

OECD GUIDELINE FOR THE TESTING OF CHEMICALS

DRAFT PROPOSAL FOR A NEW GUIDELINE: 435

***In Vitro* Membrane Barrier Test Method for Skin Corrosion**

INTRODUCTION

1. Skin corrosion refers to the production of irreversible damage to the skin, manifested as visible necrosis through the epidermis and into the dermis, following the application of a test material [as defined by the United Nations (UN) Globally Harmonised System for the Classification and Labelling of Chemical Substances and Mixtures (GHS)] (1). This Test Guideline provides an *in vitro* procedure by which the assessment of corrosivity is not carried out in live animals.

2. A number of *in vitro* test methods have been proposed as alternatives for the standard *in vivo* rabbit skin procedure (OECD TG 404)(2) used to identify corrosive substances. This Test Guideline is for an *in vitro* membrane barrier test method that can be used to identify corrosive substances. The test method utilizes an artificial membrane designed to respond to corrosive substances in a manner similar to animal skin *in situ*.

3. Skin corrosivity has traditionally been assessed by applying the test substance to the skin of living animals and assessing the extent of tissue damage after a fixed period of time (2)(3). The UN GHS tiered testing and evaluation strategy for the assessment and classification of skin corrosivity allows for the use of validated and accepted *in vitro* test methods (1). In this tiered strategy, positive results from *in vitro* test methods can be used to classify a substance as corrosive without the need for animal testing, thus reducing and refining the use of animals in testing. Substances that are negative undergo additional testing in accordance with the tiered testing strategy (1)(see supplement to Test Guideline 404(2)). The use of *in vitro* test methods to identify corrosive substances can therefore avoid the pain and distress that might occur when animals are used for this purpose.

4. Validation studies have been completed for an *in vitro* membrane barrier test method commercially available as Corrositex[®] (4)(5)(6). Based on its acknowledged validity, this validated reference test method has been recommended for use as part of a tiered testing strategy for assessing the dermal corrosion hazard potential of chemicals (5). Before an *in vitro* membrane barrier test method for skin corrosion can be used for regulatory purposes, its reliability, accuracy, and limitations for its proposed use should be determined to ensure that it is comparable to that of the validated reference test method (7)(8)(9)(10).

5. A limitation of the validated reference test method (5) is that many non-corrosive chemicals and chemical mixtures and some corrosive chemicals and chemical mixtures do not qualify for testing. Aqueous substances with a pH in the range of 4.5 to 8.5 often do not qualify for testing; however, 85% of chemicals tested in this pH range were non-corrosive in animal tests (5). The *in vitro* membrane barrier test methods may be used to test solids (soluble or insoluble in water), liquids (aqueous or non-aqueous), and emulsions; however, test chemicals and chemical mixtures not causing a colour change in the Chemical Detection System (CDS) of the validated reference test method cannot be tested with the membrane barrier test method and should be tested using other test methods. The samples may be pure chemicals, dilutions, formulations, or waste. No prior treatment of the sample is required.

6. This Test Guideline provides a third *in vitro* method for skin corrosivity testing. The other test methods are based on the use of reconstituted human skin (OECD TG 431)(11) and isolated rat skin (OECD TG 430)(12).

DEFINITIONS

7. Definitions used are provided in Annex 1.

INITIAL CONSIDERATIONS

8. The test described in this Guideline allows the identification of corrosive chemical substances and mixtures and allows the subcategorisation of corrosive substances as permitted in the GHS (Table 1)(1). In addition, such a test method may be used to make decisions on the corrosivity and non-corrosivity of specific classes of chemicals, *e.g.*, organic and inorganic acids, acid derivatives¹, and bases for certain transport testing purposes (5)(13)(14). This Test Guideline describes a generic procedure similar to a validated reference test method (5).

Table 1. The UN GHS Skin Corrosive Category and Subcategories (1)

Corrosive Category (category 1) (applies to authorities not using subcategories)	Potential Corrosive Subcategories (only applies to some authorities)	Corrosive in ≥ 1 of 3 animals	
		Exposure	Observation
Corrosive	Corrosive subcategory 1A	≤ 3 minutes	≤ 1 hour
	Corrosive subcategory 1B	> 3 minutes / ≤ 1 hour	≤ 14 days
	Corrosive subcategory 1C	> 1 hour / ≤ 4 hours	≤ 14 days

PRINCIPLE OF THE TEST

9. This test method is composed of two components, a synthetic macromolecular bio-barrier and a CDS; the basis of this test method is that it detects membrane barrier damage caused by corrosive test substances after the application of the test substance to the surface of the artificial membrane barrier (5), presumably by the same mechanism(s) of corrosion that operate on living skin.

10. Penetration of the membrane barrier (or breakthrough) might be measured by a number of procedures, including a change in the colour of a pH indicator dye or in some other property of the indicator solution below the barrier.

11. The membrane barrier should be determined to be valid, *i.e.*, relevant and reliable, for its intended use. This includes ensuring that different preparations are consistent in regard to barrier properties, *e.g.*, capable of maintaining a barrier to non-corrosive substances, able to categorize the corrosive properties of chemicals across the various subcategories of corrosivity (1). The classification assigned is based on the time it takes a substance to penetrate through the membrane barrier to the indicator solution.

¹ "Acid derivative" is a non-specific class designation and is broadly defined as an acid produced from a chemical substance either directly or by modification or partial substitution. This class includes anhydrides, halo acids, salts, and other types of chemicals.

PROCEDURE

12. The following is a generic description of the components and procedures of an artificial membrane barrier test method for corrosivity assessment (7)(15). The membrane barrier and the qualification, categorisation and indicator solutions can be constructed, prepared or obtained commercially, *e.g.*, Corrositex®. A sample test method protocol for the validated reference test method can be obtained at [<http://iccvam.niehs.nih.gov>]. Testing should be performed at ambient temperature (17-25°C) and the components should comply with the following.

Test Substance Compatibility Test

13. Prior to performing the membrane barrier test, a compatibility test is performed to determine if the test substance is detectable by the CDS. The CDS and the exposure conditions used for the compatibility test should reflect the exposure in the subsequent membrane barrier test. If the CDS does not detect the test substance, the membrane barrier test method is not suitable for evaluating the potential corrosivity of that particular test substance and a different test method should be used.

Test Substance Categorisation Test

14. If appropriate for the test method, a test substance that has been qualified by the qualification test should be subjected to a categorization test, *i.e.*, a screening test to distinguish between weak and strong acids or bases. Two different breakthrough timescales should be used for determining corrosivity and GHS skin corrosivity subcategory, based on the acid or alkali reserve of the chemical.

Membrane Barrier Test Method Components

Membrane Barrier

15. The membrane barrier should consist of two components: a proteinaceous macromolecular aqueous gel and a permeable supporting membrane. The proteinaceous gel should be impervious to liquids and solids but can be corroded and made permeable. The fully constructed membrane barrier should be stored under pre-determined conditions shown to preclude deterioration of the gel, *e.g.*, drying, microbial growth, shifting, cracking, which would degrade its performance. The acceptable storage period should be determined and membrane barrier preparations not used after that period.

16. The permeable supporting membrane provides mechanical support to the proteinaceous gel during the gelling process and exposure to the test substance. The supporting membrane should prevent sagging or shifting of the gel and be readily permeable to all test substances.

17. The proteinaceous gel, composed of protein, *e.g.*, keratin, collagen, or mixtures of proteins, forming a gel matrix, serves as the target for the test substance. The proteinaceous material is placed on the surface of the supporting membrane and allowed to gel prior to placing the membrane barrier over the indicator solution. The proteinaceous gel should be of equal thickness and density throughout, and with no air bubbles or defects that could affect its functional integrity.

Chemical Detection System (CDS)

18. The indicator solution responds to the presence of a test substance. A pH indicator dye or combination of dyes, *e.g.*, cresol red and methyl orange, that will show a colour change in response to the

presence of the test substance or other types of chemical or electrochemical reactions can be used. The measurement system can be visual or electronic.

19. Detection systems that are developed for detecting the passage of the test substance through the barrier membrane should be assessed for their relevance and reliability in order to demonstrate the range of substances that can be detected and the quantitative limits of detection.

Test Performance

Assembly of the Test Method Components

20. The membrane barrier is positioned in a vial (or tube) containing the indicator solution so that the supporting membrane is in full contact with the indicator solution and with no air bubbles present. Care should be taken to ensure that barrier integrity is maintained.

Application of the Test Substance

21. A suitable amount of the test substance, *e.g.*, 500 µL of a liquid or 500 mg of a finely powdered solid (5), is carefully layered onto the upper surface of the membrane barrier and evenly distributed. An appropriate number of replicates, *e.g.*, four (5), is prepared for each test substance and its corresponding controls. The time of applying the test substance to the membrane barrier is recorded. To ensure that short corrosion times are accurately recorded, the application times of the test substance to the replicate vials are staggered.

Measurement of Membrane Barrier Penetrations

22. Each vial is appropriately monitored and the time of the first change in the indicator solution, *i.e.*, barrier penetration, is recorded, and the elapsed time between application and penetration of the membrane barrier determined.

Controls

23. In tests that involve the use of a vehicle or solvent with the test substance, the vehicle or solvent should be compatible with the membrane barrier system, *i.e.*, not alter the integrity of the membrane barrier system, and should not alter the corrosivity of the test substance. When applicable, solvent (or vehicle) control should be tested concurrently with the test substance to demonstrate the compatibility of the solvent with the membrane barrier system.

24. A positive (corrosive) control chemical, *e.g.*, sodium hydroxide pellets (7), should be tested concurrently with the test substance to demonstrate the reliability of the test method. A second positive control that is of the same chemical class as the test substance may be useful for evaluating the relative corrosivity potential of a corrosive test substance. The positive control(s) should allow detection of penetration through the barrier membrane that is both over and under the expected (historical) performance of the assay. For this purpose, extremely corrosive (GHS subcategory 1A) or non-corrosive chemicals are of limited utility. A corrosive GHS subcategory 1B substance would allow detection of a too rapid or too slow breakthrough time. A weak substance (GHS subcategory 1C) might be employed to measure the ability of the test method to consistently distinguish between corrosive and non-corrosive substances. Regardless of the approach used, an acceptable positive control response range should be developed based on the historical range of breakthrough times for the positive control substances(s)

employed. In each study, the exact breakthrough time should be determined for the positive control so that deviations outside the acceptable range can be detected.

25. A negative (non-corrosive) control substance, *e.g.*, 10% citric acid, 6% propionic acid (7), should also be tested concurrently with the test substance as another quality control measure to demonstrate the functional integrity of the membrane barrier.

Study Acceptability Criteria

26. According to the established time parameters for each of the GHS corrosivity subcategories, the time (in minutes) elapsed between application of a test substance to the membrane barrier and barrier penetration is used to predict the corrosivity of the test substance. For a study to be considered acceptable, the concurrent positive control should give the expected penetration response time, the concurrent negative control should not be corrosive, and, when included, the concurrent solvent control should neither be corrosive nor should it alter the corrosivity potential of the test substance. To demonstrate technical proficiency with the validated reference test method, the user may evaluate the twelve chemicals recommended in Table 2. However, the performance standards described in Annex 2 of this Test Guideline should be used to demonstrate the reliability and accuracy of proposed test methods that are structurally and functionally similar to the validated reference test method (16).

Interpretation of Results and Corrosivity Classification of Test Substances

27. The time (in minutes) elapsed between application of the test substance to the membrane barrier and barrier penetration is used to classify the test substance in terms of corrosivity (1) and, if applicable, UN Packing Group (17).

DATA AND REPORTING

Data

28. The time (in minutes) elapsed between application and barrier penetration for the test substance and the positive control(s) should be reported in tabular form as individual replicate data, as well as means \pm the standard deviation for each trial.

Test Report

29. The test report should include the following information:

Test and Control Substances:

- identification data and Chemical Abstracts Services Registry Number, if known;
- physical nature and purity (major impurities);
- physico-chemical properties relevant to the conduct of the study;
- treatment of the test/control substances prior to testing, if applicable, *e.g.*, warming, grinding;
- stability, if known.

Justification of the *in vitro* membrane barrier model and protocol used.

Test Conditions:

- description of the apparatus and preparation procedures used;

- source and composition of the *in vitro* membrane barrier used;
- composition and properties of the qualification and detection solutions;
- method of detection;
- test substance amounts;
- number of replicates;
- method of application;
- observation times.

Results:

- tabulation of data from individual test samples;
- descriptions of other effects observed;
- description of the evaluation and classification criteria.

Discussion of the results

Conclusions.

LITERATURE

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- (2) OECD (2002). Test Guideline 404. OECD Guideline for Testing of Chemicals. Acute Dermal Irritation/Corrosion. Updated Guideline, adopted April 24, 2002. Available: [http://www.oecd.org/document/22/0,2340,en_2649_34377_1916054_1_1_1_1,00.html]
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- (7) ICCVAM (1997). Validation and Regulatory Acceptance of Toxicological Test Methods. A Report of the *ad hoc* Interagency Coordinating Committee on the Validation of Alternative Methods. NIEHS, NIH Publication No. 97-3981. Available: [<http://iccvam.niehs.nih.gov/docs/guidelines/validate.pdf>]
- (8) OECD (1996). Report of the OECD Workshop on “Harmonisation of Validation and Acceptance Criteria for Alternative Toxicological Test Methods”. Paris, 1996, (Solna Report) [ENV/MC/CHEM(96)9]
- (9) OECD (2002). Report of the Stockholm Conference on “Validation and Regulatory Acceptance of New and Updated Methods in Hazard Assessment”. Paris, 2002 [ENV/JM/TG/M(2002)2]
- (10) Balls, M. and Karcher, W. (1995). Comment: The Validation of Alternative Test Methods. *ATLA* 23:884-886.
- (11) OECD (2004). Test Guideline 431. OECD Guideline for Testing of Chemicals. *In Vitro* Skin Corrosion: Human Skin Model Test. Available: [http://www.oecd.org/document/22/0,2340,en_2649_34377_1916054_1_1_1_1,00.html]

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Table 2: Proficiency Chemicals

Chemical	CASRN	Chemical Class	UN GHS Subcategory*
Nitric acid	7697-37-2	Inorganic acid	1A
Phosphorus pentachloride	10026-13-8	Inorganic acid	1A
Selenic acid	7783-08-6	Inorganic acid	1A
Valeryl chloride	638-29-9	Acid derivative	1B
Sodium Hydroxide	1310-73-2	Inorganic base	1B
1-(2-Aminoethyl) piperazine	140-31-8	Organic base	1B
Benzenesulfonyl chloride	98-09-9	Acid derivative	1C
Hydroxylamine sulphate	10039-54-0	Organic acid	1C
Tetraethylenepentamine	112-57-2	Organic base	1C
Eugenol	97-53-0	Organic acid	NC
Nonyl acrylate	2664-55-3	Acid ester	NC
Sodium acid carbonate	144-55-8	Inorganic base	NC

The twelve chemicals listed above contain three substances from each of the three GHS subcategories for corrosive substances and three non-corrosive substances, and are taken from the list of 40 reference chemicals that are included in the minimum list of chemicals identified for demonstrating the accuracy and reliability of test methods that are structurally and functionally similar to the validated reference test method (see Annex 2)(5)(16).

* The corresponding UN Packing groups are I, II and III, respectively, for the UN GHS 1A, 1B and 1C subcategories. NC; Non-corrosive.

Annex 1

DEFINITIONS

Accuracy: (a) The closeness of agreement between a test method result and an accepted reference value.
(b) The proportion of correct outcomes of a test method. It is a measure of test method performance and one aspect of “relevance”. The term is often used interchangeably with “concordance”. Accuracy is highly dependent on the prevalence of positives in the population being examined.

Chemical Detection System (CDS): A visual or electronic measurement system with an indicator solution that responds to the presence of a test substance, *e.g.*, by a change in a pH indicator dye, or combination of dyes, that will show a colour change in response to the presence of the test substance or by other types of chemical or electrochemical reactions.

GHS: Globally Harmonized System of Classification and Labelling of Chemicals (GHS). A joint activity of OECD (EHS), the UN Economic and Social Council’s Sub Committee of Experts on the Transport of Dangerous Goods (UNSCETDG), the Interorganization Programme for the Sound Management of Chemicals (IOMC) and the International Labour Organization (ILO)(1).

Relevance: The extent to which a test method correctly predicts or measures the biological effect of interest in humans or another species of interest. Relevance incorporates consideration of the “accuracy” or “concordance” of a test method.

Reliability: A measure of the degree to which a test method can be performed reproducibly within and among laboratories over time. It is assessed by calculating intra- and inter-laboratory reproducibility and intra-laboratory repeatability.

Skin corrosion: The production of irreversible damage to the skin, manifested as visible necrosis through the epidermis and into the dermis, following the application of a test material (1).

Annex 2

ASSESSMENT OF THE PERFORMANCE CHARACTERISTICS OF PROPOSED *IN VITRO* MEMBRANE BARRIER TEST METHOD FOR SKIN CORROSION

INTRODUCTION

1. Test methods proposed for use under this Test Guideline should be evaluated to determine their reliability and accuracy using substances of known corrosivity and non-corrosivity. When evaluated using the recommended reference chemicals (Table 1), the proposed test methods should have reliability and accuracy that are comparable to that of the validated reference test method (1)(Table 2). The reliability and accuracy standards that should be achieved are provided in paragraphs 3 and 4. Non-corrosive and corrosive substances, ranging from strong to weak and representing relevant chemical classes are included so that the reliability and accuracy, *i.e.*, sensitivity, specificity, false positive rates, and false negative rates, of the proposed test method can be compared to that of the validated reference test method (1)(2). For purposes of transportation hazard classification, the list of corrosive substances also covers the range of UN Packing Group classifications/GHS skin corrosivity subcategories (3)(4). This will allow for the determination of whether the penetration times used to assign test substances to a UN Packing Group/GHS skin corrosivity subcategory are appropriate. The elapsed times associated with the assignment of each Packing Group/GHS skin corrosivity subcategories to a test substance should be determined for each composition of barrier, indicator, and categorization systems, and the particular test method used. The reliability of the test method, as well as its ability to over- and under-predict known corrosive substances, should be determined prior to its use for testing new substances. Where possible, the classes or types of substances that are consistently over- or under-predicted should be defined.

PERFORMANCE STANDARDS

2. Reference chemicals are used to determine if the reliability and accuracy of a proposed *in vitro* membrane barrier test method is comparable to that of the validated reference test method (2). The 40 reference chemicals listed in Table 1 include chemicals representing different chemical classes of interest and the range of corrosivity responses, *i.e.*, non-corrosive, UN Packing Group I (GHS 1A), II (GHS 1B), and III (GHS 1C) corrosives, obtained for the *in vivo* reference test method. The distribution of chemicals in this list by corrosivity and UN Packing Group classifications/GHS skin corrosivity subcategories are 12 non-corrosive and 28 corrosive chemicals. Among the 28 corrosive chemicals there are nine substances each in Packing Groups I (GHS 1A) and II (GHS 1B), and 10 substances in Packing Group III (GHS 1C). These reference chemicals represent the minimum number that should be used to evaluate the accuracy and reliability of a not previously validated membrane barrier test method for skin corrosion. In situations where a listed chemical is unavailable, other chemicals or products for which adequate *in vivo* reference data are available could be used. If desired, additional chemicals representing other chemical or product classes and for which adequate *in vivo* reference data are available can be added to the minimum list of reference chemicals to further evaluate the accuracy of the proposed test method.

3. The reliability of the proposed test method should be comparable to that of the validated reference test method. However, an assessment of inter-laboratory reproducibility is not essential if the proposed test method is to be used in one laboratory only. The inter-laboratory reproducibility for corrosive versus non-corrosive and UN Packing Group classification/GHS skin corrosivity subcategories should be at least 93% (1). In terms of membrane breakthrough times, the median coefficient of variation (CV) should not exceed 30% for studies conducted in different laboratories and should not exceed 5% for replicate measurements within a study (1).

Table 1. Reference Chemicals for Determination of Accuracy and Reliability of *In Vitro* Membrane Corrosivity Test Methods

Chemical ¹	CASRN	Chemical ² Class	Conc ² (%)	UN <i>In Vivo</i> PG ³	Validated Test Method PG	pH ²
Fluorosulfonic acid	7789-21-1	inorganic acid	neat	I	I	0
Nitric acid	7697-37-2	inorganic acid	90	I	I	0
Phosphorus pentachloride	10026-13-8	inorganic acid	98	I	I	0
Selenic acid	7783-08-6	inorganic acid	95	I	I	0
Boron trifluoride dehydrate	13319-75-0	inorganic acid	96	I	I	0.4
Phosphorus tribromide	7789-60-8	inorganic acid	97	I	I	1.0
Sulfuric acid, 10% wt.	7664-93-9	inorganic acid	10	I	I	1.2
Benzyl chloroformate	501-53-1	acid derivative	95	I	NC	2.5
1,2-Diaminopropane	78-90-0	organic base	NA	I	II	8.3
Phosphoric acid	7664-38-2	inorganic acid	85	II	II	0.4
Valeryl chloride	638-29-9	acid derivative	98	II	II	0.5
Acetic acid	64-19-7	organic acid	99+	II	II	1.9
Caprylic acid	124-07-2	organic acid	95	II	NC	2.7
Capric:caprylic acid (45:55)	68937-75-7	organic acid	95	II	NC	3.0
Ammonium hydrogen difluoride	1341-49-7	acid derivative	98	II	II	5.2
1-(2-Aminoethyl) piperazine	140-31-8	organic base	99	II	II	11.8
Ethanolamine	141-43-5	organic base	99+	II	II	11.8
Sodium hydroxide	1310-73-2	inorganic base	100	II	II	13.8
Cyanuric chloride	108-77-0	acid derivative	99	III	III	1.7
Benzenesulfonyl chloride	98-09-9	acid derivative	neat	III	III	1.8
Crotonic acid	107-93-7	organic acid	99+	III	III	2.3
Butyric anhydride	106-31-0	acid derivative	99	III	III	3.1
Hydroxylamine sulfate	10039-54-0	organic acid	97+	III	III	3.6
2-Methylbutyric acid	600-07-7	organic acid	NA	III	III	3.6
Dicyclohexylamine	101-83-7	organic base	99	III	III	9.6
<i>N,N</i> -Dimethyl benzylamine	103-83-3	organic base	99	III	III	10.7
Tetraethylenepent-amine	112-57-2	organic base	neat	III	III	11.9
2-Ethylhexylamine	104-75-6	organic base	98	III	III	12.0

Chemical ¹	CASRN	Chemical ² Class	Conc ² (%)	UN <i>In Vivo</i> PG ³	Validated Test Method PG	pH ²
Maleic acid	110-16-7	organic acid	99	NC	II	1.3
Copper(II) chloride	7447-39-4	acid derivative	97	NC	II	3.0
Eugenol	97-53-0	organic acid	NA	NC	NC	3.7
Chromium(III) fluoride	7788-97-8	acid derivative	97	NC	NC	3.9
Cinnamaldehyde	14371-10-9	electrophile	100	NC	NC	3.9
Ethyl triglycol methacrylate	39670-09-2	acid ester	neat	NC	NC	4.5
Nonyl acrylate	2664-55-3	acid ester	neat	NC	NC	6.9
Benzalkonium chloride	8001-54-5	quaternary ammonium	100	NC	NC	7.6
Sodium acid carbonate	144-55-8	inorganic base	100	NC	NC	8.3
Sodium undecylenate	3398-33-2	surfactant	33	NC	NC	8.3
Sodium carbonate, 50% aqueous	497-19-8	inorganic base	100	NC	II	11.7
Calcium carbonate	471-34-1	inorganic base	neat	NC	NC	12.6

Abbreviations: CASRN = Chemical Abstracts Service Registry Number; Conc = concentration; NA = not available; NC = non-corrosive; PG = Packing Group; UN = United Nations.

¹ The 40 reference chemicals comprise a representative selection from the 163 reference chemicals that was originally used to validate the reference test method (Corrositex®); the complete list and the selection criteria are provided in (1).

² The chemical class, the concentration tested, and the pH values were obtained from the original sources as indicated in (1). The pH values are rounded to one decimal point.

³ Within the UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS), the PG classifications correspond as follows: PG I = 1A, PG II = 1B, PG III = 1C.

4. The accuracy (sensitivity, specificity, false negative rate, false positive rate, ability to correctly identify UN Packing Group classifications/GHS skin corrosivity subcategories) of the proposed test method should be at least comparable to that of the validated test method (1)(2)(Table 2).

Table 2. Accuracy of the Validated Reference Test Method for Skin Corrosion¹

Source	No. of Chemicals	Sensitivity ²	Specificity ²	False Negative Rate ²	False Positive Rate ²	Packing Group Accuracy ³
Reference Chemicals ⁴	40	89% (25/28)	75% (9/12)	11% (3/28)	25% (3/12)	96% (24/25)

¹ Table 2 provides the accuracy of the validated reference test method in correctly identifying the corrosivity potential of the 40 reference chemicals (Table 1).

² In this analysis (1), a substance is first classified as positive or negative for corrosivity within each laboratory based on the majority of test results obtained (when replicate testing was conducted). Next, the substance is classified as positive or negative for corrosivity based on the majority of test results obtained in multiple laboratories (when multiple laboratory studies were conducted).

³ Packing Group Accuracy reflects the frequency with which the validated reference test method correctly identified the UN Packing Group classification (or GHS skin corrosivity subcategories) assigned to a corrosive substance based on *in vivo* rabbit skin test method results. This calculation is limited to substances correctly identified as corrosive by Corrositex[®].

⁴ See Table 1.

LITERATURE

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