SLOVENSKI STANDARD
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Medicinske rokavice za enkratno uporabo - 3.del: Zahteve in preskusi za biološko ovrednotenje

Medical gloves for single use - Part 3: Requirements and testing for biological evaluation

Medizinische Handschuhe zum einmaligen Gebrauch - Teil 3: Anforderungen und Prüfungen für die biologische Bewertung

Gants médicaux non réutilisables - Partie 3: Exigences et essais pour évaluation biologique

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11.140	Oprema bolnišnic	Hospital equipment

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EUROPEAN STANDARD
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English version

Medical gloves for single use - Part 3: Requirements and testing for biological evaluation

Gants médicaux à usage unique - Partie 3: Exigences et essais pour évaluation biologique

Medizinische Handschuhe zum einmaligen Gebrauch - Teil 3: Anforderungen und Prüfungen für die biologische Bewertung

This European Standard was approved by CEN on 1 April 1999.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the Central Secretariat or to any CEN member.

This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the Central Secretariat has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and United Kingdom.

EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

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Contents

Foreword

This European Standard has been prepared by Technical Committee CEN/TC 205 "Non-active medical devices", the secretariat of which is held by BSI.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by June 2000, and conflicting national standards shall be withdrawn at the latest by June 2000.

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s).

For relationship with EU Directive(s), see informative Annex ZA, which is an integral part of this standard.

According to the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom.

Annex A is normative and forms part of this European Standard. Annexes B, C, D, E and ZA are for information only.

Introduction

Adverse reactions in health care workers and patients to latex products have been reported over the last few years due to latex proteins. However, adverse reactions due to chemicals, lubricants, sterilization residues (ethylene oxide) pyrogens or residues are also described in the scientific literature. Adverse reactions are most often reported due to gloves made from natural rubber latex, but some of the reactions can also be seen due to gloves made from other polymers.

The series of horizontal standards EN ISO 10993 give guidelines concerning biological evaluation of medical devices and also includes evaluation and testing protocols for specific tests and other safety related specifications.

However it does not cover all adverse reactions (e.g, immediate type allergies) that can result from the use of medical gloves. These adverse reactions occur to specific allergens that can be present in gloves. Several factors contribute to the reaction:

a) the long-term and high frequency of skin contact by the glove user;

b) exposure to the allergens through direct contact to skin and mucosa especially if they are not intact and by inhalation of particles;

c) the occlusive nature of the glove/skin interaction over years of glove use.

This part of EN 455 therefore gives test methods that enable the biological safety of medical gloves to be evaluated as part of a risk analysis process, in accordance with EN 1441.

This part of EN 455 does not specify levels of acceptability for latex proteins and chemicals because at present there is insufficient understanding of factors relevant to safety assessment in this area, e.g. identity of allergens, sensitisation threshold and process controls. It is anticipated that, as the level of understanding is raised, the requirements of this standard will be modified. Further methods to measure and control these allergens are under development.

1 Scope

This Part of EN 455 specifies requirements for the evaluation of biological safety for medical gloves for single use. It gives requirements for labelling and glove packaging and the disclosure of information relevant to the test methods used. It also contains a review of immunological test methods for the determination of leachable proteins and allergens.

2 Normative References

This European Standard incorporates, by dated or undated reference, provisions from other publications. These normative references are cited at the appropriate places in the text and the publications are listed hereafter. For dated references subsequent amendments to or revisions of any of these publications apply to this European Standard only when incorporated in it by amendment or revision. For undated references the latest edition of the publication referred to applies.

EN 1041 Information supplied by the manufacturer with medical devices

EN 1441 Medical devices - risk analysis

EN ISO 10993 Biological evaluation of medical devices

The European Pharmacopoeia 3rd Edition, Suppl. 2.6.14, Bacterial endotoxins, 1998

The European Pharmacopoeia 3rd Edition, 2.6.8 Pyrogens, 1997

3 Definitions

For the purpose of this part of EN 455, the following definitions apply:

3.1
chemicals:
Substances added and formed during any step of the manufacturing process or in storage which may be available in the final product. These can include lubricants and chemical coatings and sterilizing agents.

3.2
endotoxins:
Lipo-polysaccharides originating from the outer cell-membrane of Gram-negative bacteria.

NOTE : Sources of endotoxins can include bacterial contamination of the raw materials, the process water used during manufacturing and manual handling of the gloves

3.3
leachable proteins:
Water soluble proteins and peptides of different molecular weights that are leachable from the final product.

NOTE : Most of these proteins originate from natural rubber latex. These and other proteins (e.g. casein) which may be added can change, alter and degrade during the manufacturing process. Proteins extracted in aqueous media have been reported to cause Type I allergic reactions.

3.4
pyrogens:
Substances creating fever in rabbits which can be related to fever and other adverse reactions in humans.

NOTE : Endotoxins are one type of pyrogen.

3.5
process limit:
Highest value of protein in gloves likely to be encountered for that manufacturing process.

4 Requirements

4.1 General

Medical gloves for single use shall be examined as described in the EN ISO 10993 series. A risk analysis in accordance with EN 1441 shall be carried out,

4.2 Leachable proteins

The manufacturer shall monitor the process limit of leachable protein in the finished gloves containing natural rubber latex by the method specified in **5.1**. Documentation of these results shall be retained. The results of the test and applied test method shall be made available on request.

This documentation will assist in deciding, in conjunction with the risk analysis, if the biological risks associated with contaminants and residues are acceptable.

4.3 Endotoxins

The manufacturer shall monitor the endotoxin contamination of sterile gloves using the test method specified in **5.2** if the gloves are labelled with 'low endotoxin content'. For such labelled gloves the endotoxin content shall not exceed the limit of 20 endotoxin units per pair of gloves.

4.4 Chemicals

Gloves shall not contain or be dressed with talcum powder (magnesium silicate). The manufacturer shall disclose, upon request, a list of chemical ingredients either added during manufacturing or already known. to be present in the product such as accelerators, antioxidants and biocides, that are known to cause adverse health effects based on current data.

4.5 Labelling

In addition to the labelling specified in EN 1041, the following labelling shall be given at least on the primary packaging:

a) Medical gloves derived directly from natural rubber latex shall be labelled with the following or equivalent:

'(Product) contains natural rubber latex which can cause allergic reactions.'

b) Powdered gloves shall be labelled as such.

Powdered sterile surgical gloves shall be labelled with the following or equivalent:

'CAUTION: Surface powder shall be removed aseptically prior to undertaking operative procedures in order to minimize the risk of adverse tissue reactions.'

NOTE 1 : This caution can be given on the inner wrapping.

c) If the manufacturer labels the gloves with a protein content, the process limit, measured as specified in **5.1**, shall be given.

NOTE 2 : This does not allow a protein labelling claim below 50 µg/g.

NOTE 3 : Safe use of this glove by or on latex-sensitized individuals has not been established.

d) The claim of "hypoallergenicity" shall not be used.

NOTE: Attention is drawn to the symbols given in EN 980.

5 Test methods

5.1 Leachable proteins

The test method for the determination of leachable protein shall be either the modified Lowry method given in annex A or a suitably validated method which has been correlated against the modified Lowry method. See Annex A for more information.

NOTE 1 : It is recognised that other validated methods for the analysis of leachable proteins exist (e.g. validated amino acid analysis method given in Annex C) and these can be used provided that they have been validated and a correlation has been established against the reference method specified in this standard. These methods are not yet suitable for routine quality control purposes.

NOTE 2 : Immunological methods for protein determination are also under development (see annex B).

5.2 Endotoxins

Except where non-removable interferences in the LAL procedures are present, selection, validation and use of technique shall be either as described in The European Pharmacopoeia 3rd Edition, Suppl. 1998 2.6.14. Bacterial endotoxins or by an equally sensitive and reproducible Limulus Amoebocyte Lysate (LAL) procedure. Where non-removable interferences in the LAL procedure are present, the bacterial endotoxin level cannot be accurately measured. In such instances a rabbit pyrogen test as described in the European Pharmacopoeia (3rd edition, 1997 2.6.8) may be applied The results shall be expressed in endotoxin units (E.U.) per pair of gloves.(1 E.U. = 1 I.U.)]

The test shall be carried out for each batch. The minimum number of pairs of gloves recommended to be tested in relation to the number of items in the batch are two pairs of gloves for a batch size under thirty, three pairs of gloves for a batch size thirty to
one hundred, and 3 % of a batch above size one hundred, up to a maximum of ten pairs of gloves per batch.

The outside surface of a pair of gloves is extracted with 40 ml of endotoxin-free water (Water LAL , European Pharmacopoeia, 3rd Edition, Suppl. 1998, 2.6.14) for not less than 40 min and not more than 60 min at a temperature between 37 °C and 40 °C in a way to ensure that all surfaces come into contact with the extraction medium. The extract is centrifuged, if necessary, for 15 min at 2000g to remove particles after which the liquid component is decanted and tested for endotoxin immediately afterwards.

NOTE : It is recognised that other methods for the analysis of endotoxins exist and these can be used for routine quality control purposes provided they

have been validated and a correlation established against the reference method specified in this European standard.

6 Test report

The test report shall include at least the following information:

— a reference to this part of EN 455;

— the type of gloves and manufacturing batch code;

— the name and address of the manufacturer or distributor and of the test laboratory if different;

— the date of the test performed;

— the description of the test method applied;

— the test results.

Annex A (normative)

Method for the determination of aqueous extractable proteins in natural rubber gloves using the modified Lowry assay

A.1 Scope

This method is for the determination of the amount of aqueous extractable proteins in gloves for medical use made from natural rubber (NR). It has been validated during interlaboratory round-robin tests. The lower quantification limit is approximately 10 µg protein per g of glove (i.e. 2 µg protein per ml of extract) depending on the glove weight.

Chemicals such as surfactants, accelerators and antioxidants added to the NR latex during the manufacture of the gloves can interfere with the colour development during the determination, some materials may reduce colour development while others can increase it. If the test method yields results that appear erroneous due to interferants, then any validated amino acid analysis method can be used (as an example see the method given in annex C).

NOTE : Persons using this method should be familiar with normal laboratory practice, This method does not purport to address all of the safety problems, if any, associated with its use. It is the responsibility of the user to establish appropriate safety and health practices and to ensure compliance with any national regulatory conditions.

A.2 Principle

Water soluble proteins are extracted in to a buffer solution and then precipitated with acids in the presence of sodium deoxycholate to concentrate them and to separate them from water soluble substances which may interfere with the determination. The precipitated proteins are redissolved in alkali and quantified colorimetrically by a modified Lowry method. The assay is based on the reaction of proteins with copper and Folin reagent in an alkaline medium to give a characteristic blue colour. Spectrophotometric measurements are performed at a fixed wavelength in the range 600 nm to 750 nm.

A.3 Reagents

A.3.1 *General*

Wherever water is called for, double distilled water or water of equivalent quality should be used. All other reagents should be of analytical quality.