Safety of dermal Diphoterine® application: An active decontamination solution for chemical splash injuries

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Abstract
Diphoterine (Laboratoire Prevor, Valmondois, France) is an active, amphoteric, polyvalent, chelating, slightly hypertonic decontamination solution for chemical splashes to the skin and eyes. It chemically bonds a large number of chemical substances present on the skin surface without causing a significant release of heat (exothermic reactions). Because of its amphoteric properties, it can bind chemically opposite substances such as acids and bases or oxidizers and reducing agents. No adverse effects have been observed in an ongoing postmarketing surveillance program during many years of use in European industrial facilities. Diphoterine has more recently been used in hospitals for delayed management of chemical burns to the skin and eyes. There is interest in having protocols for both immediate and delayed Diphoterine use for skin decontamination. Whereas studies of Diphoterine efficacy, clinical and in vitro or ex vivo, have been published or are in the process of being prepared for publication, no review has yet been published focusing solely on the safety of this decontamination solution. Therefore, all available studies on the safety of Diphoterine are described here, including recent studies demonstrating no harmful effects on the skin. Diphoterine can be used, even on damaged skin, without toxic, irritant, allergic, or sensitizing effects.

Keywords: Diphoterine; decontamination solution; chemical burns

Introduction
Diphoterine (conceived and developed by Laboratoire Prevor, Valmondois, France) is an amphoteric, polyvalent, chelating, and slightly hypertonic decontamination solution for chemical splashes to the skin and eyes. It has been used for many years in European industrial facilities, where no adverse effects have been observed in an ongoing postmarketing surveillance program. It has more recently been used in hospitals for successful delayed management of chemical burns to the skin and eyes.

A comprehensive review of the available data, published and unpublished, on the safety of this active skin decontamination solution may aid its acceptance as a replacement for traditional water washing, the efficacy of which has been questioned in the last several years [1-3]. In addition, the issue of the deleterious “wash-in” effect of skin chemical splash decontamination with hypotonic water has been recognized [4,5]. Approximately 25,000 chemicals, such as acids, bases, oxidizers, and reducing agents, have the potential to cause chemical burns or injuries [6], including dermal irritation and sensitization. Therefore, potential improvements in chemical splash countermeasures such as active decontamination solutions that chemically bind the splashed chemical substance present on the surface of the skin, whose chemical reactions do not induce significant heat release (exothermic reactions), and that have no physiologic effects on the tissues themselves deserve consideration for use as skin decontaminants.
Whereas studies of Diphtherine efficacy, clinical and in vitro or ex vivo, have been published or are in the process of being prepared for publication, no review has yet been published focusing solely on the safety of this decontamination solution. Therefore, available studies on the safety of Diphtherine are described here.

Materials and methods

All studies reviewed here were performed in independent laboratories or by independent research groups, in accordance with guidelines applicable to the specific test as well as all applicable ethical standards for experimental animal studies or human subject studies. Each guideline or standard followed is described below in the section for the reviewed study.

Acute dermal median lethal dose

Acute dermal toxicity or acute dermal median lethal dose ($LD_{50}$) was evaluated in the Sprague-Dawley CYF strain rat (study 133/9); the evaluation was performed at SafePharm Laboratories Limited, Derby, UK [7], and was designed following the Organisation for Economic Co-operation and Development (OECD) guideline for testing of chemicals 402, “Acute Dermal Toxicity.” A group of 10 animals (5 males and 5 females) received a single 24-hour, semioccluded dermal application of the test material (Diphtherine; batch D380503) to intact skin at a dose of 2,000 mg/kg body weight, corresponding to a volume of 1.95 mL/kg. Approximately 24 hours prior to the beginning of the test, the back and flanks of each animal were clipped free of hair using veterinary clippers to expose a skin area of approximately 6 cm × 12 cm. Diphtherine was not diluted and was applied uniformly to an area of skin approximating 10% of the total body surface area (TBSA) using a graduated syringe. A piece of surgical gauze (4 cm × 7 cm) was placed over the treatment area and semioccluded with a double layer of adhesive bandage (Elastoplast; Beiersdorf AG, Birmingham, UK) wrapped around the trunk of the rat. After the 24-hour exposure period, the bandage was removed and the treated skin and surrounding hair were wiped with moist cotton wool to remove any residual test material. All animals were observed for signs of toxicity and death at 1 and 4 hours after application, and subsequently at least once daily for 14 days. After euthanasia, all animals were subjected to a gross necropsy examination for any macroscopic abnormalities.

Dermal irritation in vitro

The potential dermal irritation of Diphtherine (batch D550305A*) was evaluated by an in vitro Dermal Irritation test (InVitro International, Irvine, CA, USA) [8] at the Integra (Abich) Laboratory, Milan, Italy. This test is used to predict the potential for causing dermal irritation in humans with the relationship described in Table 1 [8]. The irritant product reacts with the protein structures of a reagent matrix and its irritant potential is rendered objectively observable by a cloudy appearance that can be measured with an optical density spectrophotometer.

Cytotoxicity in murine fibroblasts

The cytotoxicity of Diphtherine (batch D951205B*) was tested in vitro at the Integra (Abich) Laboratory (study REL/003/06/IRRC/ELB) [9,10] to evaluate the cytotoxicity of finished products or raw materials intended to be used on the skin or mucosae, following the UNI EN ISO 10993-5 rule concerning the biological evaluation of medical devices [10]. The cells utilized are murine fibroblasts (3T3). This cell line is derived from albino mouse embryos. Cell viability or death is evaluated via the MTT test. The MTT assay is simple and accurate, yields reproducible results, and was originally developed by Mossman [9]. The key component is (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide), or MTT. This product is a yellowish color in solution. Mitochondrial dehydrogenases of viable cells cleave the tetrazolium ring, leading to the formation of purple crystals that are soluble in aqueous solution. The crystals are redissolved in acidified isopropanol and the resulting purple solution is measured spectrophotometrically. An increase or decrease in cell number results in a concomitant change in the amount of formazan formed, indicating the degree of cytotoxicity caused by the test material.

After exposure to the test material, the cells are washed with a washing solution, Dulbecco phosphate-buffered saline Dulbecco modified Eagle Medium (DMEM). After removal of the washing

<table>
<thead>
<tr>
<th>HIE Score</th>
<th>Predicted Dermal Irritation Classification</th>
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<tbody>
<tr>
<td>0.0-0.90</td>
<td>NonIrritant</td>
</tr>
<tr>
<td>0.90-1.20</td>
<td>Minimum irritant</td>
</tr>
<tr>
<td>1.20-2.00</td>
<td>Mild irritant</td>
</tr>
<tr>
<td>2.00-4.00</td>
<td>Irritant</td>
</tr>
<tr>
<td>&gt;4.00</td>
<td>Severe irritant</td>
</tr>
</tbody>
</table>
solution, the MTT medium is added to each culture well and the cells are incubated at 37°C.

At the end of the incubation period, the MTT medium is removed and the cells are treated with the MTT solubilization solution.

The plate is shaken on a gyrating plate, ensuring that all the crystals have dissolved from the cells and have formed a homogeneous solution. The absorbance is measured on a microplate reader, with background clearing.

The results are expressed in terms of viability:

\[
\text{% cell survival} = \frac{\text{OD treated cells} \times 100}{\text{OD nontreated cells}}
\]

where OD refers to optical density. Use of this equation provides the theoretical inhibitory concentration of 50% (IC\text{50}) value, i.e., the concentration of test compound that induces a decrease of cell survival by 50% as compared with untreated cultures. This indicates the potential irritant effect of the test compound.

Cells are seeded in 24-well plates, for 24 hours in DMEM + 10% fetal calf serum (FCS). Fresh medium is added, supplemented with only 10% FCS and with 5 scalar dilutions of the tested product ranging from 0.03 to 5 mg/mL.

The sample was dissolved in the medium. For each dilution, 3 replications were performed. After 10 and 24 hours of incubation, cells were tested for viability with the cytotoxicity (MTT) assay. Cells treated with a 2.8% saline isotonic to Diphtherine were used as negative controls. Cells treated with a known irritant surfactant, sodium lauryl sulfate (SLS), in concentrations ranging from 0.03 to 0.5 mg/mL were used as positive controls. Percent cell viability in the presence of SLS was estimated versus negative control.

**Local tolerance after single application on rabbit skin**

Local tolerance was evaluated in the New Zealand white female rabbit. The study was performed at the CERB Laboratory, Baugy, France (CERB report 20060537TL) [11] and in accordance with the guidelines concerning Good Laboratory Practice (GLP) dated March 14, 2000, published by the French Ministry of Social Affairs and National Solidarity, State Secretariat of Health, which are in accordance with the general requirements of OECD principles of GLP (ENV/MC/CHEM (98) 17) and are accepted by the US Food and Drug Administration (FDA) and the Japanese Authorities (Ministry of Health, Labour and Welfare, Pharmaceutical and Medical Devices Agency).

The local tolerance of Diphtherine (batch D761203B) was evaluated following a single, semioccluded or nonoccluded application to scarified and nonscarified rabbit skin. The study involved 2 groups of 3 animals each. Diphtherine was applied to the skin of the flanks. Approximately 24 hours before the test, the treatment regions of each rabbit were carefully clipped free of fur over an area of at least 14 cm x 6 cm. Care was taken to avoid abrading the skin.

Diphtherine 0.5 mL was applied over 4 areas to the scarified or nonscarified skin of each rabbit following the treatment site design. Adjacent surfaces of nontreated skin served as controls for the trial.

Diphtherine was applied directly on the skin with a graduated syringe over 4 areas of approximately 6 cm², and then covered with a semiocclusive microporous and nonallergenic dressing held in place with an adhesive dressing (Elastoplast) (semioccluded application). The 2 other gauze pads were held in place with only a suppil and aerated adhesive tape (nonoccluded application). The animals were fitted with these pads for 24 hours.

Scarifications approximately 2.5 cm long and 0.5 cm apart were produced on the appropriate flanks of each animal using a sterile vaccinostyle, with care taken to avoid any bleeding. The opposite flanks of each of the animals were kept intact. Diphtherine was applied only once, with an exposure duration of 24 hours using semiocclusive and nonocclusive dressings.

Before application and approximately 1 hour after removal of the dressing (time 24 hours), and once again 48 hours later (time 72 hours), any skin lesions were evaluated. Afterwards, the appearance and suppleness of the skin, rapidity of fur regrowth, appearance of the regrowth, and skin fold thickness were evaluated. Skin fold thicknesses were measured using an Oditest micrometer (Kröplin Längenmesstechnik, Schüchtern, Germany).

**Topical skin sensitization in the guinea pig**

A skin sensitization study was done in the guinea pig [12] according to the Magnusson and Kligman method [13]. The study was carried out at the CERB Laboratory (CERB report 20030418ST) in accordance with all applicable regulations and standards for protecting animal welfare.

The grading system for skin reactions followed OECD guideline 406: no visible change, 0; discrete or patchy erythema, 1; moderate and confluent
erythema, 2; and intense erythema and swelling, 3. The maximum nonirritant concentration of Diphoterine (batch D433011A) for dermal application was determined in 2 males and 2 females that had a dermal application of 0.5 mL on a 4-cm² (2 cm × 2 cm) surface area, using 1 concentration on each flank (on a 2 cm x 2 cm gauze pad held in place with an Elastoplast semiocclusive dressing).

The sensitization potential was evaluated in 30 animals, with 20 animals (10 males, 10 females) treated with Diphoterine and a negative control group of 10 animals (5 males, 5 females).

Sodium laurel sulfate (10%) in mineral oil was used for topical induction, and Diphoterine was applied on a piece of absorbent gauze and held in place for 48 hours by an Elastoplast semiabsorbent dressing. Positive controls received 0.5 mL of 1% dinitrochlorobenzene (DNCB) solution topically. Evaluation of allergenicity was done at 24 and 48 hours.

**Local skin application tolerance in normal human volunteers**

The local skin tolerance of Diphoterine was evaluated in 55 normal volunteers by the Institut Dermatologique d’Aquitaine (Aquitaine Dermatologic Institute [IDEA]), Martillac, France. The investigation was performed at Solar Test International (STI) in Romania, according to the internal standard protocol. A single application of 0.02 mL of Diphoterine (batch D970112B) was applied on the external surface of the arm and maintained in contact with the skin with an occlusive patch (Hayes chamber) for 48 hours.

Fifty-seven normal human volunteers were recruited and 55 were included in the study, male and female, with normal skin and without any dermatologic lesions on the experimental area. Eight volunteers were aged 65 to 70 years, but this had no influence on the results. Blinded clinical evaluation by a dermatologist was done 30 minutes after patch removal and took into account erythema, papules, vesicles, and blisters according to their intensity, with evaluation scores ranging from 0 to 4. The total sum of the scores divided by the number of volunteers defines the average irritation index (IIM), which allows an arbitrary classification of the test product (Diphoterine) (Table 2).

<table>
<thead>
<tr>
<th>Classification</th>
<th>IIM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonirritant</td>
<td>≤0.2</td>
</tr>
<tr>
<td>Slightly irritant</td>
<td>0.20 to ≤0.50</td>
</tr>
<tr>
<td>Moderately irritant</td>
<td>0.50 to ≤2</td>
</tr>
<tr>
<td>Very irritant</td>
<td>2 to 5</td>
</tr>
<tr>
<td>Severely irritant</td>
<td>&gt;5</td>
</tr>
</tbody>
</table>

IIM = average irritation index.

**Skin sensitization in normal human volunteers**

Diphoterine dermal sensitization potential testing was performed in 150 normal human volunteer subjects with normal skin according to the Marzulli-Malbach method [14], supervised by the Institut Dermatologique d’Aquitaine (IDEA; reference ID-07/0477). Fifty normal volunteer subjects each were evaluated in 3 research centers: the STE Center in Romania, the CIT Center in Romania, and the PROCOS Center in Poland.

Diphoterine (batch D970903A) product application was as follows: The application areas were the homolateral scapular areas (induction areas) and contralateral scapular areas (challenge areas). The applied quantity of Diphoterine was 25 μL under total occlusion. The frequency of application was 3 times per week for 48 hours (9 applications each at the 2 Romanian sites and 8 applications at the Polish site). The duration was 3 weeks during the induction phase, and 1 week during the challenge phase.

**Application conditions** were such that the test product (Diphoterine) was placed on a filter paper disk placed in the cup of the occlusive patch. A similar patch not containing any test material was applied in the same conditions and served as an untreated control. During the challenge phase, no wetting or washing was allowed in the contralateral test area. Clinical criteria for sensitization (challenge phase) were in accordance with a scale developed by the International Contact Dermatitis Group (ICDG).

**Percutaneous absorption and tolerability in vitro**

Percutaneous absorption and tolerability evaluations of Diphoterine (batch D440312A) were performed on in vitro human reconstituted 3-dimensional (3D) epidermis (SkinEthic, Nice, France) at the Integra (Aïbach) Laboratory (study REL/190/05/ASSP/ST) [9,10,15].

All tests were performed following the GLP guidelines. Diphoterine absorption was tested and controlled on 3D epidermis with exposure up to 6 hours. The in vitro experimental model consists of a unit of epidermis composed of pluristratified human keratinocytes, well differentiated at the surface of the stratum corneum at the air interface, having morphology
and functionality close to that of in vivo human skin according to the technical information from the skin supplier.

Diphoterine, 500 µL, was added to each epidermis unit. Evaluation of skin cell viability was performed following the MTT test method (described in the cytotoxicity test section above). If the viability rate is greater than 20%, then the skin tolerability in humans would be expected to be good, and if it is greater than 50%, the skin tolerability would be expected to be very good.

**Results**

**Acute dermal median lethal dose**

There were no deaths among the test animals. No signs of systemic or local toxicity were noted during the study period. All animals showed expected gains in body weight over the study period. No gross abnormalities were noted at necropsy. The acute dermal LD₅₀ of the test material in the Sprague-Dawley rat was found to be greater than 2,000 mg/kg body weight [7], signifying that Diphoterine is nonirritating and nontoxic in this test system.

**Dermal irritation in vitro**

Diphoterine was found to be nonirritant in the Dermal Irritation test [8], with a maximum human irritancy equivalent (HIE) score of 0.8.

**Cytotoxicity in murine fibroblasts**

Results obtained for viability of cells exposed to Diphoterine versus SLS are summarized in Table 3.

The estimated IC₅₀ of SLS was 0.258 mg/mL after 10 minutes of exposure and decreased to 0.08 mg/mL after 24 hours of exposure, whereas the IC₅₀ of Diphoterine was greater than 5 mg/mL, even after 24 hours of contact. Diphoterine did not show any cytotoxic effects on fibroblasts up to 24 hours.

**Local tolerance after single application on rabbit skin**

Diphoterine did not induce coloring of the application sites and did not interfere with skin lesion grading. Whatever the site and the group, no erythema and no edema were noted on the scarified or nonscarified sites covered by a semiocclusive or nonocclusive dressing. No effects on skin appearance, skin suppleness, rapidity and appearance of fur regrowth, or skin fold thickness (Table 4) were observed in any of the animals.

The scores obtained for all sites were the following: 0 for no erythema, 0 for a normal skin appearance, 0 for a return to normal skin suppleness after pinching, and 1 for a normal fur regrowth.

No effects on appearance and skin suppleness, rapidity and appearance of fur regrowth, or skin fold thickness were observed in any of the animals. No significant difference on skin fold thickness was found, whatever the site and the group.

### Table 3. Cell viability after 10 minutes and 24 hours of exposure at various doses.

<table>
<thead>
<tr>
<th></th>
<th>0.5 mg/mL</th>
<th>0.25 mg/mL</th>
<th>0.125 mg/mL</th>
<th>0.06 mg/mL</th>
<th>0.03 mg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SLS D</td>
<td>SLS D</td>
<td>SLS D</td>
<td>SLS D</td>
<td>SLS D</td>
</tr>
<tr>
<td>% Cell viability, 10-minute exposure</td>
<td>0.9</td>
<td>93.8</td>
<td>47.9</td>
<td>94.9</td>
<td>83.1</td>
</tr>
<tr>
<td>SD</td>
<td>0.2</td>
<td>2.4</td>
<td>4.6</td>
<td>1.8</td>
<td>5.0</td>
</tr>
<tr>
<td>% Cell viability, 24-hour exposure</td>
<td>0.1</td>
<td>90.4</td>
<td>0.9</td>
<td>97.0</td>
<td>3.4</td>
</tr>
<tr>
<td>SD</td>
<td>2.4</td>
<td>0.9</td>
<td>0.1</td>
<td>3.4</td>
<td>0.6</td>
</tr>
</tbody>
</table>

D = Diphoterine; SD = standard deviation; SLS = sodium lauryl sulfate.

### Table 4. Skin fold thickness evolution (N = 3).

<table>
<thead>
<tr>
<th>Mean/SEM values</th>
<th>Site 1</th>
<th>Site 2</th>
<th>Site 3</th>
<th>Site 4</th>
<th>Group 1</th>
<th>Site 1</th>
<th>Site 2</th>
<th>Site 3</th>
<th>Site 4</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>(µm)</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Predose</td>
<td>1.27</td>
<td>0.09</td>
<td>1.37</td>
<td>0.13</td>
<td>1.23</td>
<td>0.25</td>
<td>1.35</td>
<td>0.08</td>
<td>1.37</td>
<td>0.14</td>
</tr>
<tr>
<td>24 Hours</td>
<td>1.62</td>
<td>0.13</td>
<td>1.45</td>
<td>0.1</td>
<td>1.42</td>
<td>0.13</td>
<td>1.53</td>
<td>0.04</td>
<td>1.53</td>
<td>0.09</td>
</tr>
<tr>
<td>72 Hours</td>
<td>1.47</td>
<td>0.09</td>
<td>1.43</td>
<td>0.11</td>
<td>1.68</td>
<td>0.12</td>
<td>1.4</td>
<td>0.14</td>
<td>1.35</td>
<td>0.19</td>
</tr>
</tbody>
</table>

SD = standard deviation; SEM = standard error of the mean.
No dermal irritation was observed, as well as no toxic effects. Individual body weight gains were normal for all animals, and no mortality occurred during the study (72 hours of observation). Under the experimental conditions adopted, Diphotherine applied on scarified and nonscarified skin following a single, semioccluded or nonoccluded application (24 hours) induced no dermal lesions and no toxic effects in the rabbit after 72 hours.

Topical skin sensitization in the guinea pig

In the guinea pig sensitization study, Diphotherine was not irritating at 24 and 48 hours after application and was not found to have any skin-sensitizing effects [12].

Local skin application tolerance in normal human volunteers

Of 57 normal human volunteers, 55 were included in the study. The IIM was 0.00. Diphotherine can be considered nonirritant after an application of 8 consecutive hours on the skin of 55 normal human volunteers.

Skin sensitization in normal human volunteers

One hundred sixty-one volunteers completed the study. Clinical examinations during the induction phase allowed continuing Diphotherine and blank applications throughout this period and during the challenge phase. During the challenge phase, no reactions were observed. An IIM was calculated at each examination.

The IIM on day 22 was calculated for the 111 normal volunteers who had 9 successive Diphotherine applications, and was 0.09.

Diphotherine remains nonirritating during the first 5 applications, and then becomes slightly irritating (IIM = 0.25) during the 3 following applications. Thus, among 111 normal volunteers, who received 9 successive dermal applications, Diphotherine can be considered hypoallergenic, and the risk of inducing contact dermal sensitivity is minimal.

Percutaneous absorption and tolerability in vitro

Diphotherine shows high tolerability even after 6 hours of observation. Being applied for transient periods and with topical application, its biocompatibility may be considered very high. The data obtained for Diphotherine absorption through the epidermis (in µg) are summarized in Figure 1. The absorption of Diphotherine remains low compared with the amount initially applied, which means that even after several hours of contact, diffusion through the epidermis is very weak: none was present during the first 10 minutes following application and only about 3.210⁻³% of the initial applied dose was present after 6 hours of contact. The product shows a high biocompatibility toward human skin.

Discussion

These results show that Diphotherine has no physiologic interaction with the skin, as all dermal tests

![Graph](Figure 1. Absorption of Diphotherine through the epidermis in an in vitro study using human reconstituted 3D epidermis.)
induced no irritating or sensitizing effects on either normal of scarified skin, by nonocclusive or semicocclusive exposures, and with prolonged exposures. These exposure conditions, especially for the evaluation of local tolerance in normal human volunteers, are much more strict that those required by the standard protocol for Diphoterine use: a single dose within 1 minute after chemical skin contact, 100 mL for decontamination of 1 hand or foot, 200 mL for decontamination of 1 arm or thigh, and 5 liters over 5 minutes for the whole body.

Other tests have been performed to evaluate the potential toxicity of Diphoterine by other exposure routes. The acute toxicity of Diphoterine administered by the oral route (LD$_{50}$) (Centre International de Toxicologie [CIT], Eyvieux, France—rat oral toxicity, study 6564 TAR) [7] in rats was found to be greater than 2,000 mg/kg, a dose at which no signs of toxicity were observed, no deaths occurred, and no changes were noted in general behavior, expected body weight gain, or macroscopic evidence of abnormalities at necropsy. The Ames test (CIT, Ames test; bacterial reverse mutation test, study TAR 29023) has also been performed, and Diphoterine did not show any mutagenic activity in the bacterial reverse mutation test in Salmonella typhimurium and Escherichia coli.

All these toxicologic data are in accordance with the postmarketing surveillance program of Diphoterine use where no adverse effects of this skin or eye chemical decontamination solution have been reported to the manufacturer.

The low rate of Diphoterine diffusion through the skin is also a good indicator of safety, as the product remains on the surface of the skin to react with irritating or corrosive chemical products and arrests their noxious action with its amphoteric and hypertonic properties [15]. It has no apparent physiologic effect on the skin. These safety data may increase the range for the use of different dermal applications of Diphoterine, such as delayed management of the victims of chemical assaults, which continue to occur in various countries worldwide.

An experimental and comparative study [16] of concentrated hydrochloric acid burns on rat skin showed that skin flushing with Diphoterine reduced substance P release (decreased inflammation) during the first 48 hours after the burn, and was associated with better wound healing and higher concentrations of β-endorphin (indicator of pain alleviation) 7 days later when compared with normal saline solution or 10% calcium gluconate.

Several cases of successful delayed use of Diphoterine have been reported by users through the postmarketing survey, as the initial decontamination or following water washing. Data on some cases of in-hospital utilization are being prepared for submission for publication.

Conclusion

Under the experimental conditions utilized, Diphoterine showed no irritating, skin-sensitizing, or toxic effects on normal or damaged skin. These results are in accordance with the lack of adverse effects observed in workers after immediate use of Diphoterine for chemical skin or eye splash decontamination. Further clinical comparative studies should be conducted in order to demonstrate any interest of delayed Diphoterine application on chemically splashed skin.

Acknowledgements

Declaration of interest: Drs. Hall and Maibach are consultants to Laboratoire Prevor, Valmondois, France, manufacturer of Diphoterine. Drs. Mathieu and Burgher are employees of Laboratoire Prevor.

References