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Child-resistant non-reclosable packaging for pharmaceutical products — Requirements and testing

Emballages à l'épreuve des enfants, non refermables pour produits pharmaceutiques — Exigences et essais

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

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For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

This document was prepared by the European Committee for Standardization (CEN) (as EN 14375) and was adopted, under a special "fast-track procedure", by Technical Committee ISO/TC 122, *Packaging*, Subcommittee SC 3, *Performance requirements and tests for means of packaging, packages and unit loads (as required by ISO/TC 122)*.

There are no changes to the content of the EN 14375 document.

Introduction

Child-resistant packaging is used to create a physical barrier between a child and a potentially hazardous product. Various types of packaging are recognized as being child-resistant, based on performance testing against standards for specific product categories and packaging types.

Since child-resistant packaging was introduced, the incidence of accidental ingestion of potentially hazardous products by children under 5 years old has fallen. The degree to which this is due to the use of child-resistant packaging as opposed to other factors, such as greater public awareness of the hazards, is not easily assessed, but there is little doubt that child-resistant packaging has made a positive contribution to the reduction.

The use of child-resistant packaging needs to be confined to those products that are potentially hazardous, or for which any legislation makes its use mandatory, since, if used in other circumstances, there could be confusion over the degree of hazard posed by the product.

In any case, proper labelling and information by the manufacturer is important for the safe use of the product in the home.

Child-resistant packaging acts as the last line of defence if other barriers separating the child and hazardous product have failed. However, it should be recognized that it is unrealistic to expect that any functional packaging can be totally impossible for a child of 42 to 51 months inclusive to open and that child-resistant packaging cannot be a substitute for other safety precautions.

There has been an increasing use of child-resistant packaging, therefore it is desirable to achieve agreement on testing procedures in order to avoid confusion and misunderstanding in an area of great importance to the safety of young children.

The on-going development of non-reclosable packaging offers a significant area for innovation in packaging. The styles of non-reclosable packages can be wide-ranging in design.

This document aims to minimize the number of children "exposed to training" during panel testing. Since the introduction of performance testing much has been learned about the use of children for testing child-resistant packaging and attention has been focused on how the number of children involved can be reduced. Future development of standards based on mechanical test methods is needed to avoid unnecessary child panel testing and is essential in developing physical package attributes useable by manufacturers.

Child-resistant packaging is only the last in a series of protective measures, and does not release parents or guardians from their duty to keep medicinal products out of the reach of children.

Child-resistant non-reclosable packaging for pharmaceutical products — Requirements and testing

1 Scope

This document specifies performance requirements and methods of test for non-reclosable packaging that have been designated child-resistant. This document is intended for type approval only (see 3.5) and is not intended for quality assurance purposes.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
child-resistant package
package which is difficult for young children to open (or gain access to the contents), but which is possible for adults to use properly

3.2
non-reclosable child-resistant package
child-resistant package (3.1) or part of a child-resistant package which, when all or part of the contents have been removed, cannot be properly closed again

3.3
substitute product
inert substitute resembling the product it replaces

Note 1 to entry: This is sometimes referred to as a placebo product.

EXAMPLE Powder, tablets or liquids (uncoloured water), etc.

3.4
unit dose
discrete quantity of any product to be removed from its immediate packaging in its entirety

3.5
type approval
procedure to certify as child-resistant a specific type of non-reclosable package, formed from a specified set of materials

4 Requirements

4.1 General requirements

A non-reclosable child-resistant package, when tested in accordance with the requirements of this document, shall be capable of providing a satisfactory degree of resistance to opening by children (see 4.2.1) and a satisfactory level of accessibility to its contents by adults (see 4.2.2).

A non-reclosable child-resistant package, in addition to conforming to the performance requirements specified in this document (see 4.2), shall be appropriate for the contents, provide mechanical protection and function properly for the life of the content and packaging.

Manufacturers, component manufacturers, fillers and packers of such packages shall initiate and operate procedures to control the quality of packaging materials so that type approved packaging is in accordance with the requirements of this document.

NOTE ISO 9001 specifies requirements for quality management systems where organizations need to demonstrate their capability of supplying conforming products to customers.

4.2 Performance requirements

4.2.1 Child test

An individual child test shall be considered a failure in relation to unit, strip or blister packages if within 10 min the child accesses more than 8 unit doses from the packaging provided.

When tested in accordance with 5.3.2 and evaluated in accordance with 5.4.1.3, the packaging shall be deemed to be child-resistant.

NOTE The figure of eight units is based on existing national standards published by certain CEN members and does not address the issue of toxicity. Some pharmaceutical products on the market can cause harm to children by the ingestion of fewer than eight units. However, reliable data on child toxicity exists for few pharmaceutical products. A harmful dose can be established for some existing pharmaceutical products and a maximum safe dose can be established for all pharmaceutical products by one means or another. Such information is not currently available for all products and there is no central register where this information could be held. In the absence of European legislation on this topic, the drafters of EN 14375 acknowledge these concerns and believe that research and collection of data should continue with a view to considering the substitution of a toxicity based pass/fail criterion for the child panel test in a later revision.

4.2.2 Adult test

When tested in accordance with 5.3.3.2, at least 90 % of the adults shall be able to access at least 1 unit dose within the 1 min test period, without a demonstration.

To minimize the exposure of children to unnecessary testing, the adult test should be carried out before the child test.

5 Testing

5.1 Principle

Type approval for non-reclosable child-resistant packaging is obtained by a sequential test method or full panel test for children and a full panel test for adults. A test group of up to 200 children aged 42 to 51 months is divided into pairs. Each child is given a number of non-reclosable packages to be opened by whatever means they wish to use. If a child fails to gain access within 5 min, the method of opening is demonstrated by the supervisor and the child is given a further 5 min to open the package. The results are recorded sequentially, as obtained. The package is deemed child-resistant if the trail of results on the test charts passes into the acceptance zone or if at least 80 % of the children are unable to access more than eight unit doses within 10 min and at least 85 % of the children are unable to access more

than eight unit doses within the first 5 min. The package's accessibility by a test group of 100 adults is also assessed. Each adult is given a non-reclosable package, any associated opening tools and written instructions, and is allowed 5 min to familiarize themselves with the packaging. The number of adults opening the package within a 1 min test period is recorded. The package is deemed to comply with the requirements of this document if at least 90 % of the adults are able to access at least 1 unit dose in 1 min.

5.2 Samples and sample preparation

Sufficient packages shall be produced by the proposed manufacturing process to enable a representative sample to be selected by the supervisor for testing and to provide a reserve for reference purposes. Dangerous products shall not be used to fill the package to be tested; an appropriate substitute product shall be used. The material and design of the test samples shall conform to the technical specification and they shall be representative of an average batch of original packages.

Packages for the child panel test shall be unprinted.

In every test, a new package shall be provided for each member of the test group. For both the child and adult tests, there shall be at least 10 unit doses available for each participant.

Each sample package shall be checked for integrity before the test is conducted. The packages shall be presented to the children without the outer retail packaging, giving them access to the individual unit doses.

5.3 Procedure

5.3.1 General

The test procedure is carried out in two stages:

a) child test (see 5.3.2);

b) adult test (see 5.3.3).

5.3.2 Child test

5.3.2.1 Composition of child test group

The test group shall comprise no more than 200 children aged 42 to 51 months, inclusive, with approximately equal numbers of girls and boys. As far as possible, there shall be an even distribution of ages and sexes within the panel. The children shall be selected at random and shall have no apparent physical or mental disability which might affect manual dexterity. They shall not have taken part in more than one previous test and, in that test, a packaging of a different type and design shall have been used. If a child is used for more than one test there shall be at least 4 weeks between tests. Parental or guardian consent shall be obtained before the child is used as a part of the test group. Any children having been involved in a reported poisoning accident shall be excluded from the test.

Children should be selected to represent as closely, as is reasonably possible, the different social, ethnic and cultural origins or the population as a whole, and not just of the immediate district in which the test is carried out.

5.3.2.2 Test procedure

Testing shall be carried out in the presence of a test supervisor. The child test shall take place in an environment familiar to the children.

Test personnel should visit the test location beforehand and become known by the children in order to gain their confidence. Only the supervisors should be present, parents being excluded from the test.

The test shall be carried out by a sequential procedure (see 5.4.1.1 to 5.4.1.3). The number of children tested will therefore depend on the results obtained, however, the age and sex constraints specified in 5.3.2.1 shall be adhered to.

Pairs of children shall be involved in the test, each pair being monitored by one supervisor. Should a child wander off during the test, action by the supervisor shall be limited to leading the child back to its place and requesting that he or she continue the test, without any additional instruction being given concerning the opening of the package; this fact shall be included in the report (see Clause 6).

If desired, a number of pairs (up to five) can undertake tests in the same room at the same time, provided that arrangements are such that they cannot distract other pairs. They can adopt any attitude or position that they find convenient and should not be restrained. During the test, children should be removed as far as possible from extraneous distractions. If other means of observation are used, the supervisor can stand at a distance from the children.

Each child shall be given sufficient packages (see 5.2) with the request that they be opened by whatever means the child wishes to use; 10 min shall be allocated for this purpose. No attempt shall be made to prevent a child using its teeth or any other method of opening the package. However, no tools or implements shall be accessible which might be used by the child, other than those supplied by the manufacturer/filler or packer at point of sale.

Children failing to open or gain access to a minimum of 1 unit dose in the first 5 min shall then watch a single demonstration by the test supervisor of the package being opened, with no emphasis being placed on the actions of opening and with no verbal instructions. These children then have a further 5 min to open the package or gain access to its contents.

If a child leaves the test area during the test period (5 min or 10 min) or refuses to participate in the test despite encouragement, the result shall not be taken into account but the event recorded.

When tools are needed to open the package, but these are not supplied by the manufacturer, there shall be no demonstration. The test is therefore limited to the first 5 min test period.

At the conclusion of each test, the children should be warned not to play with, or attempt to open, these types of packages.

NOTE Annex A provides a summary of the requirements and guidance to be followed by test supervisors. If required by the regulatory body, an official observer will be present, but the guidance laid down in Annex A still applies.

5.3.3 Adult test

5.3.3.1 Composition of adult test group

The test group shall comprise 100 participants. These shall be selected using a screening procedure in which potential participants shall be asked the following questions.

“Are you professionally concerned with the design, manufacture or use of child-resistant packaging?”

“Have you taken part in more than one previous child resistant packaging test within the last 6 months?”

Only those participants responding with negative answers shall be selected.

In order to elicit this information and, at the same time, to ascertain whether the individual is literate, this question shall be presented on a typed or printed form and given to the person to read.

Persons with obvious physical disabilities that might affect manual dexterity shall not be approached and those unable to understand the written opening instructions discounted.

The purpose of the test shall be explained but no demonstration shall be given.

The 100 participants shall be randomly selected between the ages of 50 and 70 in accordance with the requirements given in Table 1. Not more than 30 of the adults tested shall be obtained from or tested at any one site. No individual supervisor shall administer the test to more than 35 adults.

Table 1 — Composition of the adult test group

	Age range years	Male number of participants	Female number of participants	Total number of participants
	50 to 54	8 or 7	17 or 18	25
	55 to 59	7 or 8	18 or 17	25
	60 to 70	15	35	50
Total	—	30	70	100

5.3.3.2 Test procedure

There is no need for the adults to be tested at any particular place or time. The test should be carried out by one person at a time and only the supervisor should be present.

Each adult shall be given a package, together with any associated opening tools that would be provided with the package at point of sale, and written instructions on how to open the package correctly, if any.

These can be printed in or on the package when supplied to a consumer.

Each adult shall perform the test individually. No demonstration of how to open the package shall be given by the supervisor. A period of 5 min shall be allowed for the test participants to familiarize themselves with the package to be tested by reading the opening instructions and then attempting to open it correctly. Test participants shall not be allowed to consult either the supervisor or other participants in the test.

Participants who successfully open the test package within the 5 min period shall be given a new identical package and shall be requested to open this one as quickly as possible. A 1 min test period shall be allowed for the participants to open the new packaging.

If in this period of 5 min a panellist is unable to open the package being tested they will be given a screening test. This screening test consists of asking the panellist to open and reclose the following two conventional non-child resistant closures in one minute each:

a) a 28 mm diameter continuous screw thread closure applied at 1,1 Nm torque onto a 25 ml to 50 ml cylindrical plastic container;

b) a 28 mm diameter “push-off” closure applied to a 25 ml to 50 ml round plastic container.

Panellists unable to open and reclose both of these packages in the 1 min screening test shall be discounted from the adult panel results.

Panellists who are able to open and reclose both these packages are counted as a failure in the overall result.

5.4 Evaluation

5.4.1 Child test

5.4.1.1 General

The result of each test shall be recorded on the test charts given in Figures B.1 and B.2 in accordance with 5.4.1.2. The results shall be evaluated in accordance with 5.4.1.3.

NOTE The statistical parameters governing the sampling procedures for the test charts are given in Annex C.