Evaluation of a Sample Provided by

[redacted]

Utilizing the CORROSITEX® (OECD TG 435)

November 22, 2019

INVITRO INTERNATIONAL

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November 22, 2019

[redacted]

[redacted]

Dear [redacted] and [redacted],

Enclosed is a copy of the final report detailing the results of our study of the material that was sent to us for analysis by the Corrositex® test method.

We are delighted that you have selected InVitro International to perform this analysis for you. We look forward to being able to provide additional services for you in the future.

Sincerely,

W. Richard Ulmer
President & CEO

UTILIZATION OF THE CORROSITEX® TEST METHOD TO EVALUATE A SAMPLE PROVIDED BY [redacted]

Completion Date: November 22, 2019

Client: [redacted]

Client Contact: [redacted]

Phone Number: [redacted]

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Study Technician: 11/22/2019
Shannon Beatty Date

Director of R&D, QA: 11/22/2019
Amy Wang, M.S. Date

Approved by:
President & CEO of
InVitro International, Inc. 11/22/2019
W. Richard Ulmer Date

EXECUTIVE SUMMARY

A single sample provided by [redacted] was evaluated with the Corrositex® test method to determine its corrosive potential and to designate its Packing Group classification. The results of this study may be summarized as follows:

Sample Description	Mean Corrositex® Time (minutes)	UN Packing Group	GHS Category for Skin Corrosion
NGA1 – NF - SAMI	>60	Non-corrosive	Not Category 1

EVALUATION OF A SAMPLE PROVIDED BY [redacted] UTILIZING THE CORROSITEX® TEST METHOD

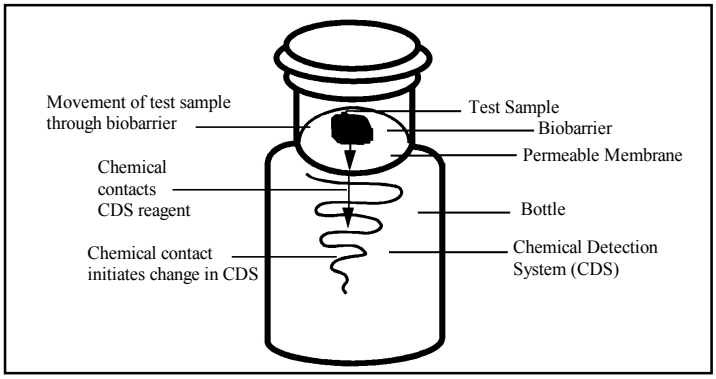
STUDY OBJECTIVE

A single sample provided by [redacted] was evaluated with the Corrositex® test method to determine its corrosive potential and to designate its Packing Group classification. To achieve this objective, the sample was subjected to a three-step testing process as described under Materials and Methods.

BACKGROUND

The Corrositex® test is an internationally accepted [1][2][3] validated test method for skin corrosion according to Globally Harmonized System (GHS) classifications. The test is a standardized, as well as reproducible method that can be employed to determine the potential corrosivity and determine the Packing Group classification of specified categories of chemical compounds under the hazardous materials transportation regulations administered by the U.S. Department of Transportation (DOT) and international dangerous goods codes. The Corrositex test predicts the *in vivo* corrosive potential of a chemical compound or mixture by using as an endpoint the time it takes for the chemical to permeate through or destroy a synthetic biobarrier. When the chemical has passed through this biobarrier, a visual change is produced in a proprietary Chemical Detection System (CDS). This assay system is depicted in Figure 1.

Figure 1. A Schematic Diagram Depicting the Biobarrier and Chemical Detection System of the Corrositex® Test Method



Occasionally, due to the limitation of the Membrane Barrier Test Method, when the test sample was not causing a detectable change in the step 1, Chemical Compatibility Test, the sample is not suitable for a standard Membrane Barrier Test Method to determine the penetration (breakthrough) time. In the database for which *in vivo* data were available, when an aqueous chemical with a pH in the range of 4.5 to 8.5 often do not qualify for testing, however, 85% of non-qualifying chemicals tested in this pH range were non-corrosive in animal tests[1][2].

MATERIALS/METHODS

The Corrositex® test is performed in three steps. First, a Chemical Compatibility Test is done to insure that the test sample and the CDS reagent are compatible. This is achieved by placing either 150 µl of a liquid or 100 mg of a solid into an aliquot of the CDS reagent and observing it for the presence of any detectable change. If a physical or color change is observed, the sample is judged to be compatible with the detection solution and the remainder of the test is performed. The second step, Chemical Timescale Category Test, utilizes appropriate indicator solutions to permit categorization of the test sample as either a Corrositex® Category 1 or Corrositex® Category 2 material. Corrositex® Category 1 materials are typically strong acids/bases, while Corrositex® Category 2 materials are typically weak acids/bases. The third step, Membrane Barrier Test Method, is performed by applying 500 µl of a liquid or 500 mg of a solid test sample to the biobarrier. When the chemical permeates through or destroys the full thickness of this biobarrier, it comes into contact with the CDS which then undergoes a simple color change. This color change is visually observed and the time required for the color change to occur is recorded. As summarized in Table 1 below, the time required to destroy the biobarrier is recorded for four sample replicates and the mean of these replicates is utilized to designate the UN Packing Group classification as I (severe corrosivity), II (moderate corrosivity), III (mild corrosivity), or Non-corrosive (NC). Positive and negative controls are analyzed concurrently to confirm the test's validity.

Table 1. Designation of UN Packing Groups/GHS Skin Corrosion Categories [(a)(b)]

	Corrositex Time (minutes)			
Corrositex Category 1	0 to 3 min.	>3 to 60 min.	>60 to 240 min.	>240 min.
Corrositex Category 2	0 to 3 min.	>3 to 30 min.	>30 to 60 min.	>60 min.
UN Packing Group	**PG I**	**PG II**	**PG III**	**Non-corrosive**
GHS Skin Corrosion Category	**GHS Skin Corrosion Category 1**			
GHS Skin Corrosion Sub-categories	**Sub-category 1A**	**Sub-category 1B**	**Sub-category 1C**	

[(a)] United Nations (UN) (2013). Globally Harmonized System of Classification and Labeling of Chemicals (GHS). Fifth revised edition, UN New York and Geneva, 2013. Ch 3.2.

[(b)] The GHS provides guidance to organize information to make a weight of evidence decision about hazardous material classification. It states that in some cases, classification of a substance may be made on the weight of evidence within a tier, and further that *in vitro* alternatives which have been validated and accepted should be used to make classification decisions. The use of Corrositex and other *in vitro* alternatives is addressed in chapter 3.2 (para. 3.2.2.2) .

RESULTS

A summary of the results obtained after evaluating the test sample is presented in Table 2.

Table 2. Summary of Corrositex® Test Results

IVI #: C4732	**Corrositex Time (minutes)**
Sample: NGA1 – NF - SAMI	**Replicate #1:** >60
Conc. Tested: Neat	**Replicate #2:** >60
pH(10%) : 10.57	**Replicate #3:** >60
Compatibility Test: Qualify	**Replicate #4:** >60
Corrositex Category: 2	**Mean ± SD:** >60
UN Packing Group: Non-corrosive **GHS Skin Corrosion Category: Not Category 1**	

DISCUSSION

A single sample obtained from [redacted] was analyzed by the Corrositex® method to determine its corrosive potential and GHS and U.N. Packing Group designations.

The results of this study indicated that the sample was compatible with the Corrositex® system and was classified as a Category 2 material. The results obtained from the evaluation of four replicate samples were highly reproducible, demonstrating that a mean time of **>60** minutes required to destroy the synthetic biobarriers. These findings lead to the designation of this sample, **NGA1 – NF - SAMI**, as a **UN Non-corrosive** and **not a GHS Category 1.**

REFERENCE

(1) ICCVAM (1999). Corrositex®. An In Vitro Test Method for Assessing Dermal Corrosivity Potentail of Chemicals. The Results of an Independent Peer Review Evaluation Coordinated by ICCVAM, NTP and NICEATM. NIEHS, NIH Publication (No. 99-4495)

(2) OECD (2015). OECD Test Guideline 435. *In Vitro* Membrane Barrier Test Method for Skin Corrosion.

(3) United Nations (UN) (2013). Globally Harmonized System of Classification and Labeling of Chemicals (GHS). Fifth revised edition, UN New York and Geneva, 2013. Ch 3.2.

REGULATORY ACCEPTANCE

(1) **DEPARTMENT OF TRANSPORTATION – DOT-E 10904.** Original exemption granted 4/28/1993

(2) **ORGANIZATION FOR ECONOMIC COOPERATION AND DEVELOPMENT (OECD).** Original adapted 7/19/2006. Updated 7/28/2015.

(3) **CONSUMER PRODUCT SAFETY COMMISSION (CPSC).** Formal Acceptance, NIEHS press release dated 3/21/2000

(4) **EUROPEAN CENTRE FOR THE VALIDATION OF ALTERNATIVE METHODS (ECVAM).** 12/2002

(5) **EPA FEDERAL REGISTER / VOL. 60, NO. 142 DERMAL CORROSION METHOD 1120.** Formal Acceptance, NIEHS press release dated 3/21/00

(6) **INTERNATIONAL AIR TRANSPORTATION ASSOCIATION (IATA).** Letter of acceptance dated December 17, 1993

(7) **OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION (OSHA).** Letter of Interpretation dated March 3, 1994. Formal Acceptance, NIEHS press release dated 3/21/00

(8) **NATIONAL INSTITUTE OF ENVIROMENTAL HEALTH SCIENCES (NIEHS).** Endorsement dated 6/22/1999

(9) **TRANSPORT CANADA – PERMIT FOR EQUIVALENT LEVEL OF SAFETY SU 4483.** Original approval 8/14/96. Full Draize Replacement Acceptance 3/5/02