AMENDMENT SHEET NO. 3
ISRAEL STANDARD SI 139

LIQUID BASED ON SYNTHETIC SURFACE ACTIVE MATERIALS FOR HAND DISHWASHING

April 2003

This is a true translation of the Hebrew original. In any case of discrepancy between the original Hebrew text and the English translation, the Hebrew version shall prevail.

This Amendment Sheet updates
Israel Standard SI 139 of January 1990
Amendment no. 1 of March 1992
Amendment no. 2 of March 1996

Clause 102. References

Israel Standards

At the end of the Clause of the list of Israel Standards, add:

SI 2302 – Classification, packaging, labelling and marking of dangerous substances.

Following the list of Israel Standards, add:

International Standards

ISO 11683 – Tactile warnings of danger – Requirements

Foreign documents

Directive 67/548/EEC – Classification, packaging and labelling of dangerous substances

Directive 1999/45/EC – Classification, packaging and labelling of dangerous preparations

A.I.S.E.[1] – Association International de la Savonnerie, de la detergence et des Produits d'Entretien (International Association for Soaps, Detergents and Maintenance Products)

Clause 105. Packaging and marking

Clause 105.1 - Packages whose content is up to 10 liters

Delete the sentence, "The cleaning liquid shall be packaged in containers that meet the requirements of Israel Standard SI 639, Type 1." and replace it with: The cleaning liquid shall be packaged in containers that meet the requirements of Israel Standard SI 2302.

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Clause 105.3 Marking of the containers

- In Amendment no. 2, delete the Clause no., "**105.3.4**" and replace it with: **105.3.5**.

Delete the text in this clause and replace it with the following:

105.3.5 The words, "לא למאכל" (meaning "Not for consumption") shall be marked in a prominent location with a letter size of at least 3 mm and a color that stands out and is different than the background. A tactile marking, where required by the Directive of the European Community 1999/45/EC, shall be added as given in the International Standard ISO 11683.

- At the end of the Clause, add subclause 105.3.6, as follows:

105.3.6 Instructions for use

Clause 201. General requirements

On line five, delete the sentence, " The liquid shall be of a class suitable for packages of type 1 in accordance with Israel Standard SI 639."

Clause 202. Chemical and physical requirements

Table 1

In the second column ("Requirement of liquid for class"), on the row for pH, add the following sentence after the values, "6.0 – 8.5": The pH may be higher than 8.5 provided that the requirements of Clause 202A are met.

Following Clause 202, add Clause 202A, as follows:

202A. Test for skin irritation

In every case that the pH of the cleaning liquid in a 1 % aqueous solution exceeds 8.5, the manufacturer or importer shall present to the test laboratory a test certificate on behalf of the manufacturer, of the performance of a skin irritation test by the "human patch test" as given in Annex B to this Standard, that certifies that the product does not cause irritation in accordance with criterion B.2 in Annex B, below. The test certificate shall be issued by a laboratory for testing skin irritation, recognized by the Israel Ministry of Health.

Clause 203. Liquid content in the container

203.1 Declared content

Delete the Clause.

Following Annex A, Annex B shall be added as follows:

ANNEX B – SKIN IRRITATION TEST BY THE "HUMAN PATCH TEST"

(Normative Annex)

B.1 General

The test is taken from the A.I.S.E. document:

Guidelines for application of Directive 1999/45/EC – A.I.S.E. – 2001,

part B – Approach to irritancy classification,

Clause 1.4 – Skin irritation – Human patch test protocol,

Appendix 3 – Human covered patch test protocol

B.2 Evaluation of test results and classification

According to the criteria for the definition of an irritant given in Directive 67/548/EEC, Appendix VI, Clause 3.2.6.1, a material is considered an "irritant" when it causes significant skin inflammation under test conditions, namely when the mean value of the results for erythema[(2)] or eschar formation or oedema formation calculated over all the test participants (at 24 + 48 + 72 hours) is 2 or more.

Consideration shall be given to special effects, such as hyperplasia, scaling, exudation or surface incrustration, discoloration and fissures.

B.3 Test procedure

The test procedure in English, verbatim, is brought below from the abovementioned A.I.S.E. document. The test shall be as specified in the Procedure, with the following additions:

1.4 Skin irritation – Human patch test protocol

1.4.1 Principle of the test method

In the second paragraph, first line, after the words:

"Patches are applied to the upper outer arm", add the following:

or to the intrascapular region of the back

Appendix 3 – Human covered patch test protocol

4. Materials and dose levels

In the second paragraph, last line, after the words:

"applied to the upper outer arm", add the following:

or to the intrascapular region of the back.

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(2) Not relevant to the translation.

1.4 SKIN IRRITATION - HUMAN PATCH TEST PROTOCOL

The Human Patch Test provides relevant information regarding skin irritation potential of preparations in view of their classification according to the Dangerous Preparations Directive.

1.4.1 Principle of the test method

The test is based upon the animal test method described in Annex V to Directive 67/548/EEC [Part B.4. Acute Toxicity, (Skin Irritation) OJEC. L251 of 19 September 1984, modified in OJEC L 383 of 29 December 1992.]

Patches are applied to the upper outer arm of human volunteers for a maximum of 4 hours, following satisfactory results from a suitable preliminary study.

The degree of irritation is read and graded at specified intervals after treatment and is further described to provide a complete evaluation of the effects.

The test procedure and grading are detailed in Appendix 3.

1.4.2 Ethical considerations

The trial will be conducted in accordance with the Declaration of Helsinki (1964) and subsequent revisions.

Prior to exposing human volunteers, all relevant safety data on the preparation and its constituents should be evaluated.

The procedures and the types of materials to be tested will be subject to ethical review and approval by an appropriate Ethics Committee. All reasonable care should be taken not to cause excessive skin reaction on the volunteers. Prior to conducting the test, written informed consent shall be obtained from each subject.

1.4.3 Good Clinical Practices

The study will be carried out according to recognised guidelines on Good Clinical Practices (e.g. EC Guidelines for Medicinal Products 111 /3976/88-EN) and will be subject to Quality Assurance procedures as appropriate.

Appendix 3

Human Covered Patch Test Protocol

Preliminary study to the Human Covered Patch Test

The preliminary study is designed to reduce the likelihood of excessive skin irritation on the volunteers and should be otherwise performed using exactly the same ethical and methodology conditions as the main study.

Grades are those described in Table I below.

Three healthy volunteers are patched on both arms with the same material. One hour after patching, one of the two patches is removed and the skin is graded immediately, one hour and 24 hours after patch removal. If a grade > 2 is observed during the first hour after patch removal, the other patch is also removed and the skin graded.

In case a grade > 2 is observed at the 1 hour or the 24 hour reading for the one-hour patch, further testing of the preparation should be discussed with the Sponsor prior to deciding on the main study.

If no grades > 2 are observed at the 1 hour reading for the one-hour patch, the other patch is left in place for a total of 4 hours and the skin is graded as described in the main study.

If no grades > 2 are observed at both 1 and 24 hours readings for the one-hour patch, the main study will proceed with 7 other volunteers so that 10 volunteers in total will have been exposed for 4 hours.

Main Study

1. Selection of Subjects

Only healthy volunteers should be used for the test.

The eligibility of each subject will be determined prior to the study e.g. by means of a questionnaire. Exclusion criteria include:

- pregnancy or nursing condition
- skin cancer
- any active skin condition including allergy
- sunburn, acne, scar tissue or tattoos on the test site
- use of medication unless considered irrelevant by the physician involved
- past medical history considered relevant by the physician involved
- heavy alcohol consumption
- participation in another skin clinical test within the last 2 months.

2. Number of Subjects

The number of volunteers used in the main study should be determined on the basis of statistical validation. Previous studies have demonstrated that ten volunteers is usually a suitable number.

3. Patch Composition

The use of commercially available patches, e.g. Webril^{R} non woven cotton squares on semi occlusive tape (e.g. Micropore^{R}), is recommended to minimize inter-laboratory variation.

4. Materials and Dose Levels

Materials considered to be highly irritant or corrosive namely on the basis of their pH-Alkaline/Acidic Reserve (See Appendix 2) would not be tested unless other valid data indicate otherwise. It is the responsibility of the Sponsor to characterize the test materials prior to the study.

Liquid test materials are applied undiluted on the patch prior to skin application. Solids should be moistened sufficiently with water to ensure good contact with the skin. In practice pre-wetting the patch before adding the powder is suitable. 0.2 up to 0.5 ml or g should be used depending on the patch size (e.g. 0.2 ml is suitable for a 1.5 x 1.5 cm patch). The patch is applied to the upper outer arm.

Several test materials may be tested on each subject.

5. Reference Material

A standard reference material may be used in order to check intra and inter-laboratory variation. The concentration of use needs determination by experimentation.

6. Exposure

If two or more products are tested simultaneously the arrangement of the treatment sites on the arm is randomised so that the relative positions of the treatments are different for each panellist. During the test the treatments are identified by code letters. The order of treatments on each panellist is not decoded until the end of the test to preclude bias in the assessment.

In the main study a 4 hour application period is normally employed.

After the appropriate treatment time, the patch is removed, residues are washed off gently with water and the treatment sites are marked.

7. Observation Times

Treatment sites are examined before patch application and are assessed at 1 hour, 24 hours, 48 hours and 72 hours after patch removal or until the reaction has returned to normal.

8. Assessment of reactions

Treatment sites are assessed according to the scoring scale of Annex V to Directive 67/548/EEC. Details of the scoring methods are summarised in the following Table I.

The incidence and extent of exudation or surface encrustation, and discolouration of the treated site will also be assessed. Any other effects and subjective comments made by the volunteers are also recorded.

One examiner will conduct all assessments. Data can be recorded on pre-prepared forms such as that shown in Table II.

TABLE I

Grading of skin reaction

Erythema Scores

0	=	No erythema
1	=	Very slight erythema
2	=	Well-defined erythema
3	=	Moderate to severe erythema
4	=	Severe erythema

Oedema Scores

0	=	No oedema
1	=	Very slight oedema (barely perceptible)
2	=	Slight oedema (edges of area well defined by definite raising)
3	=	Moderate oedema (edges raised by approximately 1 mm)
4	=	Severe oedema (raised > 1 mm and extending beyond the area of exposure)

Exudation or Surface Encrustation

0	=	No effects
1	=	Up to one half of the treated area affected
2	=	More than one half of the treated area affected

Other Effects: (describe)

TABLE II

Example of report sheet

Skin Irritation — 4 Hour Human Patch Test
Individual Panellist Scores

Panellist N° : _____ Test N° : _____

Test Material: _____ Concentration: _____

Assessment Time (hrs)	1	24	48	72
Erythema				
Oedema				
Exudation/Crust Formation				

Average erythema score (24/48/72 hrs): _____

Average oedema score (24/48/72) hrs : _____

Reference Material: _____ Concentration: _____

Assessment Time (hrs)	1	24	48	72
Erythema				
Oedema				
Exudation/Crust Formation				

Average erythema score (24/48/72 hrs): _____

Average oedema score (24/48/72) hrs: _____