carcinogenic risk must be assumed for the absorption quantities calculated here. Therefore N-nitrosodi-n-butylamine is marked with "H".				▲
930-55-2	N-ニトロソピロリジン	【DFG】 ・ N-nitrosopyrrolidine is a proven genotoxic carcinogen for which, however, no safe exposure level can be estimated. Therefore, even small amounts absorbed percutaneously must be assumed to increase the carcinogenic risk. N-nitrosopyrrolidine is therefore marked with "H".				▲
944-22-9	O-エチル-S-フェニル=エチルホスホノチオロチオナート (別名：ホノホス)	【ACGIH】 ・ Since fonofos is associated with a relatively low dermal LD50 in rats and has caused death when given dermally to rabbits, a skin notation is warranted.		●		
999-61-1	アクリル酸2-ヒドロキシプロピル	【ACGIH】 ・ LD50 values reported for rabbits, to which HPA was topicalyappiled,waranted asignment of the Skin notation.		●		
1024-57-3	１，４，５，６，７，８，８ーヘプタクロロー２，３ーエポキシー３ａ，４，７，７ａーテトラヒドロー４，７ーメタノー１Ｈーインデン　(別名：ヘプタクロルエポキシド)	【ACGIH】 ・ A Skin notation is assigned, based on the systemic toxicity and mortality in animals followiing dermal aplicattiioin of the insecticides.		●		
1116-54-7	N-ニトロソジエタノールアミン	【DFG】 ・ A study on the genesis of skin and lung tumors after repeated dermal exposure of nude mice to a 4% solution of N-nitrosodimethylamine in acetone revealed no skin and lung tumors after 20 weeks of treatment and 80 weeks of observation. However, in contrast to the control group, some lung adenomas appeared, which were considered by the author to indicate dermal penetration (Iversen 1980). ・ In vitro studies of the penetration of N-nitrosodimethylamine through human cadaver skin (static diffusion cell) showed the uptake of approximately 20 µg in the receptor solution after 3 hours when an "infinite-dose" solution of 1 g N-nitrosodimethylamine/l isopropyl myristate was used. This corresponds to a flux of 7 µg/cm2 and hour. In the "finite dose" studies, the authors discuss the evaporation of N-nitrosodimethylamine during the experiments, so that the absorption values (1-4%) are probably significantly too low (Brain et al. 1995). ・ Based on the experimentally determined physicochemical data (miscible with water, log KOW -0.57; SRC 2004), the dermal flux is 1.603 mg/cm2 and hour using the model of Fiserova-Bergerova et al. 1990 and 0.251 mg/cm2 and hour using the model of Guy and Potts 1993. This would correspond to a total intake of 3206 mg and 502 mg, respectively, for a one-hour exposure of both hands and forearms (approximately 2000 cm2).		▲	▲	▲
1120-71-4	１，２ーオキサチオラン＝２，２ージオキシド (別名：1,3-プロパンスルトン)	【DFG】 ・ Since 1,3-propane sultone penetrates the skin in toxic amounts and induces systemic tumours after skin application [29], it is given the designation "H". As a carcinogenic and unequivocally mutagenic substance, it cannot be classified in any of the pregnancy groups. Pregnant women should avoid any occupational contact with 1,3-propane sultone.		▲		
1300-73-8	キシリジン	【ACGIH】 ・ Based on the central nervous system effects and methemoglobin formation seen in cats that received repeated cutaneous applications of 2,4-xylidine, the Skin notation is warranted.		●		
1303-28-2	五酸化ニ砒素	【DFG】 ・ Arsenic and its inorganic arsenic compounds were previously not designated with an “H” (for substances that can be absorbed through the skin in toxicologically relevant amounts) (documentation “Arsenic and its inorganic compounds (with the exception of arsine)” 2005; supplement “Arsenic and its inorganic compounds (with the exception of arsine)” 2014). ・ Arsenic and its inorganic arsenic compounds are classified in Category 1 for carcinogenic substances and in Category 3 A for germ cell mutagens. No MAK value could be established. No safe concentration range can therefore be estimated for exposure to the skin-penetrating compounds, so that an increased carcinogenic or genotoxic risk should be assumed even for low amounts absorbed percutaneously. Dermal penetration has been demonstrated for pentavalent arsenic compounds, for trivalent arsenic compounds it may be assumed. The extent of penetration doubtless depends on the solubility of the substance, so that the inorganic arsenic compounds, with the exception of arsenic itself and gallium arsenide, which are both very poorly soluble in water, are designated with an “H”.				▲

1319-77-3	クレゾール	【ACGIH】 ・ A Skin notation is warranted because dermal LD 50 values, along with evidence from accidental human exposure, show that systemic toxicity can result from skin exposure (Larcan et al., 1974; Green, 1975). ・ Dermal LD 50 values for rats of 620, 1100, 750, and 825 mg/kg body weight were derived for o-, p-, m-, and m-/p-cresols, respectively (IPCS, 1995). Dermal LD50 values for a single dose applied to the skin of three female albino New Zealand rabbits were: 2000, 890, 2380, 300 mg/kg body weight for technical cresol (mixed isomers), o-, p-, and m-cresols, respectively. ・ In addition, o-, m- and p-cresols showed tumor-promoting activity in the skin of groups of about 30 albino mice exposed to DMBA (dimethylbenzanthracene) in acetone (Boutwell and Bosch, 1959). ・ Exogenous cresols are absorbed rapidly across the skin, lungs, and gastrointestinal tract and spread quickly through the body. In vitro human skin is very permeable to cresols (Roberts et al., 1977). In vitro, 70% of the p-cresol applied to mouse skin was transported in six hours (Hinz et al., 1991). ・ In some cases, fatalities are thought to have been a result of skin contact with preparations containing cresols causing severe skin burns, scarring, and systemic toxicity (Larcan et al., 1974; Green, 1975).	●	●	●	
1321-64-8	ペンタクロロナフタレン	【ACGIH】 ・ A Skin notation is assigned based on the demonstrated absorption of pentachloronaphthalene through the intact skin of treated animals.		●		
1321-65-9	トリクロロナフタレン	【ACGIH】 ・ Based on data showing chlorinated naphthalenes can be absorbed dermally, a Skin notation is appropriate for trichloronaphthalene. 【DFG】 ・ Absorption through the skin was seen with pentachloronaphthalene and is also probable for all other chlorinated naphthalenes. All chlorinated naphthalenes are therefore designated with an “H”. ・ Because of the lack of data, the possibility cannot be excluded that even when the MAK value for trichloronaphthalenes is set at 1 mg/m3 and for pentachloronaphthalenes at 0.1 mg/m3, liver damage may occur in individual persons. This also applies for other chlorinated naphthalenes, such as monochlorinated and dichlorinated naphthalenes, which are considered to be more like trichlorinated naphthalenes, and tetrachlorinated, hexachlorinated and higher chlorinated naphthalenes, which are considered to be more like pentachlorinated naphthalenes. Chlorinated naphthalenes are therefore included in Section IIb of the List of MAK and BAT Values.]		● ▲		▲
1327-53-3	三酸化ニヒ素(亜ヒ酸)	【DFG】 ・ Arsenic and its inorganic arsenic compounds were previously not designated with an “H” (for substances that can be absorbed through the skin in toxicologically relevant amounts) (documentation “Arsenic and its inorganic compounds (with the exception of arsine)” 2005; supplement “Arsenic and its inorganic compounds (with the exception of arsine)” 2014). Arsenic and its inorganic arsenic compounds are classified in Category 1 for carcinogenic substances and in Category 3 A for germ cell mutagens. No MAK value could be established. No safe concentration range can therefore be estimated for exposure to the skin-penetrating compounds, so that an increased carcinogenic or genotoxic risk should be assumed even for low amounts absorbed percutaneously. Dermal penetration has been demonstrated for pentavalent arsenic compounds, for trivalent arsenic compounds it may be assumed. The extent of penetration doubtless depends on the solubility of the substance, so that the inorganic arsenic compounds, with the exception of arsenic itself and gallium arsenide, which are both very poorly soluble in water, are designated with an “H”.				▲
1330-20-7	キシレン	【DFG】 ・ As described in Section 2, dermal exposure to liquid xylene can contribute consider-ably to the body burden and the toxic effects. Xylene is therefore designated with an “H”.As a result of a lack of data, xylene is at present not designated with an “S” (for sub-stances with sensitization potential).	▲	▲		▲
1331-22-2	メチルシクロヘキサノン（異性体混合物）	【産衛】 メチルシクロヘキサノンの生体作用は、大量曝露では麻酔性と皮膚・粘膜に対する刺激作用が特徴である.また皮膚吸収も認められ, 経皮吸収によるウサギの最小致死量は4.9~7.2g/kg, LD50 は 1.77g/kgとされている (LD50: ラットの経口投与で 2.14g/kg, マウスの腹腔内投与で200mg/kg,)		★		
1335-87-1	ヘキサクロロナフタレン	【ACGIH】 ・ Reports of systemic toxicity in animals and humans following dermal contact with hexachloronaphthalene warrant assignment of the Skin notation.	●	●		
1336-36-3 11097-69-1 53469-21-9	ポリクロロビフェニル	【ACGIH】 ・ The recommended Skin notation is based on the reported fatty degeneration of the liver following dermal application of PCB 1242 to experimental animals.		●		
1402-68-2	アフラトキシン	【DFG】 ・ Both in vitro and in vivo experiments show a low dermal penetration capacity of aflatoxin B1 through animal and human skin, but systemic effects in mice after epidermal application. Since aflatoxins are genotoxic carcinogens proven for humans, for which no MAK value can be given at present, an additional carcinogenic risk must be assumed for the measured resorption rates. Therefore, aflatoxins are marked with "H".		▲	▲	▲
1477-55-0	メタ - キシリレンジアミン	【ACGIH】 ・ By analogy with p-phenylenediamine, a TLV-Ceiling of 0.018 ppm with a Skin notation has been recommended since 1976. However, the Skin notation was deleted in the case of p-phenylenediamine in 1991. ・ A dermal LD50 value of 2000 mg/kg was found for rabbits.		●		●

1569-02-4	プロピレングリコールエチルエーテル (別名：1-エトキシ-2-プロパノール)	【ACGIH】 ・ A Skin notation is recommended because data show that significant amounts can be absorbed through the skin and contribute significantly to overall exposure at the recommended TLV- TWA (Korinth et al., 2012). ・ A dermal LD50 of 8100 mg/kg (9 mL/kg) was reported in rabbits. No skin irritation was observed; however, marked CNS depression was reported and deaths occurred within 48 hours (Boatman, 2001). ・ As with other propylene glycol ethers, PGEE is expected to be readily absorbed through the skin and respiratory tract. The a- isomer is metabolized by alcohol dehydrogenase with propylene glycol and carbon dioxide as the principal metabolites (Miller et al., 1983), with a small amount excreted as glucuronide and sulfate conjugates. The ß- isomer, ・ The rate of pure PGEE penetration in vitro through human skin was determined to be approximately 1400 + 400 µg/cm²/hour and increased by around 50% to around 2100 ± 100 µg/cm²/hour when applied as a 50% aqueous solution (Korinth et al., 2012). Therefore, the amount that could be absorbed over the course of an 8-hour work shift through 100 cm² of exposed skin could be as much as 1680 mg. This approximates the dose of 2125 mg associated with 8 hours of exposure at the TLV- TWA of 50 ppm (assuming 100% absorption).		●	●	●
1675-54-3	ビスフェノールAジグリシジルエーテル	【DFG】 ・ The in vivo studies demonstrate that glycidaldehyde formed from bisphenol A diglycidyl ether can bind to DNA in the skin. Because the DNA is contained in structures under the skin barrier, this DNA binding must be seen as a systemic effect, especially as it cannot be assumed that a substance which binds to dermal DNA is captured entirely by this reaction. Therefore and because bisphenol A diglycidyl ether is a genotoxic substance, the designation with an “H” is retained.				▲
1746-01-6	2,3,7,8-テトラクロロジベンゾ-1,4-ジオキシン	【DFG】 ・ In vitro studies indicate only a slow dermal penetration ability of TCDD through human skin. However, due to the strong cumulative ability of TCDD, a marking with "H" is carried out.			▲	
1763-23-1	ペルフルオロ（オクタン－１－スルホン酸）	【DFG】 ・ No dermal toxicity studies are available for PFOS. In a toxicokinetic study in rabbits, a PFOS concentration of 130 mg/l serum was measured 28 days after a single dermal application of 5000 mg/kg body weight. This is about 10 times higher than the systemic NOAEL in monkeys. Accumulation and increased serum levels of PFOS have to be expected after repeated exposure because of its long half-life. Since absorption through the skin is relatively important for the body burden as compared with inhalation because of the very low MAK value, PFOS and its salts have been labelled with “H”.		▲		▲
1910-42-5	1,1'-ジメチル-4,4'-ビピリジニウム=ジクロリド (別名：パラコートジクロリド)	【ACGIH】 ・ A Skin notation is recommended, as a single dermal application to rodents produces genotoxicity (D'Souza et al., 2005) and repeated applications cause decreased sperm count and increased sperm abnormalities (D'Souza et al., 2006). The acute dermal LD50 for rats is reporrted as 80 mg/kg (Kimbraugh and Gaines, 1970), while in rabbits, the subacute dermal LD50 (20 days) is 4.5 mg/ kg/day (McElligott, 1972).		●		
2074-50-2	パラコートジメチルサルフェート	【ACGIH】 ・ A Skin notation is recommended, as a single dermal application to rodents produces genotoxicity (D'Souza et al., 2005) and repeated applications cause decreased sperm count and increased sperm abnormalities (D'Souza et al., 2006). The acute dermal LD50 for rats is reporrted as 80 mg/kg (Kimbraugh and Gaines, 1970), while in rabbits, the subacute dermal LD50 (20 days) is 4.5 mg/ kg/day (McElligott, 1972).		●		
2104-64-5	O-エチル=O-4-ニトロフェニル=フェニルホスホノチオアート (別名：EPN)	【ACGIH】 ・ A Skin notation is assigned because relatively low doses applied to rabbit skin produced lethality. ・ Dermal LD50 values were 230 and 25 mg/kg for male and female rats, respectively, when EPN was applied in acetone to their shaved backs. (8) A dermal LD50 for the rabbit was 30 mg/kg, (10) and the lethal range for dermal exposure to EPN in rabbits was 30 to 50 mg/kg in males and 150 to 900 mg/kg in females. ・ Delayed neurotoxicity was produced in cats following the administration of either a single dermal dose of 22.5, 45, 112.5, or 225 mg/kg (0.2 to 5.0 times the dermal LD50 of 45 mg/kg) or repeated doses of 0.5, 1.0, or 2.0 mg/kg technical grade EPN. (20) Single dermal doses of 9.0 mg/kg and repeated dermal doses of 0.1 mg/kg were without effect. The cat appears about 10 times less sensitive than the hen to EPN-induced delayed neurotoxicity.		●		
2234-13-1	オクタクロロナフタレン	【ACGIH】 ・ Exposure of animals to chlorinated naphthalenes has produced severe liver injury, and skin absorption has been suggested. Accordingly, and by analogy with hexachloronaphthalene, a TLV-TWA of 0.1 mg/m³ and a TLV-STEL of 0.3 mg/m³, with a Skin notation, are recommended for octachloronaphthalene.		●		●
2243-62-1	1,5-ジアミノナフタレン	【DFG】 ・ There are no data for the absorption of the substance through the skin. The models predict only very slight absorption through the skin. The calculations for the related 2-naphthylamine predict an even lower level of absorption, yet it is designated with an ”H”. In analogy to other aminoaromatic substances and naphthalene itself, which are designated with an ”H”, and in view of its carcinogenic effects, also 1,5-diaminonaphthalene has been designated with an ”H”. There are no data available that would justify classification of the substance in a category for germ cell mutagenicity.				▲
2425-06-1	N-（1,1,2,2-テトラクロロエチルチオ）-1,2,3,6-テトラヒドロフタルイミド【キャプタフォル】	【ACGIH】 ・ Although the lethal dose following acute exposure to captafol is very high, the reported effects following dermal contact in humans (Krieger, 2001; Arimatsu, 1970) suggest a Skin notation should be recommended.		●		
2426-08-6	ノルマル-ブチル=2,3-エポキシプロピルエーテル	【ACGIH】 ・ A Skin notation is warranted, based on the finding that male germ cell mutagenicity results from the application of BGE to the skin.		●		

2431-50-7	2,3,4-トリクロロ-1-ブテン	【DFG】 ・ A dermal LD50 is not available. However, an insufficiently documented study indicates mortality by dermal application. Physicochemical data similar to 1,4-dichloro-2-butene suggest similarly good dermal absorption. 1,4-Dichloro-2-butene is marked "H" due to the demonstrated dermal absorption (dermal LD50 = 735 mg/kg bw see justification "1,4-dichlorobutene" 2000). By analogy, 2,3,4-trichloro-1-butene is also marked with "H", since a significant absorption via the skin can be assumed.		▲		▲
2465-27-2	オーラミン塩酸塩	【DFG】 ・ The data situation is insufficient, but the structural relationship with other aromatic amines suggests a relevant dermal uptake of the substance. The substances are proven genotoxic carcinogens for which, however, no safe exposure can be estimated. Therefore, even small percutaneously absorbed amounts must be assumed to increase the carcinogenic risk. The substances are therefore marked with "H".				▲
2528-36-1	りん酸ジ-ノルマル-ブチル=フェニル	【ACGIH】 ・ Based on the significanlt reduction of cholineslterase activities in rabbits treated with dibutyl phenylphosphate by dermal application, a Skin notation is assigned.		●		
2687-91-4	1-エチルピロリジン-2-オン	【DFG】 ・ There are no quantitative data available for the absorption of N-ethyl-2-pyrrolidone through the skin. Model calculations for the exposure of both hands and forearms for 1 hour to a saturated aqueous solution yielded the dermal absorption of between 80 and 444 mg (1.1 and 6.3 mg/kg body weight at a body weight of 70 kg; see Section 4.1). An extrapolated dose of 17.5 mg/kg body weight was obtained for humans on the basis of the dose of 100 mg/kg body weight from the 90-day feeding study in rats (toxicokinetic species-specific correction value (1:4), daily exposure of the animals in comparison with the 5 days per week exposure at the workplace (7:5) and extrapolation from animal studies to humans). As the estimated dermal absorption is more than 25% of the extrapolated oral dose for humans, the dermal route of exposure may significantly contribute to the total body burden. Therefore, N-ethyl-2-pyrrolidone has been designated with an “H” (for substances which can be absorbed through the skin).				▲
2807-30-9	2-プロポキシエタノール	【DFG】 ・ The dermal LD50 for guinea pigs after occlusive contact with the substance for 24 hours is between 1000 and 5000 mg/kg body weight (Katz et al. 1984). In the rabbit, dermal LD50 values of 960 (Smyth et al. 1969) and 870 mg/kg body weight were found (Boatman 1994). These values indicate that the substance is readily absorbed by the skin. ・ Groups of 5 guinea pigs were given doses of 0.5 ml undiluted 2-propoxyethanol applied non-occlusively to the dorsal skin daily for 11 days; the skin irritation observed was somewhat more severe than after short-term occlusive exposure (see Section 6.3). Mortality was not observed, systemic effects were not investigated (Katz et al. 1984). ・ As the substance is readily absorbed in dangerous amounts by the skin it is designated with an “H”. ・ No data have been published on the effects in man of 2-propoxyethanol. The eye irritation found in animal experiments and the effects in man of the homologous 2-butoxyethanol (see documentation from 1983 in Volume 6 of the present series) suggest that irritative effects of 2-propoxyethanol on the eyes and nose are also to be expected in man.		▲	▲	
2921-88-2	チオりん酸O,O-ジエチル-O-(3,5,6-トリクロロ-2-ピリジル) (別名：クロルピリホス)	【ACGIH】 ・ A Skin notation is assigned because relativeliy low doses apped to rabit skin produced lethality. Effects following exposure from dermal contact with chlorpyrifos have not been reported in humans, and dermal absorption does not appear to be extraordinarily high. However, animal studies suggest that dermal absorption may be signiflcant, and the lethal dose follawing appllication the skin of riabbits is relatively low hence, a Skin notation is assigned.		●		
3333-52-6	テトラメチルコハク酸ニトリル	【ACGIH】 ・ A Skin notation is assigned based on the dermal lethal dose for rabbits of 100 mg/kg (DuPont, 1970) and dermal LDL of 79.4 mg/kg in rabbits (Monsanto Co., 1974), on the acute lethality of TMSN (Doherty et al., 1982), and on reports that other structurally related dinitriles, e.g., adiponitrile and succinonitrile, can be absorbed dermally, causing systemic toxicity and death in animals (Hartung, 1991) (see the current TLV Documentation for Adiponitrile).		●		●
3383-96-8	テメホス	【ACGIH】 ・ A Skin notation is assigned because symptoms of organophosphate poisoning have been seen in humans and animals following dermal contact.	●	●		
3689-24-5	オキシビス（チオホスホン酸）O,O,O',O'-テトラエチル【スルホテップ】	【ACGIH】 ・ A Skin notation is assigned because symptoms of organophosphate poisoning have been seen following dermal contact in animals.		●		
3766-81-2	2-s-ブチルフェニルN-メチルカーバメート	【産衛】 ラットの急性経口 LD50 は 524mg/kg (雄) 425 mg/kg (雌) であり, 急性経皮LD50 は 5,000mg/kg (雄,雌) である		★		
3811-73-2	ナトリウム＝１－オキソ－１λ（５）－ピリジン－２－チオラート	【DFG】 ・ Sodium pyrithione is readily absorbed from the gastrointestinal tract and through the skin; independent of the route of uptake, the substance is of low toxicity. Even single high doses cause reversible damage to the peripheral nervous system of rodents; such damage is not seen in monkeys or dogs even after exposure for several days or a year. As a warning that the substance can readily be absorbed through the skin, it is designated with an “H”. ・ Studies with sodium 2,6-14C-pyrithione and 8 test persons have demonstrated that the dermal absorption of sodium pyrithione depends markedly on the solvent used. ・ After dermal application of radioactively labelled sodium pyrithione, 1 % to 7 % of the applied radioactivity was detected in the urine of monkeys (Min et al. 1970, Parekh et al. 1970), rats (Min et al. 1970, Olin Corporation 1989e, Parekh et al. 1970), mice (Olin Corporation 1975), rabbits (Howlett and Van Abbe 1975) and pigs (Wedig et al. 1974). ・ After dermal application of sodium pyrithione to rats, muscle damage and paralysis of the hind limbs were observed. The NOEL (no observed effect level) was given as 5 mg/kg body weight and day (Olin Corporation 1988b). ・ The NOEL for embryotoxic or teratogenic effects is thus 3.5 or 3 mg/kg body weight and day for rats given the substance orally or dermally and 5 mg/kg body weight and day for rabbits after dermal application.	▲	▲		
3825-26-1	ペンタデカフルオロオクタン酸アンモニウム	【ACGIH】 ・ A Skin notation is assigned, based on liver damage and elevated blood organofluoride levels in dermally treated rats.		●		

3926-62-3	クロロ酢酸ナトリウム	【DFG】 ・ For humans, a dermal uptake of 3.7 mg of monochloroacetate can be estimated from an in vitro study (Xu et al. 2002) for exposure to a 0.5% non-irritant solution of monochloroacetic acid, assuming a one-hour exposure of 2000 cm2 of skin surface. From the above conversions of the NOAELs of the oral rat studies, the systemic tolerable concentration for humans is approximately 4 mg/m3 and, assuming 100% inhalation absorption and 10 m3 respiratory volume, the tolerable intake is 40 mg. Thus, dermal uptake is less than 25% of the systemically tolerable amount. Therefore, monochloroacetic acid is not marked with "H". ・ If, as calculated above, an uptake of 3.7 mg for 0.5% monochloroacetic acid is taken as a basis, an uptake of 37 mg would be expected for a non-irritant 5% monochloroacetate solution using linear extrapolation. For monochloroacetate, the same tolerable amount derived above of approximately 40 mg applies. Thus, dermal uptake is more than 25% of the systemically tolerable amount, and sodium monochloroacetate is marked "H".			▲	▲
4170-30-3	2-ブテナール（別名:クロトンアルデヒド（(E)-2-ブテナールと(Z)-2-ブテナールの異性体混合物））	【ACGIH】 ・ A Skin notation is assigned based on the dermal LD50 of 26 mg/kg of body weight for crotonaldehyde-treated guinea pigs.		●		
4685-14-7	1,1'-ジメチル-4,4'-ビピリジニウム（別名：パラコート）	【ACGIH】 ・ A Skin notation is recommended, as a single dermal application to rodents produces genotoxicity (D'Souza et al., 2005) and repeated applications cause decreased sperm count and increased sperm abnormalities (D'Souza et al., 2006). The acute dermal LD50 for rats is reporrted as 80 mg/kg (Kimbraugh and Gaines, 1970), while in rabbits, the subacute dermal LD50 (20 days) is 4.5 mg/ kg/day (McElligott, 1972).		●		
5216-25-1	p-（トリクロロメチル）クロロベンゼン（別名p - クロロベンゾトリクロリド）	【DFG】 ・ The tumours detected in the gastrointestinal tract after dermal application are probably also a result of ingestion of the substance. A genotoxic potential for the substance is indicated by the positive results obtained in gene mutation tests with prokaryotes and mammalian cells. Therefore p-chlorobenzotrichloride is classified in Category IIIA2 in the “List of MAK and BAT Values”. Because of the marked dermal absorption, the substance must be designated with an “H”.		▲		
5392-40-5	3,7 - ジメチル - 2,6 - オクタジエナール（別名シトラール）	【ACGIH】 ・ There is evidence that citral can penetrate the skin of rats and is rapidly transported around the body affecting, for example, the rat's prostate; therefore, a Skin notation is justified (Servadio et al., 1986; Geldof et al., 1992; Scolnik et al., 1994a; Engelstein et al., 1996).		●		
6423-43-4	二硝酸プロピレン	【ACGIH】 ・ Because PGDN can readily be absorbed through the skin causing systemic effectls andl by analogy with EGON, the Skin notation is considered appropriate. ・ A 20-day subacute dermal toxicity study at 1 g PGDN/kg showed minor skin irritation; however, at 2 g/kg, rabbits became weak and cyanotic with profound dyspnea. One of five rabbits died; reduced hemoglobin and hematocrit values were documented at death. At the 4-g/kg dose, methemoglobin values increased to 34.5% at death. These latter observations, coupled with greatly increased serum and urinary nitrates, indicate ready absorption through the skin. ・ A group of 87 workers employed in the manufacture of torpedoes was studied to evaluate the possible acute and chronic neurophysiologic toxicity of PGDN. During the period when actual tests were conducted, airborne PGDN peak concentrations ranged from nondetectable to 0.22 ppm. Nearly 90% of all measured peak concentrations were at or below 0.1 ppm. Evaluation of these workers included both quantitative oculomotor functions and quantitative ataxia tests. Although some acute effects were measured, there was no evidence for chronic neurotoxicity. The only headache, which occurred during the study, was that of a worker exposed during an accidental spill. The authors (6) postulated that headaches were a result of exposure to higher airborne levels or that perhaps dermal absorption had contributed to the total absorbed dose.	●	●		●
6923-22-4	りん酸ジメチル=（E）-1-メチル-2-（N-メチルカルバモイル）ビニル	【ACGIH】 ・ A Skin notation is assigned because symptoms of organophosphate poisoning, including lethality, have been seen folllowiing dermal testri'ng in rats (LD50 values,112 to 126 mg/kg).		●		
7439-97-6	水銀	【ACGIH】 ・ Elemental mercury has been rapidly absorbed by inhalation, moderately absorbed tthrough ttne skin and slowly absorbed through the gastrointestinaltract. Inorganic mercury compounds have been absorbed somewhat less rapidly th rougtn inhalation, being influenced by chemical and physical characteristics. ・ There is extensive literature on animals exposed by different routes of exposure to various forms of mercury compounds. The extensive review by Friberg and Vostal(3) contained detailed information on the uptake, distribution, absorption, and effects of mercury exposure in animals. ・ Skin absorption of mercury has long been recognized as a route of exposure for mercury. Friberg and Vostal(3) discussed this aspect in detail. Hursh et al. (33) conducted a skin absorption study from airborne mercury vapor on five individuals and reported that the rate of uptake through the skin was 2.2% of the rate through the lung. ・ Data clearly indicate that mercury can affect both male and female reproductive outcomes. It has not been possible to unequivocally determine a safe exposure level for protection of reproduction function in either male or female workers, particularly since many studies did not adequately evaluate dermal exposure.	●	●		
7440-28-0	タリウム及びその化合物	【ACGIH】 ・ The observations of percutaneous absorption in animals (Butcher, 1964), reports of toxic effects including alopecia in workers (Richeson, 1958), and toxicity following topical use of thallium for treatment of ringworm (AMACD, 1957) support the need for a Skin notation.	●	●		

7440-38-2	砒素	【DFG】 ・ Arsenic and its inorganic arsenic compounds were previously not designated with an “H” (for substances that can be absorbed through the skin in toxicologically relevant amounts) (documentation “Arsenic and its inorganic compounds (with the exception of arsine)” 2005; supplement “Arsenic and its inorganic compounds (with the exception of arsine)” 2014). ・ Arsenic and its inorganic arsenic compounds are classified in Category 1 for carcinogenic substances and in Category 3 A for germ cell mutagens. No MAK value could be established. No safe concentration range can therefore be estimated for exposure to the skin-penetrating compounds, so that an increased carcinogenic or genotoxic risk should be assumed even for low amounts absorbed percutaneously. Dermal penetration has been demonstrated for pentavalent arsenic compounds, for trivalent arsenic compounds it may be assumed. The extent of penetration doubtless depends on the solubility of the substance, so that the inorganic arsenic compounds, with the exception of arsenic itself and gallium arsenide, which are both very poorly soluble in water, are designated with an “H”.				▲
7440-41-7	ベリリウム	【ACGIH】 ・ There are no human data for skin absorption; however, considering that the lethal dose to rabbits following dermal exposure was 390 mg/kg, a Skin notation for this chemical is recommended.		●		
7440-48-4	コバルト	【DFG】 ・ Several studies in volunteers and laboratory animals are available that demonstrate dermal uptake of water-soluble cobalt compounds in vivo. In addition, in vitro studies have shown that metallic cobalt can also penetrate human skin. ・ Since cobalt and its compounds are substances that have been shown to be clearly genotoxic carcinogens in animal studies, the dermal penetration levels found in subject trials suggest that dermal exposure may pose an additional cancer risk. Therefore, cobalt and cobalt compounds are marked with "H".	▲	▲		▲
7440-61-1	ウラン	【DFG】 ・ In rabbits, dermal application of various soluble uranium compounds caused mortality and a marked increase in the elimination of protein with the urine. As far as the poorly soluble uranium compounds uranium tetrafluoride, uranium dioxide, uranyl peroxide or triuranium octaoxide are concerned, no mortality and no signs of intoxication were found in rabbits after dermal application. The elimination of protein with the urine was, however, increased. Thus, in spite of the experimental limitations, this study provides evidence for the absorption of uranium compounds through the skin. ・ On the basis of the flux from the study of Petitot et al. 2004, the absorption of 36.1 µg uranyl nitrate per hour through intact pig skin can be calculated for an exposed skin surface of 2000 cm2. This rate of dermal absorption can make a relevant contribution to the body burden. Soluble uranium compounds, uranium and poorly soluble uranium compounds are therefore given the designation “H” (for substances which can be absorbed through the skin).		▲		▲
7664-39-3	フッ化水素酸	【ACGIH】 ・ Because of concern for the corrosive and skin penetrating properties of hydrogen fluoride, a Skin notation is assigned.		●		
7778-39-4	砒酸	【DFG】 ・ Arsenic and its inorganic arsenic compounds were previously not designated with an “H” (for substances that can be absorbed through the skin in toxicologically relevant amounts) (documentation “Arsenic and its inorganic compounds (with the exception of arsine)” 2005; supplement “Arsenic and its inorganic compounds (with the exception of arsine)” 2014). ・ Arsenic and its inorganic arsenic compounds are classified in Category 1 for carcinogenic substances and in Category 3 A for germ cell mutagens. No MAK value could be established. No safe concentration range can therefore be estimated for exposure to the skin-penetrating compounds, so that an increased carcinogenic or genotoxic risk should be assumed even for low amounts absorbed percutaneously. Dermal penetration has been demonstrated for pentavalent arsenic compounds, for trivalent arsenic compounds it may be assumed. The extent of penetration doubtless depends on the solubility of the substance, so that the inorganic arsenic compounds, with the exception of arsenic itself and gallium arsenide, which are both very poorly soluble in water, are designated with an “H”.				▲
7784-46-5	亜砒酸ナトリウム	【DFG】 ・ Arsenic and its inorganic arsenic compounds were previously not designated with an “H” (for substances that can be absorbed through the skin in toxicologically relevant amounts) (documentation “Arsenic and its inorganic compounds (with the exception of arsine)” 2005; supplement “Arsenic and its inorganic compounds (with the exception of arsine)” 2014). ・ Arsenic and its inorganic arsenic compounds are classified in Category 1 for carcinogenic substances and in Category 3 A for germ cell mutagens. No MAK value could be established. No safe concentration range can therefore be estimated for exposure to the skin-penetrating compounds, so that an increased carcinogenic or genotoxic risk should be assumed even for low amounts absorbed percutaneously. Dermal penetration has been demonstrated for pentavalent arsenic compounds, for trivalent arsenic compounds it may be assumed. The extent of penetration doubtless depends on the solubility of the substance, so that the inorganic arsenic compounds, with the exception of arsenic itself and gallium arsenide, which are both very poorly soluble in water, are designated with an “H”.				▲
7786-34-7	りん酸ジメチル＝１－メトキシカルボニル－１－プロペン－２－イル　（別名：メビンホス）	【ACGIH】 ・ A skin notation is assigned because symptoms of organophosphate poisoning, including lethality, have been seen following dermal application to rats (LD50 from 4 to 5 mg/kg).		●		
7803-57-8	ヒドラジン一水和物	【産衛】 許容濃度勧告では、無水ヒドラジン(302-01-2)およびヒドラジン一水和物(7803-57-8)は、ひとまとめにして、「皮」が付されている。無水ヒドラジン (302-01-2)の場合は、ACGIH, OSHA, DFGでSkin Notationあり.				
8001-35-2	塩素化カンフェン（別名：トキサフェン）	【ACGIH】 ・ A Skin notation is assigned based on the absorption of chlorinated camphene through intact and abraded skin of treated rabbits leading to systemic CNS effects and lethality.		●		

8006-64-2	テレピン油	【DFG】 ・ The dermally absorbed quantities of α-pinene and β-pinene calculated from in vitro penetration experiments with human epidermis and whole skin diverge greatly from 78 mg to 266 g and 43 mg to 81 g, respectively, assuming one-hour exposure to turpentine oil of 2000 cm2 of skin. It is unclear which of the two experiments is more relevant for the in vivo situation. An 8-hour exposure to the substance at the level of the MAK value (28 mg/m3) would result in the uptake of 280 mg turpentine oil, assuming complete absorption at a respiratory volume of 10 m3. Even taking the lower of the two values obtained for dermal absorption as a basis, the uptake of α-pinene and β-pinene through the skin is in sum more than 25% of the systemically tolerable amount, so that turpentine oil is designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).			▲	▲
8008-20-6	灯油	【ACGIH】 ・ Based on the systemic toxicities reported in rodents and in humans after repeated topical applications of kerosene or jet fuel, the skin notation is warranted.	●	●		
8022-00-2	ジメチルエチルメルカプトエチルチオホスフェイト【メチルジメトン】	【ACGIH】 ・ A Skin notation is assigned, based on the cholinergic and liver response seen in rats following repeated dermal exposures to relatively low doses of methyldemeton. ・ Rats receiving 15 daily dermal applications of methyl demeton at 5 mg/kg/day failed to show any overt signs of toxicity. However, partially reversible degeneration and necrosis of the liver, and reversible cholinesterase inhibition in the brain and serum were noted. 【NIOSH OSHA PEL Project Documentation 1988】 Dermal toxicity is reported to be moderate, with an LD(50) of approximately 400 mg/kg (Heath and Vandekar 1965, as cited in ACGIH 1986/Ex. 1-3, p. 388).		● ■		
8052-42-4	アスファルト (ストレートアスファルト)	【DFG】 ・ Bitumen, vapour and aerosols, is designated with an “H” because skin penetration by the carcinogenic substances has been demonstrated in animal studies. ・ Ten male nonsmokers were exposed to 20 mg/m3 of vapors and aerosols from bitumen (bitumen B65, 88% vapor content, bitumen condensate standard) for eight hours at rest using a respirator. This was to determine the exclusive absorption of bitumen through the skin. Two of these subjects were also exposed without a respirator. Urine was analyzed for metabolites of chrysene, phenanthrene, and pyrene before, during, and up to 24 hours after exposure. Thus, the dermally and inhalationally absorbed fractions could be measured via urinary metabolite excretion. The dermally absorbed fraction of chrysene, phenanthrene, and pyrene in the total intake after exposure via air was about 50 to 60% (Walter and Knecht 2007). ・ These DNA adducts could be observed in the same tissues of BD4 rats in previous studies by the same research group (Genevois et al. 1996) after dermal application. ・ Systemic DNA adducts are formed after epicutaneous application of bitumen vapor condensates to rats (Genevois et al. 1996; Begründung 2001). A subject study (Walter and Knecht 2007) indicates a good absorption of bitumen emissions from the gas phase. The previous marking with "H" is therefore retained.		▲		
8065-48-3	チオりん酸Ｏ，Ｏ－ジエチル－エチルチオエチル（別名：ジメトン）	【ACGIH】 ・ The Skin notation is assigned since symptoms of organophosphate poisoning have been seen following dermal contact in animals (lethal concentration in rodents was in the 10 to 15 mg/kg range).		●		
9016-87-9	α－（イソシアナトベンジル）－ω－（イソシアナトフェニル）ポリ［（イソシアナトフェニレン）メチレン］	【DFG】 ・ The available studies indicate that, after dermal exposure, MDI and PMDI mainly react with molecular components of the skin, and thus only very small quantities are absorbed systemically in unchanged form. In humans, intensive skin contact with MDI can, however, play a role in the induction of specific hyperreactivity of the airways. As technical-grade PMDI contains a considerable amount of monomeric MDI, similar effects are to be assumed. As the prevention of respiratory sensitization was one of the decisive criteria for establishing the MAK value, and this critical effect can also be caused by skin contact, both MDI and PMDI are designated with an “H” (for substances which can be absorbed through the skin).				▲
10595-95-6	N-ニトロソメチルエチルアミン	【DFG】 ・ Since N-nitrosomethylethylamine is a genotoxic carcinogen that has been proven in animal experiments and for which no MAK value can currently be stated, an additional carcinogenic risk must be assumed for the absorption quantities calculated here. Therefore N-nitrosomethylethylamine is marked with "H".				▲
11070-44-3	テトラヒドロメチル無水フタル酸	【ACGIH】 ・ A Skin notation is based on animal data demonstrating the potential to cause respiratory sensitization following dermal absorption (Dearman et al., 2000).		●		
11097-69-1	ポリクロロビフェニル	【ACGIH】 ・ A Skin notation is recommended based on the liver toxicity reported among animals treated dermally with PCB 1254.		●		
12079-65-1	シクロペンタジエニルトリカルボニルマンガン	【ACGIH】 ・ Systemic toxicity, including mortality, in rats treated by tail immersion in MCT warrants assignment of the Skin notation.		●		
12108-13-3	2-メチルシクロペンタジエニルトリカルボニルマンガン	【ACGIH】 ・ MMT penetrates intact skin very rapidly, producing adverse effects on the CNS.	●	●		
13071-79-9	テルブホス	【ACGIH】 ・ A Skin notation is assigned because of the potency seen following dermal application to animals; lethality in rodents occurs with exposure of approximately 1 mg/kg.		●		
13429-07-7	1-（2-メトキシ-2-メチルエトキシ）-2-プロパノール	【NIOSH OSHA PEL Project Documentation 1988】 ・ 34590-94-8参照				
13463-41-7	2-ピリジンチオール-1-オキシドの亜鉛塩（別名：ジンクピリチオン）	【DFG】 ・ As a warning that the substance can readily be absorbed through the skin, it is designated with an “H”. ・ Sodium pyrithione is readily absorbed from the gastrointestinal tract and through the intact skin. The substance is excreted rapidly in the form of urinary metabolites. ・ The LD50 of sodium pyrithione after application of single dermal doses to rabbits (Olin Corporation 1987c) is of the same order of magnitude (1800 mg/kg body weight) as that found after administration of single oral doses to rats (Olin Corporation 1987b)		▲		

13530-65-9	クロム酸亜鉛	【ACGIH】 ・ Skin notation is assigned for Cr(VI) compounds based on the systemic absorption of chromium following dermal exposures to water-soluble Cr(VI) compounds, which can be detected by increased chromium excretion in the urine.				●
14977-61-8	オキシ塩化クロム（ＶＩ）(別名：塩化クロミル)	【ACGIH】 ・ In the absence of human or animal toxicity information for chromyl chloride, and no specific occupational exposure data, the recommended TLV is based on that for water-soluble Cr(VI) compounds.				●
16752-77-5	S-メチル-N-[（メチルカルバモイル）オキシ]チオアセトイミデート	【ACGIH】 ・A Skin notation is recommended based on AChE inhibitory signs when the compound was applied to rabbit skin (Brock, 1989) and in humans after dermal exposure (Cable and Doherty, 1999; Tsatsakis et al., 2001).	●	●		
17702-41-9	デカボラン	【ACGIH】 ・ A Skin notation is assigned, based on data that indicates the high hazard from dermal absorption, with systemic toxicity, including CNS effects. ・ The LD50 values for dermal application to rabbits and rats are 71 ppm and 740 ppm, respectively. The symptoms of acute decaborane toxicity are loss of coordination, convulsions, weakness, tremors, hyperexcitability, and narcosis with primary tissue effects on the kidneys and liver. ・ Significant health hazards were found from all practical routes of entry, especially the skin. By some routes of administration (percutaneous) and in some species (rats and rabbits), but not in all, toxicity to the CNS was intensified over that from single exposures.	●	●		
22224-92-6	N - イソプロピルアミノホスホン酸O - エチル - O -（3 - メチル - 4 - メチルチオフェニル）　（別名フェナミホス）	【ACGIH】 ・ A Skin notation is assigned since lethality has occurred in animals dermally exposed to fenamiphos. ・ In vitro dermal absorption of pure fenamiphos by human and rat skin accounted for 0.42% to 9.95% of the applied dose. ・ Dermal LD50 values for technical fenamiphos were 72 to 154 mg/kg in rats and 178 to 225 mg/kg in rabbits. ・ In rabbits whose clipped dorsal skin was treated with 0, 0.5, 2.5, or 10 mg/kg fenamiphos for 6 hours/day on 21 consecutive days, slight erythema of abraded skin lasting 3 to 6 days plus inhibition of plasma, RBC, and brain cholinesterase occurred at doses of 2.5 and 10 mg/kg. Cholinergic effects were not reported at any dose.		●	●	
22781-23-3	2,2-ジメチル-1,3-ベンゾジオキソール-4-イル-N-メチルカルバマート (別名：ベンダイオカルブ)	【ACGIH】 ・ A Skin notation is assigned because clinical signs of neurotoxicity have been seen following dermal contact with repeated exposures of 50 mg/ kg bendliocarb producing AChE inhibition in rats (Sanderson, 1972 as cited in FAO and WHO, 1982).		●		
25154-54-5	ジニトロベンゼン (異性体混合物)	【ACGIH】 ・ A Skin notation is assigned, based on the ready absorpt ion of dinitrobenzene through the skin and its established contribution to systemic toxicity. 【NIOSH】 ・ DNB is potentially capable of causing adverse systemic effects following skin con- tact. A critical review of available data has resulted in the following SK assignment for DNB: SK: SYS (Methemoglobinemia Limited human data) ・ Ishihara et al. [1976] reported a case of m-DNB intoxication involving a woman exposed to an aque- ous mixture containing 0.5% (weight by weight; w/w) m-DNB while handling parts immersed in the aqueous mixture. After ruling out the possibility of exposure via the inhalation of vaporized m-DNB, Ishihara et al. [1976] concluded that the main route of exposure was dermal absorp- tion, despite the use of personal protective equipment in the form of latex gloves. Ad- ditional evidence of the ability of DNB to be dermally absorbed was identified in an investigation of the onset of five cases of methemoglobinemia in workers employed as steam-press operators in a rubber plant [NIOSH 1987]. The workers applied an adhesive to bond metal studs into rubber bumper strips, without wearing gloves. Bulk analysis revealed that the adhesive was contaminated with p-DNB (1% w/w). The report indicated that the main route of entry for p-DNB was skin absorption. The workers experienced yellowing of the hands, cyanosis of the lips and nail beds, headache, dizziness, nausea, chest pain, confusion, and difficulty in concentration [NIOSH 1987]. ・ No in vivo or in vitro toxicokinetic stud- ies that evaluated the potential of DNB to be absorbed through human or animal skin were identified. ・ No dermal lethal concentration (LDLo) for humans has been identified for DNB. In addition, no dermal LD50 value (the dose resulting in 50% mortality in the exposed. population) for animals has been reported. No additional acute toxicity was identi- fied for DNB. ・ On the basis of this algorithm, a ratio of the skin dose to the inhalation dose (SI ratio) of 0.12 was cal- culated for DNB. An SI ratio of ≥0.1 indi- cates that a chemical is capable of produc- ing systemic toxicity from skin exposure [NIOSH 2009].	● ■			■
25321-14-6	ジニトロトルエン (異性体混合物)	【ACGIH】 ・ Studies of workers in the explosives industry indicate that dermal contact may be the major route of absorption from exposure to DNT. Accordingly, a Skin notation is assigned. Biological monitoring of workers exposed to DNT provides additional support for the TLV Skin notation.	●			
26471-62-5	メチル-1,3-フェニレン=ジイソシアネート	【ACGIH】 ・ A Skin notation is also warranted because induction of respiratory hypersensitivity, a systemic response, occurs by this route.	●	●		
26530-20-1	2-n-オクチル-4-イソチアゾリン-3-オン	【DFG】 ・ 2-Octyl-4-isothiazolin-3-one is designated with an “H” because, on the one hand, the LD50 values obtained in the dermal test with rabbits and the oral test with rats are similar and, on the other hand, the lowest observed effect level (LOEL) for systemic effects in the 90-day dermal test was very low, about 15 mg/kg body weight and day. In addition, it has been demonstrated in vivo and in vitro that the substance readily penetrates the skin.		▲	▲	
26628-22-8	アジ化ナトリウム	【NIOSH OSHA PEL Project Documentation 1988】 ・ Dr. Hecker of Abbott Laboratories (Ex. 3-678) commented that the limit for sodium azide should include a skin notation, and Sax and Lewis (Dangerous Properties of Industrial Materials, 7th ed., 1989) report the dermal LD(50) in rabbits to be 20 mg/kg, demonstrating that sodium azide readily penetrates the skin and causes systemic poisoning. Grace Ziem, an independent occupational physician, also supported a skin notation for sodium azide (Ex. 46). In the final rule, OSHA is therefore adding a skin notation for sodium azide.				

26952-21-6	イソオクタノール	【ACGIH】 ・ Systemic toxicity in the form of central nervous system depression, dyspnea, and ataxia following dermal administration to rabbits of isooctyl alcohol warrant recommendation of a Skin notation.		●		
31242-93-0	塩素化ジフェニルオキシド	【DFG】 ・ Since dermal administration of 0.2 ml of a 10% hexachlorodiphenyl oxide emulsion once a week for four weeks to the inner ear of 4 rabbits resulted in systemic effects (Powers et al. 1975), the previous marking with "H" remains in place.		▲		
34590-94-8	ジプロピレングリコールメチルエーテル	【NIOSH OSHA PEL Project Documentation 1988】 ・ Rowe and associates (1954/Ex. 1-435) reported a single acute oral LD(50) for rats of 5.4 ml/kg. Even at the highest levels tested (not further specified), no single application of DPGME to the skin of rabbits was lethal, although some narcosis and transient weight loss did occur. However, a significant number of deaths occurred in a group of rabbits treated with 65 repeated dermal applications containing DPGME concentrations of 3 ml/kg or higher during a 90-day period. ・ The ARCO Chemical Company (Ex. 3-740) questioned the appropriateness of a skin notation for this substance. In response to ARCO, the Agency notes that DPGME, applied essentially according to the Draize method, is absorbed in sufficient quantities through rabbit skin to cause transient narcosis, although the absorption rate was not considered acutely dangerous (Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C, p. 3990, Clayton and Clayton 1982). Topical administration of 10 mg/kg DPGME five times per week for 13 weeks to shaved rabbit skin caused six deaths among seven animals (Chemical Hazards of the Workplace, 2nd ed., p. 221, Proctor, Hughes, and Fischman, 1988). To date, there are no human data demonstrating that dermal contact with DPGME is without a significant adverse health risk; therefore, in accordance with the policy described in Section VI.C.18, OSHA finds that the available evidence does not meet the criterion for deleting an existing skin notation.		■		
35400-43-2	ジチオりん酸O-エチル-O-（4-メチルチオフェニル）-S-n-プロピル	【ACGIH】 ・ A skin notation is assigned because mortality was seen in animals given relatively low acute dermal doses (Jones, 1994).		●		
35554-44-0	（RS） - 1 - （ベータ - アリルオキシ - 2,4 - ジクロロフェネチル）イミダゾール（別名イマザリル）	【DFG】 ・ After exposure at the level of the MAK value, the amount absorbed is 20 mg for a respiratory volume of 10 m3 per day. Assuming standard conditions (2000 cm2, 1 hour), the absorbed quantities calculated using the models are in the range between 3 and 213 mg. Epicutaneous exposure could thus contribute to systemic toxicity. The substance is therefore designated with an “H” (for substances that can be absorbed through the skin).				▲
53469-21-9	ポリクロロビフェニル	【ACGIH】 ・ A Skin notation is recommended based on the liver toxicity reported among animals treated dermally with PCB 1254. ・ The material was shown to be absorbed through the skin, causing fatty degeneration of the liver in exposed animals.		●		
95465-99-9	S,S-ビス（1-メチルプロピル）=O-エチル=ホスホロジチオアート（別名：カズサホス）	【ACGIH】 ・ A Skin notation is assigned because symptoms of organophosphate poisoning have been seen following dermal contact in animals (lethal concentration in rodents is in the 40- 70 mg/kg range) (De Prospo, 1986; Rand, 1983b).		●		
111988-49-9	チアクロプリド	【ACGIH】 ・ A Skin notation is recommended because repeated dermal application to Wistar rats induces liver and tlilyroid responses similar to those elicited by inhalation and feeding (Kroetlinger and Sander, 1997 as cited in FAO and WHO, 2008).		●		
592-01-8	シアン化カルシウム	【ACGIH】 ・ HCN and, though less direct, the cyanide salts can be absorbed through the skin and produce systemic toxicity, including death. Accordingly, a Skin notation is assigned for HCN and the salts. ・ Inorganic cyanides were also reported to be rapid-acting acute poisons to humans and exhibit a dose-response relationship. The primary route of entry in the workplace is by inhalation, and for HCN, absorption through the skin. 【DFG】 ・ In an in vitro study, the permeability constant of human skin for aqueous solutions of cyanides was found to be 3.5 × 10−4 cm/hour. The permeability for an aqueous solution of HCN is almost 30 times higher, 10−2 cm/hour. A further study showed that toxic effects occur within 5 minutes after accidental exposure of a worker's hand to aqueous HCN solution. The designation “H” is therefore retained. The low dermal LD50 of HCN and cyanide salts also supports this designation.	● ▲	● ▲	▲	

別添2 急性経皮毒性区分1に分類されていた18物質

番号	CAS	物質名	用途等	OEL	log Kow	Vapor P	ばく露経路	動物種	LD50, 100*	文献	原文入手
1	77-77-0	Divinyl sulfone ジビニルスルホン	クロス架橋剤	-	0.6	0.78	skin	rabbit	22 uL/kg	American Industrial Hygiene Association Journal., 23(95), 1962 [PMID:13914538]	○
							subcutaneous	rat	14 mg/kg	Journal of Pharmacology and Experimental Therapeutics., 93(1), 1948	-
							subcutaneous	mouse	16 mg/kg		
2	78-97-7	Lactonitrile	溶剤、乳酸、酢酸エチル合成の中間体	-	-0.3	0.119	skin	rabbit	20 uL/kg	American Industrial Hygiene Association Journal., 30(470), 1969 [PMID:5823428]	○
							subcutaneous	rabbit	5.2 mg/kg	Archives Internationales de Pharmacodynamie et de Therapie., 5(161), 1899	-
3	82-66-6	diphacinone ダイファノシン	農薬 (殺鼠剤)	-	3.7	1.30E-10	skin	rat	200 mg/kg	Pesticide Manual., 9(310), 1991	-
4	88-85-7	Butaphene ブタフェン (ジノセブ)	フェノール系除草剤，殺ダニ剤，農業殺菌剤	-	3.6	8.50E-02	skin	rat	80 mg/kg	World Review of Pest Control., 9(119), 1970	-
							subcutaneous	rat	20 mg/kg	Journal of Pharmacy and Pharmacology., 4(1062), 1952 [PMID:13023562]	○
							skin	mouse	40 mg/kg	Toxicology and Applied Pharmacology., 7(353), 1965	○
							skin	rabbit	80 mg/kg	Pesticide Manual., 9(306), 1991	-
							skin	guinea pig	500 mg/kg	Journal of Industrial Hygiene and Toxicology., 30(10), 1948	○
5	92-13-7	pilocarpine ピロカルピン	医薬品 (緑内障点眼)	−	1.1	−	subcutaneous	rat	366 mg/kg	Drugs in Japan, 6(APP-16), 1982	-
							subcutaneous	mouse	90.9 mg/kg		
6	107-11-9	allylamine アリルアミン	農薬原料、高分子化合物の改質剤	-	0.1	242	skin	rabbit	35 mg/kg	Archives of Environmental Health, 1,343,1960	○
7	107-16-4	Glycolonitrile グリコロニトリル	溶剤、殺菌剤、防カビ剤および医薬品の合成時の有機中間体	NIOSH	-0.7	0.8	skin	rabbit	5 mg/kg	American Industrial Hygiene Association Journal, 23,95,1962	○
							subcutaneous	mouse	15 mg/kg	Archives Internationales de Pharmacodynamie et de Therapie., 12(447), 1904	-
8	119-38-0	Isolan イソラン	アブラムシ駆除剤、殺虫剤	-	1.4	1.30E-03	skin	rat	5.6 mg/kg	Wirksubstanzen der Pflanzenschutz und Schadlingsbekampfungsmittel, Perkow, W., Berlin, Verlag Paul Parey, 1971-1976, -(-), 1971/1976	-
9	297-78-9	isobenzan イソベンザン (テロドリン)	有機塩素系殺虫殺菌剤	-	4.6	2.92E-03	skin	rabbit	12 mg/kg	Pesticide Chemicals Official Compendium, Association of the American Pesticide Control Officials, Inc., 1966., -(1099), 1966	-
							skin	guinea pig	2 mg/kg	Aldrin Dieldrin Endrin and Telodrin: An Epidemiological and Toxicological Study of Long-Ter Occupational Exposure, Jager, K.W., New York, Elsevier Science Pub. Co., 1970, -(88), 1970	-
							skin	rat	5 mg/kg	World Review of Pest Control., 9(119), 1970	-
10	297-97-2	O,O-Diethyl O-(2-pyrazinyl) thiophosphate (Thionazin) チオナジン	土壌殺虫剤、殺線虫剤	-	2	3.00E-03	skin	rat	8 mg/kg	Special Publication of the Entomological Society of America., 78-1(46), 1978	-
							skin	guinea pig	10 mg/kg	Guide to the Chemicals Used in Crop Protection., 6(498), 1973	-
							skin	duck	7 mg/kg	Toxicology and Applied Pharmacology., 47(451), 1979 [PMID:442090]	○
11	333-29-9	Phosfolan ジエチル-(1,3-ジチオシクロペンチリデン)-チオホスホルアミド	殺虫剤・防虫剤	−	3.6	-	skin	rabbit	23 mg/kg	Guide to the Chemicals Used in Crop Protection., 6(200), 1973	-
							skin	bird - wild	10 mg/kg	Toxicology and Applied Pharmacology., 26(154), 1973 [PMID:4748134]	○

12	351-05-3	p-Bromo-2-fluoroacetanilide モノフルオール酢酸パラブロムアニリド	殺虫剤・防虫剤	−	2.7	-	skin	rat	7 mg/kg	Agricultural and Biological Chemistry., 31(1294), 1967	○
							skin	mouse	71 mg/kg	Agricultural and Biological Chemistry., 31(1294), 1967	
13	470-90-6	Chlorfenvinphos クロルフェンビンホス	農薬（殺虫剤）（失効農薬）	−	3.1	7.50E−06	skin	mouse	336 mg/kg	Oyo Yakuri. Pharmacometrics. (Oyo Yakuri Kenkyukai, CPO Box 180, Sendai 980-91, Japan) V.1- 1967-	-
							skin	rabbit	400 mg/kg	Toxicology and Applied Pharmacology. (Academic Press, Inc., 1 E. First St., Duluth, MN 55802) V.1- 1959-	-
							skin	rat	26.4 mg/kg	Acta Physiologica Polonica. (Karger-Libri, POB CH-4009, Warszawa, Switzerland) V.1-41, 1950-90.	-
14	556-61-6	Methyl isothiocyanate イソチオシアン酸メチル	農業用土壌燻蒸剤	-	0.9	3.54	skin	rat	2780 mg/kg	Wirksubstanzen der Pflanzenschutz und Schadlingsbekampfungsmittel, Perkow, W., Berlin, Verlag Paul Parey, 1971-1976, -(-), 1971/1976	-
							skin	mouse	1820 mg/kg		-
							skin	rabbit	33 mg/kg	Toxicology and Applied Pharmacology., 42(417), 1977 [PMID:595018]	○
15	786-19-6	carbophenothion カルボフェノチオン	殺虫・殺ダニ剤	-	5.3	3.00E-07	skin	rat	27 mg/kg	Toxicology and Applied Pharmacology., 2(88), 1960 [PMID:13825957]	○
							skin	rabbit	1270 mg/kg	Pesticide Chemicals Official Compendium, Association of the American Pesticide Control Officials, Inc., 1966., -(200), 1966	-
							subcutaneous	chicken	640 mg/kg	Biochemical Pharmacology., 12(1377), 1963 [PMID:14096425]	○
16	5827-05-4	S-(ethylsulfinyl)methyl O,O-di(isopropyl) dithiophosphate Aphidan アフィダン	有機リン系殺虫剤	-	2.7	-	skin	rat	28 mg/kg	Pesticide Manual., 8(361), 1987	-
							skin	mouse	1300 mg/kg		
17	12185-10-3	Phosphorus (yellow) 黄りん	赤りん、りん酸、りん化合物（塩化りん、硫化りん）の原料、高純度りん（半導体用）	ACGIH NIOSH OSHA DFG	/	2.60E-02	skin	rat	29 mg/kg	Ben-Hur N, Giladi A, Neuman Z, et al. 1972. Phosphorus burns: A pathophysiological study. Br J Plast Surg 25:238-244.	○
							skin	rat	100 mg/kg	Ben-Hur N, Appelbaum J. 1973. Biochemistry, histopathology and treatment of phosphorus burns: An experimental study. Isr J Med Sci 9:40-48.	-
							skin	rat	* 181.8 mg/kg	Eldad A. Simon GA. 1991. The phosphorus burn - a preliminary comparative experimental study of various forms of treatment. Burns 17:198-200.	○
18	13194-48-4	ethoprophos エトプロホス	殺虫剤 (失効農薬)	-	3.6	3.80E-04	skin	duck	11 mg/kg	Toxicology and Applied Pharmacology, 47,451,1979	○
							skin	chicken	3 mg/kg	Toxicologist, 5,26,1985	-
							skin	rabbit	2.4 mg/kg	United States Patent Document. (U.S. Patent Office, Box 9, Washington, DC 20231), #6193990	-
							skin	rat	60 mg/kg	World Review of Pest Control. (London, UK) V.1-10, 1962-71. Discontinued., 9,119,1970	-