Association Internationale de la Savonnerie, de la Détergence et des Produits d'Entretien
International Association for Soaps, Detergents and Maintenance Products

LIQUID LAUNDRY DETERGENT CAPSULES GUIDELINES ON CLP IMPLEMENTATION

Version 2.0

26 November 2018

Overview

This document provides guidance on the implementation of Regulation (EU) No 1297/2014 of 5 December 2014, amending the CLP Regulation (EC) No 1272/2008 with specific measures related to liquid consumer laundry detergents in soluble packaging for single use.

It focuses on practical technical measures concerning the outer packaging and the soluble packaging (*i.e.* the capsule itself).

DISCLAIMER

Although all efforts have been made to try to ensure that the advice and interpretation given in these guidelines is correct, A.I.S.E. emphasises that it can accept no liability for any errors or omissions or for any loss or damage of any kind arising from their use. These Guidelines have not been endorsed by authorities at the date of publication.

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HISTORY OF THIS DOCUMENT

Date	Publication	Comments
February 2015	Liquid Laundry Detergent Capsules Guidelines On CLP Implementation Version 1.0	Original document
November 2018	Liquid Laundry Detergent Capsules Guidelines On CLP Implementation Version 2.0	- Annex IV and Annex V were merged into a new Annex IV that covers the two capsule integrity tests. In this new Annex, (1) the scope of the tests is expanded to also cover in-market inspections; (2) the pre-conditioning is refined to ensure full consistency with the test conditions; (3) statistical criteria are put forward appropriate for in-market inspection; and (4) the statistical criteria for design purposes are removed. - Update of the tonnage assumptions for the environmental risk assessment of denatonium benzoate (Annex III). - Reference to the A.I.S.E. Test Protocol for Superior Child Impeding Closures in section 3.3 on closures. - Typographical and layout corrections.

FOREWORD

These Guidelines address the requirements of Regulation (EU) No 1297/2014 (hereunder referred to as the Soluble Packaging Regulation)[1]. All other legislation applicable to detergent products and their packaging remains unchanged thus continues to apply, *e.g.*

- the number of doses and the nominal quantity to be indicated on the outer packaging in line with the Detergents Regulation (EC) No 648/2004[2] and provisions of the CLP Regulation (EC) No 1272/2008[3]
- classification, labelling and packaging of detergents according to the CLP Regulation
- labelling of allergens according to the Detergents Regulation
- other packaging requirements from *e.g.* the EU Packaging and Waste Directive, or the UN 'Orange Book' on the Transport of Dangerous Goods concerning packaging
- the REACH Regulation[4]
- other applicable legislation.

It should be borne in mind that, since all other CLP requirements concerning classification, labelling and packaging apply and since in the CLP Soluble Packaging Regulation the film is considered as packaging, the film can be excluded from the mixture composition used for deriving classification. In addition, the film (regarded as a specific form of packaging) will have to bear a label if the mixture it contains is hazardous. Specific provisions for 'reduced labelling' as well as a 'full' labelling derogation are foreseen in Article 29 and Annex I, Parts 1.5.1 and 1.5.2. of the CLP Regulation, which can be summarised as follows:

- 'Full' labelling derogation according to Article 29(2) and Annex I Part 1.5.2.2: when sold to the general public, if the capsule content is less than or equal to 25 mL and if the mixture is not classified in the following categories concerning human health: Acute Toxicity (any category), Skin corrosion Category 1A/1B/1C, Serious eye damage Category 1, Skin sensitisation Category 1, Respiratory sensitisation Category 1, Specific Target Organ Toxicity Single Exposure 'STOT SE' or Repeated Exposure 'STOT RE' (any category), CMR 1A/1B/2,[5] Aspiration hazard Category 1.

- 'Reduced labelling' in line with Article 29(1), and CLP Annex I Part 1.5.1: as the capsules are in such a shape and form and are too small to meet the requirements of CLP Article 31 (full labelling) in the languages of the Member States where LLDC are placed on the market, the capsules should bear at least the hazard pictogram(s), the product identifier and the name and phone number of the supplier, provided that all elements defined in CLP Article 17 (full labelling elements) are labelled on the outer packaging.

While the Soluble Packaging Regulation applies only to Liquid Laundry Detergent Capsules classified as hazardous, A.I.S.E. has put in place a new voluntary Product Stewardship Programme to address other unit dose products such as non-hazardous liquid laundry capsules and liquid detergent capsules other than laundry (e.g. automatic dishwasher, floor cleaners, etc.). More information can be found on A.I.S.E.'s website:

http://www.aise.eu/our-activities/product-stewardship-programmes/liquid-laundry-detergent-capsules-634/aise-product-stewardship-programme-for-liquid-laundry-detergent-capsules.aspx

Further, A.I.S.E. launched a voluntary consumer education campaign 'Keep Caps From Kids' consisting of a dedicated multi-lingual website and a communications toolkit (video, web banner, leaflets) aiming at securing safe use and storage of liquid laundry detergent capsules. The toolkit is made available to all partners.

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[1] *http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R1297&from=EN*
[2] *http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32004R0648&from=EN*
[3] *http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:en:PDF*
[4] *http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32006R1907&from=en*
[5] *Mixtures classified as CMR 1A/1B cannot be sold to the general public anyway under Annex XVII of the REACH Regulation*

1. OVERVIEW OF CLP MEASURES FOR LLDC

Regulation (EU) No 1297/2014 amends Annex II to the CLP Regulation (EC) No 1272/2008 setting out 'Special rules for labelling and packaging of certain substances and mixtures', by adding a new section under Part 3 'Special rules on packaging' concerning **liquid consumer laundry detergents in soluble packaging for single use** (referred to as Liquid Laundry Detergent Capsules = LLDC in this document).

Regulation (EU) No 1297/2014 also amends Article 35(2) of the CLP Regulation concerning 'Packaging'.

It was published on 6 December 2014 and entered into force on 26 December 2014.

The following technical measures are required under Regulation (EU) No 1297/2014:

	New CLP requirement for LLDCs
Outer packaging: visibility of content	*The outer packaging shall be **opaque or obscure** so that it impedes the visibility of the product or individual doses.*
Outer packaging: on-pack labelling	*The outer packaging shall bear the precautionary statement P102 "Keep out of reach of children" at a **visible place** and in a **format** that attracts attention.*
Outer packaging: closures	*The outer packaging shall be an **easily reclosable**, **self-standing** container and shall be fitted with a **closure** that* - *impedes the ability of young children to open the packaging by requiring **coordinated action of both hands with a strength** that makes it difficult for young children to open it; and that* - *maintains its functionality under conditions of **repeated opening and closing** for the entire life span of the outer packaging.*
Capsule soluble film: aversive agent	*The [soluble packaging / capsule] shall **contain an aversive agent** in a concentration which is safe, and which elicits oral repulsive behaviour within a **maximum time of 6 seconds**, in case of accidental oral exposure.*
Capsule soluble film integrity: containment function	*The [soluble packaging / capsule] shall retain its liquid content **for at least 30 seconds** when the soluble packaging is placed **in water at 20 °C**;*
Capsule soluble film integrity: mechanical integrity	*The [soluble packaging / capsule] shall resist **mechanical compressive strength of at least 300 N** under **standard** test conditions.*

TIMEFRAME:

The measures must be in place by **1 June 2015**.

For products already placed in the market by that date, shelf withdrawal is not required. The Regulation allows for **a transition period until 31 December 2015** (Article 2 of Regulation (EU) No 1297/2014)**.**

2. SCOPE AND DEFINITIONS

Regulation (EU) No 1297/2014 applies to "*liquid consumer laundry detergents in soluble packaging for single use*".

'Detergent' and 'consumer laundry detergent' are defined in Article 2(1) of the Detergents Regulation (EC) No 648/2004. Regulation (EU) No 1297/2014 makes explicit reference to these definitions.

This implies that soluble unit doses of laundry detergent possibly sold to professional users do not fall in the scope of the Soluble Packaging Regulation.

'Liquid' is defined in the Annex I Part 1.0 to the CLP Regulation.

> *Liquid means a substance or mixture which:*
> *(i) at 50 °C has a vapour pressure of not more than 300 kPa (3 bar);*
> *(ii) is not completely gaseous at 20°C and at a standard pressure of 101,3 kPa; and*
> *(iii) which has a melting point or initial melting point of 20°C or less at a standard pressure of 101,3 kPa.*

For multi-compartment products containing several product forms in one unit dose (*e.g.* partly liquid, partly solid), the European Commission has clarified that, in the absence of any specific provision as to a potential threshold quantity to qualify 'liquid', there is no limit. Unit doses containing **any quantity of liquid laundry detergent are deemed to be falling in the scope of the CLP measures**.

Some 'gels' may qualify as 'liquid' under this definition.

'Hazardous': since CLP Article 35(2) refers to '*packaging containing a hazardous substance or mixtures supplied to the general public*', it is understood that the new provisions apply only to hazardous LLDC *i.e.* detergent mixtures meeting the CLP classification criteria for one or more than one hazard class and category. Non-classified detergent mixtures (irrespective whether they contain one or more hazardous substances) are neither covered by the requirements of Article 35(2) nor by the Soluble Packaging Regulation.

3. OUTER PACKAGING

In this context, 'outer packaging' means the packaging unit that is purchased by a consumer as a single unit (in most cases a box/tub or a stand-up pouch) and that contains a given number of unit doses[6].

3.1. Visibility

This requirement is *de facto* equivalent to the requirements from the A.I.S.E. Product Stewardship Programme for LLDC.

Note: For stand-up pouches, it may be necessary to maintain a transparent window at the bottom of the pack to allow for production control (*e.g.* absence of leaks). This is because pouches are sealed during the production process but need to be inspected for leakers: the detection window allows inspecting without the need for destructive testing (opening the pouch to check thus 'destroying' the product). This transparent window must not be visible when the pouch is standing on a horizontal surface. It should be no larger than required for inspecting leaks.

[6] *Note: 'outer packaging' as referred to in Article 33 of CLP may apply to another layer of packaging such as the transport package.*

Illustrations of opaque or obscure packaging are shown below:

3.2. On-pack labelling

The Soluble Packaging Regulation requires the precautionary statement P102 “Keep out of reach of children” to be visible and in a format that attracts attention.

A.I.S.E. recommends companies to combine two practices:

- ensure primarily that the P102 statement from the CLP Regulation is included in the CLP label and is made more prominent than the other P statements and
- repeat a similar message at a different place on the outer packaging in an attention-grabbing format, *e.g.* P102 statement and/or the relevant A.I.S.E. safe use icons.

P102 STATEMENT IN THE CLP LABEL AREA:

It should be noted that, under the CLP Regulation, the P102 statement applies to consumer products (substances or mixtures), ‘*as appropriate*’. In the ECHA Guidance on labelling and packaging in accordance with CLP, P102 is ‘*highly recommended for substances and mixtures sold to the general public, except for those only classified as hazardous to the environment*’. In addition, according to Article 32(1) of CLP, precautionary statements should be located together with other CLP labels elements (hazard pictograms, signal word, hazard statements).

It is therefore recommended to apply the P102 statement for all LLDC classified as hazardous and to **emphasise the P102 statement in the CLP label** in order to make it stand out versus the other precautionary statements. This can be done using for example a different contrasting colour and/ or using bold or capital characters.

SAFE USE INSTRUCTIONS IN AN ATTENTION-GRABBING FORMAT:

A.I.S.E. recommends adding an attention-grabbing safe storage message on top or on front of the outer packaging in the form of a phrase and/or an icon.

Under its Product Stewardship Programme for LLDCs from December 2012[7], A.I.S.E. has developed a set of voluntary safe use icons[8] and recommends presenting these icons visibly, in the form of patches. The following requirements apply under the voluntary A.I.S.E PSP:

- Priority icons shall be featured in a patch and displayed on pack as follows:
  - 'Keep out of reach of children' (or 'Keep away from children' for a limited transition period, since this has been the text used under the A.I.S.E. PSP commitment), using official translations of P102 provided in Annex IV to the CLP Regulation;
  - 'Close the lid properly' or 'Close the bag properly' (as appropriate), using official A.I.S.E. translations (available from www.aise.eu/end_user_info).
- Minimum size of the icon: 20 x 20 mm
- Text: the icon should be accompanied with the text from the P102 statement 'keep out of reach of children' or 'keep away from children' and a minimum size of 10 points (reference font: Futura Condensed). Multilingual versions of this patch are allowed but the minimum size requirements remain valid for all languages. 'Silent icons' (icons only, without the corresponding text or with the title only) are considered as an option for multi-lingual labels, but this is not the preferred option.
- Colour of the icon: black or dark blue.
- Location of the patch displaying the icons: Patch to be placed on pack (as per A.I.S.E. guidelines and models), with yellow background (reference colour recommended: yellow CMYK: 100%).
- Recommended positioning of patch on packaging: on top or front of the pack. Excluded: underneath the outer packaging. In any event, **the patch should be readily seen by consumers.**
- General introduction sentence: 'Handle and store safely' (or its corresponding translation provided by A.I.S.E. on the link mentioned above), with a minimum size of 13 points (reference font: Futura Bold), preferably in capital letters.
- Others: patch to include copyright and website reference as follows: copyright ©A.I.S.E. together with the link: www.keepcapsfromkids.eu (minimum size: 10 points – reference font : Futura Condensed). Since A.I.S.E. previously recommended www.cleanright.eu, the transition to the new website reference can be progressively implemented by companies when updating their labels. This transition from 'cleanright' to 'keepcapsfromkids' may take place after 1 June 2015 for practical printing reasons, since this is a voluntary measure.

[7] *http://www.aise.eu/our-activities/product-stewardship-programmes/liquid-laundry-detergent-capsules-634/aise-product-stewardship-programme-for-liquid-laundry-detergent-capsules.aspx*
[8] *A.I.S.E. Safe use icons are available on: www.aise.eu/end_user_info*

FROM PATCHES USED UNTIL 2014/2015 UNDER A.I.S.E.'s PSP FOR LLDC

Patch for boxes	Patch for stand-up pouches
	

TO NEW PATCHES (to be used progressively as practically feasible)

WITH TITLE AND TEXT (PREFERRED OPTION)	WITH TITLE ONLY	SILENT
		
		

The A.I.S.E. 'yellow safety patch' which has been used since 2013 on packs of liquid laundry detergents was proven extremely successful in delivering in a consistent, attractive and powerful way the key safe use advice, thanks to the contrasted yellow and dark colours, the size and the location requirements. The icons make it understandable by a vast majority of the population.

Therefore, A.I.S.E. recommends following its LLDC PSP requirements concerning on-pack safe use communication in addition to highlighting the P102 statement in the CLP label area for compliance with the Soluble Packaging Regulation.

Although the CLP requirement concerns only the '*Keep out of reach of children*' message, A.I.S.E. advises to continue displaying the second icon related to closure ("Close the lid properly" or "Close the bag properly") in line with the PSP Use Patch Instructions. Other A.I.S.E icons can continue to be used in other areas of the label, as appropriate.

3.3. Closures

The closure of the LLDC outer packaging must meet two main requirements that need to be balanced:

i. impede young children from opening the packaging and
ii. for adults, allow easy regular opening and reclosing after use.

These functionalities must be maintained during the packaging life span.

In addition, the pack (*i.e*. the 'outer packaging' in the Soluble Packaging Regulation) should be self-standing and should remain so throughout the life span of the pack.

With regard to closure design, the Soluble Packaging Regulation refers qualitatively to two elements: '*requiring coordinated action of both hands*' and '*a strength'* for opening.

These requirements apply '*without prejudice to the requirements of section 3.1 [*of Annex II to CLP*]'* which prescribe child-resistant fastenings for specific mixture classifications (such as skin corrosive products). A.I.S.E.'s understanding is that the closure requirements for Soluble Packaging are different from child-resistant fastenings in section 3.1. and apply independently, without conflict. So section 3.1 of Annex II continues to apply for certain mixture classifications and, in addition, the new section 3.3. applies to LLDCs regardless of their classification.

A.I.S.E. suggests the following interpretation of Soluble Packaging Regulation's requirements:

- '*coordinated action of both hands'* for opening: in the lack of clear design description in the legal text, it is up to each company to assess the design against compliance with this general requirement. It builds on the fact that the key differentiator between adults and children is mental capacity, logic and dexterity. Coordination may include the required use of hands to secure a pack to enable the opening of a closure system (*e.g*. stand-up pouches).
- '*with a strength'* for opening: is to be seen in the context of the target age group, namely children below the age of 6 years. No strength value is specified in the legal text but it should be sufficient so that the closure cannot be opened unintentionally (*e.g.* by simply touching the outer packaging). Again, it should be borne in mind that they key differentiator between adults and children is dexterity and logic rather than strength.
- '*easily reclosable'*: the outer packaging closure must be able to be closed by adults in a single action, such as but not limited to, one clip to be pushed, a gentle pressure on the lid to lock, one zipper to be activated.
- '*maintains its functionality under conditions of repeated opening and closing for the entire life span'*: the closure system must meet the above criteria on opening and reclosing for the designed life of the packaging, which corresponds to at least the number of capsules/unit doses in the outer packaging .

For information, in 2017, A.I.S.E. introduced the Test Protocol for Superior Child Impeding Closures, as part of the voluntary A.I.S.E. Product Stewardship Programme For Liquid Detergent Capsules - 2017. This protocol offers a performance standard for 'child-impeding closures' that are not fully 'child- resistant' (in the meaning of ISO 8371). While CLP and the Soluble Film Regulation do not require meeting such performance criteria, nevertheless, companies may consider evaluating their LLDC outer packaging using this test protocol.

4. AVERSIVE AGENT IN THE SOLUBLE FILM

According to the Soluble Packaging Regulation, the soluble packaging (*i.e*. the capsule wall) must **contain an aversive agent** in a concentration which is safe, and which elicits oral repulsive behaviour within a **maximum time of 6 seconds**, in case of accidental oral exposure.

This measure is intended to further reduce the chance of ingestion of the liquid content in case a child left unattended has managed to gain access to a capsule and places it in his/her mouth.

A.I.S.E. has developed and evaluated a **protocol to determine effective levels of aversive agent** contained in soluble packaging *i.e.* in the soluble film. The resulting study protocol is provided in Annex I.

The objectives of this work were:

- To develop a method for measuring the oral rejection time, as a function of the level of aversive agent in the film;
- To prove the concept of effectiveness testing (at different concentrations of aversive agent), in other words to establish a 'benchmark test'.

One grade of film and one particular aversive agent were selected for the study.

The A.I.S.E. study has shown that, for the particular aversive agent and film selected, it was possible to determine a level of aversive agent sufficient to elicit a median oral rejection in less than 6 seconds. Above this concentration, the 'dose-response' curve was flat, *i.e.* higher levels of aversive agent were not found to lead to lower rejection times. A summary of the study findings is provided in Annex II.

For ethical reasons, the study was run on young adults instead of children. This is a conservative approach, because a child's palate is much more sensitive than that of adults. Infants have around 30,000 taste buds spread throughout their mouths. By the time adulthood is reached, only about a third of these remain, mostly on the tongue. The decreasing sensitivity to bitterness with age was demonstrated by Mennella et al. (2005)[9]. Consequently, it is reasonable to assume that the observed oral rejection times with young adults are similar to or higher than what may be expected with young children.

It is important to note that it is up to each company to demonstrate effectiveness of the aversive agent chosen to their own situation (soluble film/agents) at design stage. This is because:

- different aversive agents may lead to different human responses and
- the effective concentration of aversive agent may be affected by the polymer chemical composition, presence of other chemicals in the film, etc.

It is advised to foresee a safety margin so that the effectiveness of the aversive agent is maintained during the whole life cycle of the product.

Companies will need to document the levels of aversive agent used and the rationale, and **keep such records for 10 years** (in line with the general REACH and CLP record keeping deadlines).

Further, the Soluble Packaging Regulation requires the **effective concentration of aversive agent to be safe**. A.I.S.E. recommends to determine that the concentration chosen is safe in case of ingestion of the amount of film contained in one capsule, by means of a human health toxicological risk assessment, based on the highest level of aversive agent contained in the soluble packaging at any time of the product life cycle and adapted to the target age group (young children, including babies). The safety data sheet of the aversive agent is a useful source of toxicological data but may not be sufficient to run a full risk assessment.

Environmental safety should also be documented. It should be reminded that the REACH Registration is the main mechanism to assess environmental safety of substances and demonstrate the use is safe (unless a

[9] *Julie A. Mennella, M. Yanina Pepino, and Danielle R. Reed. Genetic and environmental determinants of bitter perception and sweet preferences. Pediatrics, 2005, 115 (2), e216-e222*

particular substance does not need to be registered by law). Annex III provides an example of a screening environmental risk assessment for one particular aversive agent (denatonium benzoate) showing that, even under conservative assumptions, the addition of this bittering agent in unit dose soluble films is of no concern from an environmental perspective.

5. CAPSULE INTEGRITY

Two specific requirements apply under the Soluble Packaging Regulation in relation to capsule integrity: mechanical resistance and liquid containment.

Both the mechanical and the containment function tests are understood as **'design' tests.** They serve a safety purpose in the qualification of products / validation of processes. They are not considered as quality control tests since it is impossible in practice to test every single capsule.

These tests should be performed on an appropriate, representative number of capsules at design stage and should be repeated, at the minimum, at every substantial design change in product, film specification, formulation or manufacturing process.

The capsules will be tested at least 24 hours after production after having been conditioned in an environment with a standard temperature and relative humidity. More details are provided in the test protocols (Annex IV).

5.1. Liquid containment function

The Soluble Packaging Regulation requires the soluble packaging to retain its liquid content for at least 30 seconds when the capsule is in contact with water. Some of the testing parameters are set by the Regulation (water, temperature).

To A.I.S.E.'s knowledge, no standard method exists for such type of test.

Building on the experience from its members, A.I.S.E. has developed a **containment function test protocol**, which is provided in Annex IV to this document.

5.2. Mechanical integrity

The Soluble Packaging Regulation requires the soluble packaging to resist to a mechanical compression strength of 300 N under standard test conditions.

A.I.S.E. recommends running a **dynamometric test**: the purpose of such compression test is to assess the mechanical integrity of a capsule submitted to a compressive strength.

Building on the experience from its members, A.I.S.E. has developed a test protocol, which is provided in Annex IV to this document.

ANNEX I

Study Protocol:

Assessment of the effectiveness of an aversive agent in soluble film for liquid laundry detergent capsules

Objective

The objective of this test is to determine the effectiveness of a given aversive agent contained in a given soluble packaging film. The dose-response relationship of the level of aversive agent with the observed oral rejection time is investigated. From this, the level of aversive agent that is expected to lead to a rejection time below 6 seconds is determined.

General study description

The response of test panellists to tasting water-soluble film with different levels of aversive agent is to be observed. From this, a dose-response relationship is to be established that links the deterring effect (rejection of the film) with the level of the aversive agent.

The test panel shall consist of young adults, as a proxy for the target audience for the safety measures on liquid laundry detergent capsules (i.e. young children). There are reliable indications that, especially for bitter taste, children are usually more sensitive than adults.

The test product is the water-soluble film containing (different levels of) the aversive agent. The film shall be used in isolation for tasting: actual detergent capsules shall not be used, to ensure the safety of the panellists.

Each panellist, unaware of what to expect, will be given a sheet of the soluble film containing a given level of aversive agent, and will be asked to lick the film to experience the taste. It will then be recorded whether the panellist rejects the film and if so, after how much time. Panellists are only allowed to participate once, to avoid any bias due to prior experience with a bad tasting sample.

A concentration series will be tested, in two rounds. First, in a screening round, a broad range of levels of aversive agent in film shall be assessed, as well as an untreated blank. Subsequently, based on the screening round results, suitable aversive agent test levels shall be defined for a definitive testing round, aiming to refine the dose-response relationship for those levels leading to a rejection time close to the target of maximum 6 seconds.

Test material

The test material is a combination of one specific water-soluble film type with one specific aversive agent, at different concentration levels. Both the water-soluble film and the aversive agent tested shall be identified in the study report and/or in the study sponsor's confidential study placement documentation. The results of the study are specific to the type/grade of water-soluble film and the type/grade of aversive agent used. Consequently, results cannot be extrapolated to substantially different combinations of film and aversive agent[10].

Preparation of water-soluble film treated with aversive agent

Water-soluble films with different levels of the aversive agent shall be prepared:

- Screening test: untreated (blank) - 10ppm - 100ppm - 1000ppm - 10000ppm (*)(**)
  (*) a toxicological safety assessment shall be conducted prior to the study. if toxicological concerns exist with the highest screening levels, an alternative concentration series with lower levels should be used.
  (**) a range with a different upper level may be used if pre-existing information suggests this is more appropriate.

- Final test: 6 levels (no blank) to be determined based on the outcome of the screening test

Accuracy of the aversive agent's levels in the film, and homogeneity of its distribution, shall be ensured by the producer of the treated film.

[10] *It is also up to each company to select the aversive agent they deem appropriate for their products, taking into account that some limitations of use related to Intellectual Property may apply to certain aversive agents, films or technologies.*

Preparation of the film sheets for taste testing

The treated water-soluble films shall be cut into strips of 3cm by 10cm. For each test concentration, at least 12 replicates shall be prepared. The strips of film shall then be placed in individual bags, to ensure contamination is not an additional variable for the study.

Subsequently, for each concentration, the strips shall be split into two equal batches - one batch for male panellists, one batch for female panellists. The sets of test specimens for female and male panellists shall be kept separate and identified as such.

These test specimens shall be individually labelled using a coding system that links the specimen to its aversive agent level. The coding shall not disclose the level of aversive agent neither to the panellists, nor to the persons directly handing the test specimens to the panellists. This is to avoid any bias, by applying a double-blind approach. For the same reason, preparation, packing and labelling of the film strips shall be done by different persons than those conducting the study with the panellists.

Test Panel

A test panel with as many participants as there are test specimens (i.e. in total 10 test concentrations + one blank, with minimum 12 replicates each, hence a total of at least 132 panellists) is required to conduct this study for one film / aversive agent combination.

For ethical considerations, the test panel shall not consist of young children, but instead, as a proxy, young adults shall be used. It should be noted that this is expected to lead to some difference in the results, as adults tend to 'think' about the bad taste that is happening rather than react and spit it out. The study has been designed to eliminate as much of the adults 'over thinking' to the test as possible, attempting to gage a 'true' reaction time.

The test panel shall consist of the following individuals:

- young adults, in the age group of 18-25 years old
- equal mix male / female
- exclusion criteria:
    - smokers shall be excluded.
    - panellists with prior experience on tests of aversive agents in this context shall be excluded.

Each panellist shall participate to only one single tasting session, to avoid a biased response driven by prior experience.

Test Design and Instructions

The test shall be conducted in two rounds:

1. a screening round in which a wide range of levels of the aversive agent is assessed;
2. a final round in which the dose-response relation close to the rejection time target is refined.

In the screening round, there shall be 4 test concentrations in addition to a blank (untreated film). In the final round, there shall be 6 test concentrations, and no blank. There shall be at least 12 replicates for each concentration. Hence, in total, there will be at least 132 tasting sessions (5x12=60 for the screening round, and 6x12=72 for the final round). If deemed necessary based on the results of the screening round, a higher number of replicates may be used for the final round.

The levels of aversive agent for the screening round are predetermined. The levels for the final round are to be defined based on the screening results. Consequently, the final round can only be organized several weeks after the screening round, to allow for processing of the screening data, and for preparation and shipment of the film and test specimens.

For the actual testing, the test specimens shall be provided to the person conducting the study in two batches: one for female panellists, and one for male panellists. As outline above, each of these batches shall contain an equal number of replicates for each test concentration. Consequently, every test concentration shall be tested with an equal number of males and females, to avoid any potential bias driven by the panellists' gender.

For every tasting session (one panellist, one level of the aversive agent) the following method shall be followed:

1. The test shall be conducted such that participating panellists cannot see the reaction of others in the test, and cannot talk to others who have just completed the test. The panellists shall not be informed about the presence of an aversive agent in the sample. The persons providing the test samples to the panellists shall not be informed about the level of the aversive agent in the sample.

2. The panellist shall drink a defined small amount (50ml) of still water.
3. The following exact instructions shall be given to the panellist: "*This is a taste test and it is what we call 'double-blind', meaning I do not know what taste you are going to receive. It could be anything from a neutral non-taste to something pleasant or unpleasant, it could be salty, sweet, acidic*[11]*, etc. If, when you are licking it, you think the taste is neutral or pleasant, I want you to continue licking it until I tell you to stop. If, when you are licking it, you discern that the taste is something unpleasant, I want you to stop licking it immediately. You are going to take the film that is in the bag and hold it in your hands and lick it like so...*" and then the panellist will be shown how to hold and lick the film.
4. At the moment of contact of the film strip with the tongue / mouth, a timer shall be started, and no further instructions shall be provided to the panellist. Each panellist's reaction may be filmed for future reference.
5. It shall be recorded whether the panellist rejected the test specimen prior to the strip's dissolution in half, and if so, exactly after how many seconds the rejection occurred.
6. Participants shall be given something to eat or drink to remove the bad taste. What is to be offered will depend on the aversive agent under study. For example, for bittering agents, strong dark chocolate is known to effectively remove the bitter taste. In addition, flavoured lip balm shall be offered in case the bad flavour has travelled to the lips of the panellists.
7. Exclude the panellist from any further participation to this test or similar tests in the future.

Analysis and reporting of results

All raw data collected during the study shall be reported, except for the identities of the panellists (that are to remain confidential to the testing laboratory). Note that these identities shall be archived by the testing laboratory for further reference, to avoid their participation in other similar studies in the future.

Among the panellists, it is expected that there will be a natural variability in taste receptor sensitivity, primarily driven by genetic differences. People who lack sensitivity in the receptors that are targeted by a specific aversive agent, will experience the aversive taste to a limited extent, if at all (irrespective of the concentration of the aversive agent). For example, in Sibert & Frude (1991)[12], in a test where children were given orange juice spiked with a common aversive agent (denatonium benzoate) at a level known to be effective, over 15% of the test subjects showed no evident response.

The aim of the study is to determine the appropriate aversive level that leads to oral rejection within 6 seconds of the initial exposure. For non-sensitive subjects, this rejection time cannot be achieved, irrespective of the level of aversive agent used. Consequently, data from non-sensitive subjects should be ignored when determining the appropriate level. Hence, the median of the different replicates at a given level shall be used as the relevant metric for comparison with the 6 second target.

By means of suitable statistical methods (to be determined case-by-case, depending e.g. on the distribution shape and amount of scatter of the data) it shall be determined which levels of aversive agent have led to a median rejection time below the target of 6 seconds, with at least 90% confidence. If feasible (depending on the quality of the data), a mathematical dose-response relationship shall also be developed, that allows to determine rejection time as a function of the aversive agent level. Furthermore, it shall be determined up to which level of aversive agent the observed rejection time is not significantly different from the blank; and as of which level of aversive agent the observed rejection time no longer decreased.

The final outcome of the study is the determination of the lowest aversive agent level that is expected to lead to a median rejection time (either observed as tested; or calculated if a mathematical dose-response relationship could be developed) below 6 seconds, with at least 90% confidence.

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[11] *The actual description of the taste of the aversive agent under study shall not be used here. For example if a bittering agent is used, the word 'bitter' shall not be mentioned; if the aversive agent has an acidic taste, the word 'acidic' shall not be used, etc.*

[12] *Sibert J.R. & Frude N. (1991). Bittering agents in the prevention of accidental poisoning: children's reactions to Denatonium Benzoate (Bitrex). Archives of Emergency Medicine, 1991, 8, 1-7.*

ANNEX II

Summary of Intertek study findings:

"Assessment of the Effectiveness of an Aversive Agent in Soluble Film for Liquid Laundry Detergent Capsules".

Executive Summary

- The proposed test method to assess the effectiveness of an aversive agent in soluble film for liquid laundry detergent capsules was found to be practically feasible, and to allow defining an aversive agent's effective level in the context of Commission Regulation (EU) No 1297/2014.
- It is recommended to use the median oral rejection time as the appropriate metric to assess compliance with the requirements. Non-parametric statistical methods are needed, because the rejection times between panellists are not normally distributed. Specifically, a certain percentage of the population is typically less or not sensitive to a given aversive agent due to natural variability (genetic predisposition), which leads to skewed distributions and scattered observational data. This implies that a sufficient number of replicates (at least 12 but ideally more) is required per tested level of aversive agent, to ensure robustness of the results.
- For one specific grade of PVA film, treated with the bittering agent denatonium benzoate, a dose-response relationship was observed with a decreasing rejection time up to 220ppm. The rejection time remained the same when the aversive agent's level was further increased beyond this level. The median rejection time for levels >= 220 ppm was 2.7 seconds, and was demonstrated to be significantly less than 6 seconds with >95% confidence.

Background

Commissioned by A.I.S.E., Intertek carried out a study to measure the reaction time of young adults when coming into oral contact with soluble film treated with an aversive agent. The response of the test panellists to tasting water-soluble film with different levels of aversive agent was observed. From this, a dose-response relationship was established that links the deterring effect (rejection of the film) with the level of the aversive agent.

The objectives of this study were twofold:

(1) the development of a method for measuring the oral rejection time by young adults, as a function of the level of aversive agent present in water-soluble film of detergent capsules; and

(2) proof of the concept with one specific commonly-used aversive agent and one specific film.

For the method development, a pilot study was conducted with internal Intertek employees. Next, through a screening study with 50 panellists (5 tested levels, 10 replicates each), it was determined what are the appropriate levels of the aversive agent to be tested in more detail. A final study was then conducted with 72 panellists (6 tested levels, 12 replicates each). A follow-up study with orange juice that was spiked with the aversive agent, was conducted afterwards with 10 panellists, to assess whether these may have been non-sensitive to the aversive agent. All these studies were conducted at the Intertek facility in Oak Brook, Illinois in the US.

Method Development

Overall, it can be concluded that the developed test protocol is practically feasible and that it can be used to determine the effective level of an aversive agent leading to rejection within a defined time period.

The most suitable method of delivery was found to be a sheet of film (3x10cm), to be licked by the panellists until discerning that the taste is something unpleasant. Clear wording was developed to have unambiguous instructions for the panellists. This was well understood (with only 1 exception out of 132 panellists).

To rule out any difference due to different taste sensitivities between males and females, both genders should be equally represented and each gender group should receive the same distribution of aversive agent levels tested.

The observed rejection times (especially for those aversive agent levels that lead to a substantial repulsive effect), were found to not follow a normal distribution. A majority (75-80%) was clustered around a short rejection time,

while the remainder was very scattered. This is directly driven by the biology: genetically, a certain part of the population has less (or no) effective receptors for the specific aversive taste. As such, it can be anticipated that similar distribution shapes may be found with other aversive agents and/or other soluble films than the ones used for the method development. It should be noted that follow-up to assess possible non-sensitivity of panellists with long rejection times was not found to add substantial value. Instead, appropriate statistical methods should be used that implicitly take into account the 'biological outliers'.

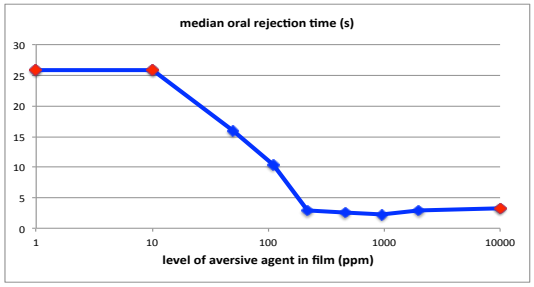
As a consequence of the non-normality, the use of mean rejection time is not relevant. Instead, the median should be used, as this is independent of the distribution shape at its extremes. Using Sign Analysis (a non-parametric method) it can be assessed whether the observed median is significantly below the required threshold of 6 seconds, with a given level of statistical confidence (e.g. 90% or 95%).

Another consequence of the non-normality is that a sufficiently high number of replicates is required for each tested level. 12 replicates per level, as applied in the final round of this study, is judged to be a minimum. But a larger number of replicates is to be preferred, to increase statistical robustness.

Proof of concept for a specific PVA film containing Denatonium Benzoate

As a proof of concept, the method was applied to determine the required effective level of one specific aversive agent (a bittering agent: denatonium benzoate) selected based on its commonality and one specific polyvinyl alcohol (PVA) film grade (Monosol M8630).

No reduction of the oral rejection time versus untreated film was seen up to 10 ppm of denatonium benzoate in the film. At 50 ppm, a clearly lower rejection time was observed, and this further decreased at 110 ppm and again at 220 ppm, where a median value of less than 3 seconds was reached. Higher levels did not cause the median rejection time to drop further[13]. The dose-response relationship is shown in the below chart. Please note that for the ppm levels a logarithmic scale was used. The data shown are from the final study except the data points in red (screening study).



The observed dose-response relationship is statistically supported by the Mann-Whitney test. This shows that the rejection times at the higher levels were not significantly different from those at 220 ppm (i.e. flat dose-response beyond 220 ppm). Further, this test shows that all treatment levels in the final study led to significantly lower rejection times than the 0 ppm blank, and that the rejection time at 220 ppm was significantly less than at 110 ppm. Finally the test shows that the rejection time at 10 ppm (screening round) was not less than for the blank.

The median oral rejection time for denatonium benzoate levels in film >= 220ppm (in the final study) was on average 2.7 seconds. Sign analysis shows that for each of these levels, the median was significantly below 6 seconds, with a confidence level of >95%. The 75th percentile of the observed rejection times was also below 6 seconds for all levels >= 220ppm (in the final study), however, statistical significance could not be demonstrated.

It can be concluded that, for the specific film grade that was tested, a denatonium benzoate level of 220 ppm in the film is adequate to meet the requirements of Commission Regulation (EU) No 1297/2014.

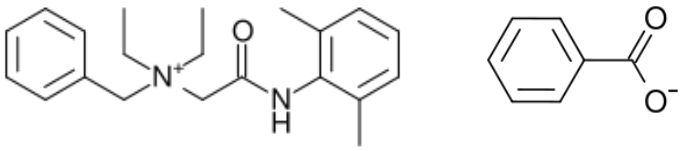
[13] *To note: the median of 9.8 seconds observed in the screening round for 1000 ppm is judged to be an artifact caused by the too limited number of replicates. When the observed rejection times for 1000 ppm (screening round) and those for the very similar level of 960 ppm (final round) are grouped, the median is 3 seconds.*

ANNEX III

Screening environmental risk assessment for Denatonium Benzoate (example of aversive agent)

Substance identification

Denatonium benzoate is a salt of the quaternary ammonium cation denatonium with the inert anion benzoate:



CAS	3734-33-6
Molecular formula	$C_{28}H_{34}N_2O_3$
Molar mass	446.581

Environmental properties

Ecotoxicity

In the European Classification & Labelling notification process (ECHA, 2015), denatonium benzoate was notified as Aquatic Chronic 3 (H412) by most notifiers.

In the EU Ecolabel DID LIST (European Commission, 2014), denatonium benzoate is included (ingredient nr. 2604). As the relevant acute LC50, a value of 13 mg/L is mentioned. Chronic data are absent.

The following ecotoxicologal data are reported in several safety data sheets (from multiple suppliers) of denatonium benzoate, and/or in regulatory reviews (e.g. US CPSC 1992; Health Canada, 2011):

- Fish: 96h LC50 Rainbow Trout: >1000 mg/L
- Invertebrates: 96h LC50 Shrimp (salt water): 400 mg/L
- Invertebrates: 48hr EC50 Daphnia magna: 13 mg/L
- No effects on bacteria up to 150 mg/L

The Predicted No-Effect Concentration (PNEC) can be derived from the lowest acute data point, in this case for the water flea Daphnia magna (which is also the value used for the EU ecolabel). The assessment factor to extrapolate from an acute EC50 to the ecosystem safe level is a factor 1000. Hence, the PNEC = 13 µg/L.

Biodegradability

The active cation denatonium was not found to be either biodegraded or adsorbed to sludge in a Semi-Continuous Activated Sludge (SCAS) study (Corby et al., 1993). As a SCAS test simulates fate in actual sewage treatment plants, it is fair to assume that denatonium benzoate will not be removed in sewage treatment.

Furthermore (cf. CPSC, 1992), in an OECD 301D test, no chemical deterioration of Denatonium benzoate was observed. In the Zahn-Wellens test (OECD 302B), a 36% breakdown was found after 28 days. A carbon dioxide production test showed that denatoinum benzoate is poorly metabolized (4.5% after 28 days).

In the EU Ecolabel DID LIST, denatonium benzoate is assumed to be not removed in sewage treatment (DF=1).

Bioaccumulation

Denatonium benzoate is highly water soluble (45 g/L) and has a low octanol/water partitioning coefficient (Kow = 0.91) (cf. Health Canada, 2011). Consequently, there is no risk for bioaccumulation.

Environmental Risk Assessment

Tonnage Estimate

Denatonium benzoate is manufactured and/or imported in the European Economic Area in 100 - 1000 tonnes per year (ECHA web site). For the purpose of this screening assessment one could conservatively assume a total of 1000 ton per year, which is equivalent to 2000 mg per capita per year in the EU (with 500 million people).

The incremental consumption of denatonium benzoate in the context of liquid laundry detergent capsules, can be estimated as follows:

- One laundry capsule of 5cm x 5cm with a film thickness of 100 µm has 5 x 5 x 0.01 x 2 sides = 0.5 cm^3 of soluble film as outer packaging. With a density of 1.3 this corresponds to 0.65 g of film per capsule.
- When 200 [respectively 1000] ppm is used as aversive agent contained in the film, this leads to the presence of 130 [resp. 650] µg of denatonium benzoate per capsule.
- In the United Kingdom, which is to date the most mature market for laundry capsules, on average about 20 capsules are sold per year per inhabitant (total market: 1150 million capsules; population of 64 million).
- This corresponds to 2.6 [resp. 13] mg of denatonium benzoate per capita per year.

Consequently, an assessment of the assumed current tonnage of 1000 ton/year in the EU (= 2000 mg/cap.year) covers any potential increase due to the introduction of denatonium benzoate in the soluble film of laundry capsules at the envisaged levels.

Risk Assessment

The average water use per person per year in the EU is 100-200 L per capita per day (EEA web site). Conservatively, a water use of 100 L/day is assumed.

Assuming 1000 ton/year in the EU, the concentration of denatonium benzoate in household waste water is 2000 mg/cap.year divided by 365 days/year x 100 L/cap.day = 55 µg/L. As denatonium benzoate is not removed in sewage treatment plants, this is also the predicted concentration for treated effluent. Finally, the Predicted Environmental Concentration (PEC) in river water, taking into account a standard dilution factor of 10, is 5.5 µg/L.

The aquatic PNEC for denatonium benzoate is 13 µg/L (derived from Daphnia magna acute data with an assessment factor of 1000).

The PEC/PNEC ratio for denatonium benzoate is 55 / 13 = 0.4 < 1. It should be noted that this is based on a conservative tonnage estimate of total consumption, which is also nearly three orders of magnitude higher than the expected use of this substance for laundry capsules.

Conclusion

Using conservative assumptions, especially regarding tonnage, this screening assessment shows no concerns with the environmental safety of denatonium benzoate. The incremental use of denatonium benzoate as aversive agent in laundry detergent capsules is minimal compared to the assumed total tonnage, and is not anticipated to negatively impact this conclusion.

References

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ANNEX IV

Capsule integrity test protocol

Scope

This provides guidance on the test design, execution and interpretation to evaluate the integrity of the capsules when in contact with water, and when subjected to pressure.

The tests are suitable for in-market compliance inspections as well as for the evaluation of product and process design and for quality control purposes.

The tests are non-destructive, i.e. each sample is subjected to the conditions defined in the legislation as the threshold for compliance. For each sample, the outcome of the test is either “pass” or “fail”. It is allowed to continue the testing beyond the legal threshold, extending the test with a destructive phase, to determine what is the critical parameter value at which the tested capsule fails. However, this aspect of the test is not part of the A.I.S.E. guidance and these data are not recommended for a compliance assessment.

Sample conditioning prior to testing

Sample conditioning is an important measure to be adopted to ensure test reproducibility. Therefore, capsules shall be tested immediately after having been conditioned at a temperature of 20±1°C) and at 50±2% Relative Humidity for at least 24 hours in the original outer packaging opened to the conditioning atmosphere.

Note that for in-market products testing, only products that were appropriately transported, stored and conditioned can provide relevant and reproducible results according to the accepted international quality standards (see for instance ASTM standard D4332 13).

Capsule integrity when in contact with water

A beaker of sufficient capacity is filled with at least 1 L of demineralised water. The water temperature shall be stabilised at 20±1°C.

One pre-conditioned capsule is gently introduced into the beaker until it is entirely submerged. The capsule shall be surrounded by water on all sides. In case the density is such that the capsule either floats or sinks, the capsule shall be placed inside a device that prevents floating or sinking (e.g. a metal cage, a netting bag, or similar) and that allows visual observation.

A 30 seconds timer shall be started as soon as the capsule is submerged.

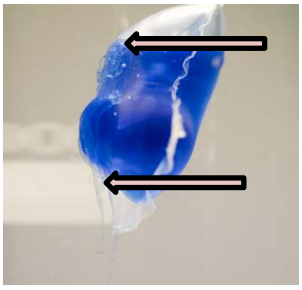
The capsule shall be carefully observed during 30 seconds, for any visual evidence of liquid leaving the capsule.

The following pictures illustrate the observable stages of containment loss (for illustration only - visual observations may differ depending on the capsule design, colour size or shape).

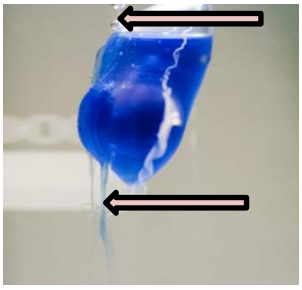
1) Prior to product release with fully closed containment.
2) The moment in time when first release of product is observed.
3) Further progress of content release and air escapes from the capsule.

Stage 1

Stage 2



Stage 3



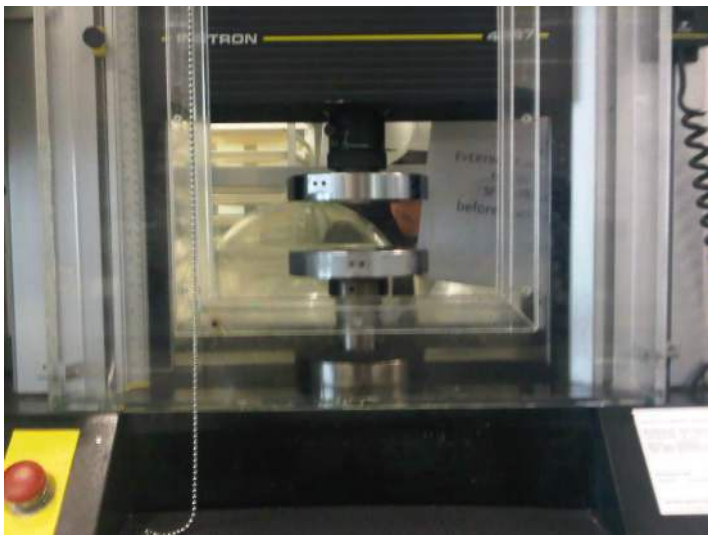
The critical liquid content release time is 30 seconds. An individual capsule successfully passes the test if no release of liquid content occurred during the 30 seconds of submersion. Optionally, the test can be continued beyond this duration.

Capsule integrity when subjected to pressure

The dynamometric test shall be conducted under conditions that are similar to the conditioning atmosphere (room temperature / approximately 50% Relative Humidity).

One capsule is subjected to an increasing compression force, between two flat plates of a surface larger than the surface area of the capsule, at a rate of 200-250 mm/min. This can be achieved with standard equipment such as e.g. Instron model 5566 (see picture below), or equivalent. During the test, the capsule is to be placed inside a transparent plastic bag to avoid spillage or splashes. It shall be positioned between the two plates that apply the force, resting on its largest surface area.

While the capsule is carefully observed, the compression force shall be gradually increased either until 300N is reached, or a lower force in case the capsule already releases its content.



The critical mechanical compression resistance is 300N. An individual capsule successfully passes the test if no release of liquid content occurred during compression up to a force of 300N. Optionally, the test can be continued beyond this threshold.

Statistical criteria for inspections using the capsule integrity tests

For inspections, to determine whether a batch of capsules is non-compliant with the capsule integrity criteria, A.I.S.E. recommends to adopt methods and quality criteria validated according to international procedures as provided by the ISO 2859-4 standard[14] with a declared quality level of 5% non-conforming items. At Level 2 (i.e. with a limiting number of 2 defects), this implies that the sample size is n=16. In other words, from a statistical point of view, test results for 16 samples contradict the declared quality level if the number of defects is >2, while the declared quality level is not contradicted if the number of defects is <= 2.

[14] *ISO (2002). Sampling procedures for inspection by attributes — Part 4: Procedures for assessment of declared quality levels. ISO 2859-4:2002(en). International Organization for Standardization, Geneva, Switzerland.*