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Medical gloves for single use - Part 4: Requirements and testing for shelf life determination

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English Version

Medical gloves for single use - Part 4: Requirements and testing for shelf life determination

Gants médicaux non réutilisables - Partie 4: Exigences et essais relatifs à la détermination de la durée de conservation

Medizinische Handschuhe zum einmaligen Gebrauch - Teil 4: Anforderungen und Prüfung zur Bestimmung der Mindesthaltbarkeit

This European Standard was approved by CEN on 20 June 2009.

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Foreword

This document (EN 455-4:2009) has been prepared by Technical Committee CEN/TC 205 “Non-active medical devices”, the secretariat of which is held by DIN.

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of an identical text or by endorsement, at the latest by January 2010, and conflicting national standards shall be withdrawn at the latest by January 2010.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN [and/or CENELEC] shall not be held responsible for identifying any or all such patent rights.

This part of EN 455 gives requirements and test methods for shelf life determination of medical gloves as part of a risk management process, in accordance with EN ISO 14971. EN 455 consists of the following parts under the general title "Medical gloves for single use":

— Part 1: Requirements and testing for freedom from holes

— Part 2: Requirements and testing for physical properties

— Part 3: Requirements and testing for biological evaluation

— Part 4: Requirements and testing for shelf life determination

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EC Directive 93/42/EEC.

For relationship with EC Directive 93/42/EEC, see informative Annex ZA, which is an integral part of this document.

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

Introduction

Medical Gloves are intended to be a barrier to agents responsible for the transmission of infections. In order to help ensure effectiveness, it is essential that gloves fit the hand properly, are free from holes and have adequate physical strength so as not to fail during use. All these issues are addressed in the EN 455 series.

This European Standard covers the minimum properties that address certain essential requirements detailed in the Medical Devices Directive (93/42/EEC). Manufacturers are required to conduct stability tests to estimate the shelf life of any new or modified glove before the product is placed on the market and to initiate real time stability studies. The real time stability test can be considered as part of the manufacturers' requirement to conduct post-marketing surveillance on their products. These requirements are intended to ensure that manufacturers have adequate data to support shelf life claims before products are placed on the market and that these data are available for review by regulatory authorities.

1 Scope

This part of EN 455 specifies requirements for shelf life for medical gloves for single use. It also specifies the requirements for labelling and the disclosure of information relevant to the test methods used.

This European Standard applies to existing, new and significantly changed designs. Existing designs that do not currently have ageing data available should generate that data within a reasonable period of time.

This European Standard does not specify the size of a lot. Attention is drawn to the difficulties that can be associated with the distribution and control of very large lots. The recommended maximum individual lot size for production is 500 000.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

EN 455 (all parts), *Medical gloves for single use*

EN 1041, *Information supplied by the manufacturer of medical devices*

EN ISO 11607 (all parts), *Packaging for terminally sterilized medical devices*

3 Terms and definitions

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

3.1
Arrhenius equation
relation between the activation energy (E_A), the absolute temperature (T), and the rate constant of a degradation reaction [k(T)]

NOTE The shelf life of a rubber product is predicted based on the Arrhenius principle of chemical reaction rates. The Arrhenius equation has the basic form:

$$k(T) = A \cdot e^{\frac{-E_A}{RT}}$$

where

A = constant (min^{-1}),

E_A = Activation Energy (J/mol),

R = the Universal Gas Constant (8,314 J · mol^{-1} · K^{-1}),

T = Absolute Temperature (K),

$k(T)$ (min^{-1}) is the rate constant for the degradation process.

An alternate way of expressing the Arrhenius equation is:

$$\ln k(T) = \ln A - (\frac{E_A}{RT})$$

The time required for the physical properties to deteriorate to the threshold value is inversely proportional to the rate constant *k(T)*.

3.2
consumer package
package, intended for distribution to a consumer, containing loose gloves or individual pairs of gloves

NOTE For example a primary pack (peelpack) for sterile product or a dispenser box for non-sterile product.

3.3
expiry date
stated date after which the gloves shall not be used

3.4
lot
collection of gloves of the same design, colour, shape, size and formulation, manufactured at essentially the same time, using the same process, raw materials of the same specifications, common equipment and packed in the same type of individual container

3.5
shelf life
time from date of manufacture to the claimed expiry date

3.6
significant change
change that could reasonably be expected to impact the safety or effectiveness of a medical device

NOTE It could include a change to any of the following:

a) the manufacturing process, facility or equipment;

b) the manufacturing quality control procedures, including the methods, tests or procedures used to control the quality, purity and sterility of the device or of the materials used in its manufacture;

c) the design of the device, including its performance characteristics, principles of operation and specifications of materials; and

d) the intended use of the device, including any new or extended use, any addition or deletion of a contra-indication for the device and any change to the period used to establish its expiry date.

3.7
threshold value
maximum or minimum value for a property being tested

4 Requirements

4.1 General

Medical gloves shall comply with the requirements of the EN 455 series of standards until the end of their stated shelf life provided they are stored according to the instructions supplied by the manufacturer.

Manufacturers shall test the properties that are reasonably expected to alter over the shelf life of the product. These properties shall include, but are not limited to, force at break, freedom from holes and, in the case of sterile gloves, pack integrity. This European Standard defines the methods to determine shelf life of medical gloves before any new product or products for which there has been a significant change to formulation or process can be marketed.

Since it is impracticable to complete real time ageing studies before introducing products to the market, accelerated stability studies based on kinetic principles can be used to assign a provisional shelf life. Such provisional shelf lives assigned shall be verified by real time studies.

Shelf life claims based on accelerated ageing shall not exceed three years. Data supporting the shelf life claims made by the manufacturer shall be made available on request.

4.2 Shelf life and resistance to degradation

Before a new or significantly modified product is placed on the market this European Standard requires:

— a completed real time study as described in 5.1 to determine shelf life or

— a real time study as described in 5.1 to determine shelf life shall have commenced and an accelerated ageing study as described in 5.2 shall have been completed.

It is recommended that the shelf life should be determined at the specific storage conditions specified for the product by the manufacturer (e.g. 25 °C). The manufacturer shall state the temperature along with the shelf life or expiry date. Accelerated ageing studies (5.2) shall be carried out on gloves from the same production lots as used for real time determination of shelf life (5.1).

NOTE For guidance on mean kinetic temperature see EN ISO 291.

4.3 Product changes

Whenever there is any significant change to the product the manufacturer shall re-determine shelf life.

4.4 Labelling

At the end of the shelf life the labelling shall remain readable according to EN 1041.

4.5 Sterile barrier integrity

For sterile products the requirements of EN ISO 11607 series apply. Attention is drawn to the maintenance of the sterility for the given shelf life of the product.

NOTE Depending on the utilised packaging material, it might occur that the packaging material will not withstand certain elevated temperatures that are being used to predict the shelf life by means of accelerated ageing testing. In these cases it might be advisable to conduct the accelerated ageing testing at lower temperatures.

4.6 Storage conditions

Manufacturers shall provide storage instructions to the end user. These may be printed on the consumer package or supplied in an accompanying document.

5 Test methods

5.1 Real time shelf life determination

The test method for the determination of shelf life using real time studies shall be that given in Annex A or a suitably validated method that has been shown to be equivalent to Annex A.

If the real time data indicates a shorter shelf life than that claimed on the basis of accelerated ageing the manufacturer shall notify the relevant regulatory authorities. The manufacturer shall change the shelf life claims for

the product to one based upon the real time study. For gloves placed on the market, real time stability studies shall be completed for the full period of the shelf life claim.

5.2 Accelerated shelf life determination

Pending the completion of real time studies, accelerated stability studies shall be used to estimate the shelf life. Examples of methods for accelerated studies and data analysis are provided in Annex B. Data generated from such studies shall support the claim that the gloves fulfil the requirements in Clause 4 for the duration of the labelled shelf life at temperature as determined by the manufacturer.

NOTE Guidance for selection of temperature is given in EN ISO 2578.

6 Test report

The test report shall contain at least the following information:

a) Reference to the appropriate standards;

b) Sample details:

   1) Complete identification of the material tested;

   2) Dimensions and method of the preparation of the test pieces, with reference to relevant European Standards;

   3) Selected properties, with reference to relevant European Standards;

   4) Threshold value of the selected property;

   5) Times and temperatures of the conditioning of test pieces;

c) Details of the ageing conditions;

d) Test data and analysis according to the relevant standards;

e) Confirmed shelf life claim.

Annex A
(normative)

Method for the determination of shelf life by real time stability studies

A.1 Principle

Gloves in consumer packages are conditioned at the temperature as defined by the manufacturer (e.g. 25 °C) for the intended shelf life period and then tested for compliance.

NOTE 25 °C is the mean kinetic temperature for temperate climates.

A.2 Procedure

A sufficient number of gloves (taken from a minimum of three lots of gloves packed in their consumer packaging or, in the case of sterile gloves, the peelpack) shall be placed in a specified environment and conditioned to assess at intervals of one year or less:

a) median of the Force at Break (13 gloves per interval) according to EN 455-2,

b) freedom from holes according to according to EN 455-1,

c) that the glove is fit for the intended purpose, and

d) pack integrity (sterile gloves).

The lots shall be tested individually and the results for each lot reported individually – lots may not be combined. Each lot must pass all the requirements of the test to allow a shelf life claim for the stated interval.

NOTE It is strongly recommended that additional gloves be conditioned as spares in case there is a need for any retesting or in case additional time points are required.

A.3 Confirmation of shelf life claim

Upon completion of A.2, the shelf life claim shall be up to that period, not to exceed five years, for which the gloves have complied with the requirements of this European Standard.

Annex B
(informative)

Guidance on conducting and analyzing accelerated ageing studies

B.1 Principle

Accelerated ageing studies may be used to estimate provisional shelf lives. This informative annex describes a general protocol that may be used for conducting accelerated ageing studies to estimate shelf life for market introduction while real time studies are in progress. It also offers guidelines on analyzing these studies to predict provisional shelf life using the Arrhenius relationship.

B.2 Background

Before commencing accelerated ageing studies, consideration should be given to the specific mechanisms of degradation that may apply to the type of material from which the gloves are made. Some materials, for example, may exhibit excellent resistance to thermal and oxidative degradation but may be susceptible to rapid degradation by hydrolysis if not protected from moisture. Accelerated ageing studies are usually undertaken at elevated temperatures to increase the rate of degradation but other potentially important factors, such as humidity, also need to be taken into account.

It should also be recognized that the use of high temperatures may cause effects to occur that are not relevant to the normal ageing processes observed under ambient conditions. For example, some thermoplastic materials may exhibit excessive softening or partial melting at the higher temperatures typically used for accelerated ageing studies. There is also evidence that for some natural rubber latex formulations the mechanism of degradation changes at temperatures in excess of 50°C. The temperature range used for testing some types of gloves may therefore be restricted.

The shelf life of a glove may be limited by other factors than deterioration in the strength of the material. For example the material may increase in modulus and the shelf life may therefore be limited by the glove becoming too stiff or brittle. In such cases it may be more appropriate to monitor modulus in addition to strength.

Because of the errors and uncertainties inherent in the determination of shelf lives using accelerated ageing methods shelf life claims should be limited to a maximum of 3 years.

B.3 Procedure for conducting accelerated ageing studies

B.3.1 Pilot Study and Estimate of Provisional Shelf Life

A pilot study is undertaken first to establish the effect of temperatures on the rates of degradation of the product and make an estimate of the shelf life of the product. Gloves, packed in their consumer packaging or, in the case of sterile gloves, the peelpack, from three production lots are conditioned in ovens at selected temperatures. At appropriate time intervals, remove samples of gloves from the oven, and determine the Force at Break according to EN 455-2, plus any other tests though likely to enable comparison of the glove characteristics such as extensibility or modulus of elasticity.

It is recommended that a minimum of four elevated temperatures are used. A minimum of 5 time points at each temperature is recommended and the study should continue for at least 120 days and preferably 180 days. It is recommended that at least 7 gloves are tested at each time / temperature point.

If the results are to be compared with those for gloves for which real time stability data is available then equivalent samples of those gloves should be conditioned at the same time.

Estimate of the provisional shelf life of the product at 25°C (or other storage temperature specified by the manufacturer) using one or more of the procedure described in sections B.4, B.5 and B.6.

B.3.2 Verification of provisional shelf life estimate

Using data from the pilot study select one or more combinations of ageing time and temperature that are expected to cause the same degree of degradation that will occur over the estimated shelf life of the product at 25°C (or other storage temperature specified by the manufacturer). The ageing conditions should be chosen with a view to replicating the mode of failure at 25°C that is predicted by the pilot stability study. The choice of reference conditions is most easily achieved using Arrhenius shift factors assuming that a reasonable Arrhenius plot has been obtained and a reliable estimate of the activation energy is available. For convenience the ageing temperatures can be selected as 70°C (if applicable) and 50°C.

NOTE 1 The verification study may be started before the pilot study is completed but there should be a suitable time delay to allow data from the pilot study to be collected and analysed in order to determine when the verification samples should be tested.

NOTE 2 In the example cited in this annex where the activation energy has been estimated to be 142 kJ/mol, 22 days at 50˚C, 5 days at 60˚C and 1 day at 70˚C would be approximately equivalent to 5 years at 25˚C.

Take samples of gloves packed in their consumer packaging or, in the case of sterile gloves, the peelpack from three lots. The same three lots should be used as for the pilot accelerated ageing study if the verification study is started within 2 months of starting the pilot study. Otherwise fresh lots of gloves should be used. Condition the samples at the selected ageing temperature for the selected time. Test the samples for compliance with the requirements of the EN 455 series of standards including the following:

a) median of the Force at Break (13 gloves per interval) according to EN 455-2,

b) freedom from holes according to EN 455-1,

c) that the glove is fit for the intended purpose, and

d) pack integrity (sterile gloves).

The estimate of provisional shelf life is confirmed if the product complies with the requirements of the EN 455 series of standards after storage at the selected ageing temperature and time.

B.4 Analysis of accelerated ageing data to estimate provisional shelf life

For many products, shelf life estimates can be predicted by extrapolation from accelerated ageing studies using the Arrhenius equation. Details of the procedure are given in ISO 11346. The application of the Arrhenius equation should be considered first. Details of how to construct an Arrhenius plot are given in B.5

Alternatively the results of accelerated ageing data may be analyzed by a number of other methods or as stipulated by the manufacturer's regulatory authority. A useful method is to compare the rates of change of properties with those of a glove of similar formulation for which the shelf life has already been determined by a real time study. Manufacturers are not limited to any specific method of analysis of accelerated ageing studies and are encouraged to investigate the various methods available.

B.5 Application of the Arrhenius equation to accelerated ageing data

B.5.1 Background

For many chemical reactions the rate at which the reaction occurs varies with temperature according to the Arrhenius Equation:

$$k(T) = A \cdot e^{\frac{-E_A}{RT}} \qquad \text{(B.1)}$$

where

A is a constant,

E_A is the activation energy,

R is the gas constant (8,314 J · mol^{-1} · K^{-1}),

T is the absolute temperature,

$k(T)$ is the rate constant for the particular chemical reaction concerned.

It can be shown that the time required for a reaction to reach a specified threshold, is inversely proportional to the rate constant $k(T)$. The Arrhenius equation can therefore be re-written in terms of the time required to reach a specified threshold, $t_{(x\%)}$, as:

$$\frac{C}{t_{(x\%)}} = A \cdot e^{\frac{-E_A}{RT}} \qquad \text{(B.2)}$$

where

C is a constant.

Taking logs of both sides and rearranging equation (B.2) becomes;

$$\ln t_{(x\%)} = \frac{E_A}{RT} - \ln\frac{A}{C} \qquad \text{(B.3)}$$

If it is assumed that there is a direct relationship between the underlying chemical changes and the observed change in the physical property being observed then equations (B.3) also models the time required for that physical property to reach a specified threshold.

If the Arrhenius equation is applicable then it follows from equation (B.3) that a straight line will be obtained by plotting $\ln t_{(x\%)}$ against $1/T$ (K^{-1}). Assuming that a straight line is obtained then it is very easy to extrapolate the line and determine time required for the predetermined degree of change to occur at the target temperature. The activation energy E_A can be readily calculated from the slope of the line recognizing that:

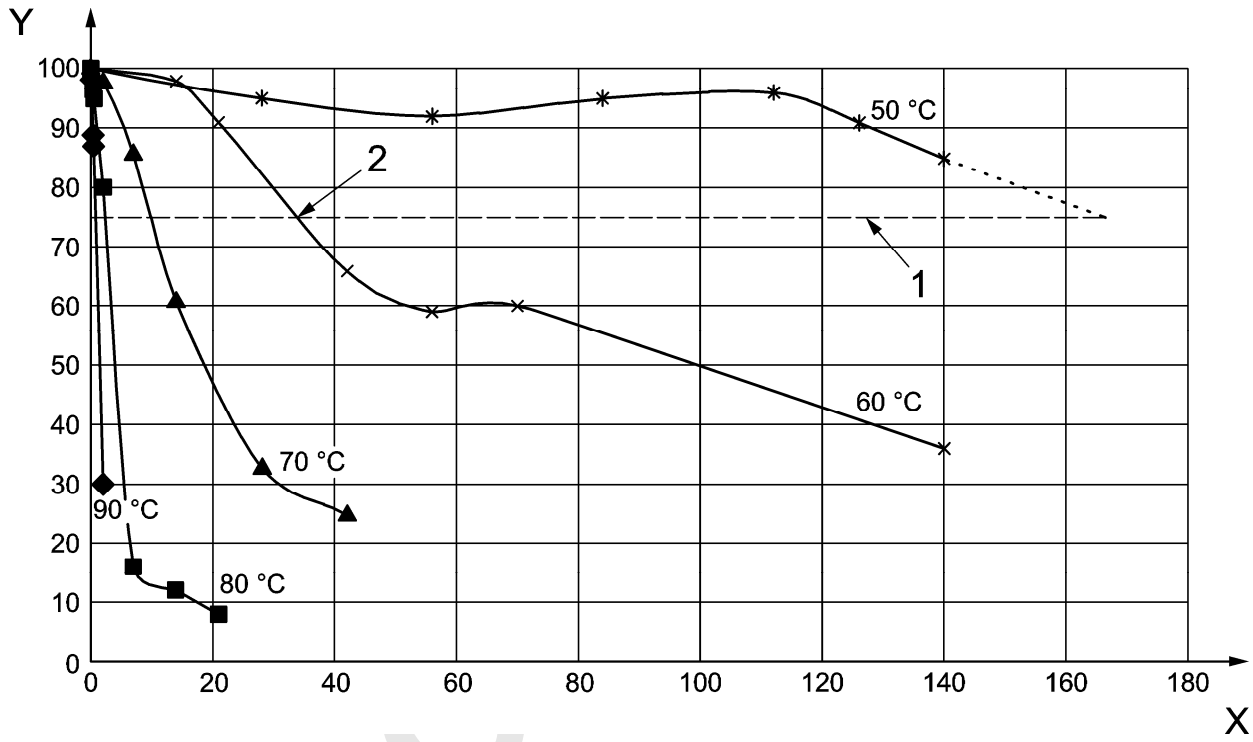
$$m = \frac{E_A}{RT} \qquad \text{(B.4)}$$

where

m is the slope of the line.

B.5.2 Estimating the Time Required to Reach a Specified Threshold Value

The first stage in preparing an Arrhenius plot is to determine how long it takes at each temperature for the physical property under investigation to reach a predetermined threshold. Ideally the threshold value should represent the maximum change that can be tolerated before the glove is at risk of failing the requirements specified in clause 4, but this may not always be possible, particularly at lower temperatures and with stable materials. The difference between initial and threshold values should nevertheless be sufficiently large compared to the background variability to allow the time to be estimated accurately. It may be necessary to extrapolate data obtained at lower ageing temperatures in order to determine the time to reach the threshold value. Figure B.1 illustrates how this is done assuming a threshold value of 75% retained force at break.



Key

X t in days **Y** Initial force at break in %

1 75% threshold **2** Time to reach threshold at 60˚C

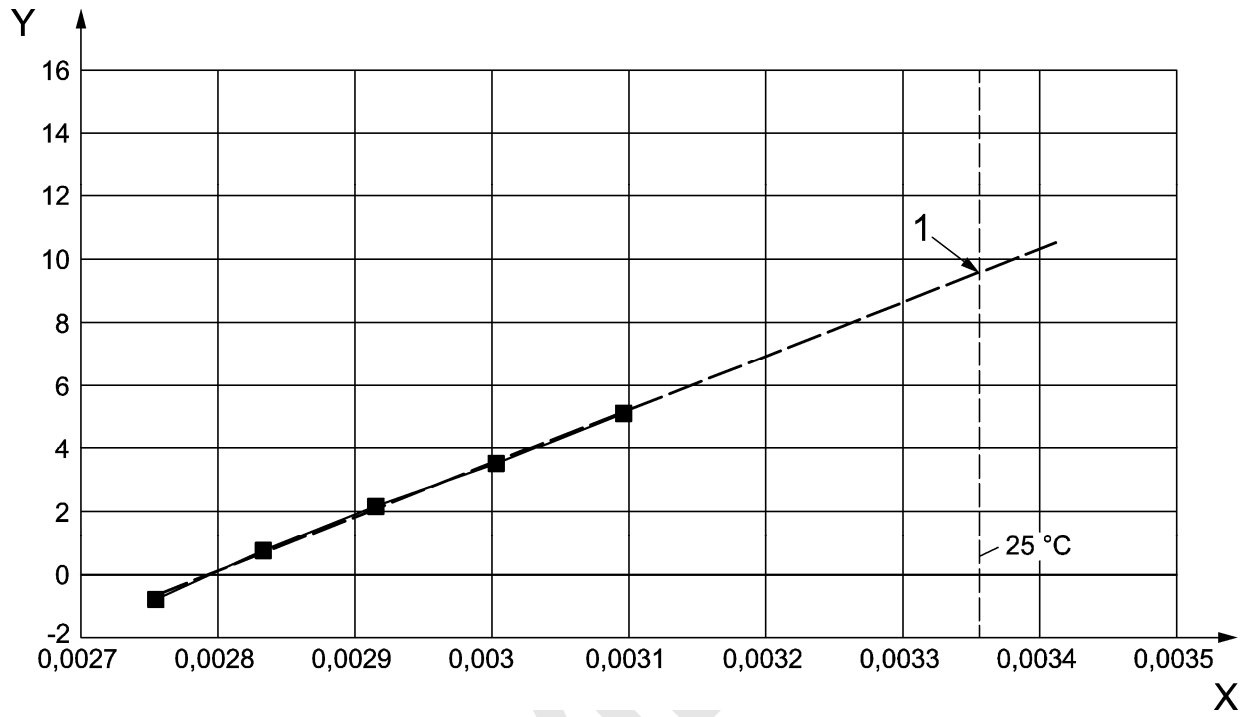
Figure B.1 — Estimating the time to reach a specified threshold

NOTE Estimating the time to reach a specified threshold is often easier if linear regression methods can be used to fit a straight line through the data. In order to do this it may be necessary to apply an appropriate transformation to the data first. Many chemical processes follow first order kinetics, i.e. the rate of change is proportional to the instantaneous value of the variable under consideration. If the rate of change of a specific property follows first order kinetics then a straight line can be obtained by plotting the natural log (ln) of the property against time.

In some ageing processes sudden changes in the rate of degradation can occur, for example when all the antioxidant is consumed. If it is necessary to extrapolate data to determine the time required to reach the specified threshold then consideration should be given to the possibility of such effects.

B.5.3 Constructing the Arrhenius plot and estimating the activation energy

The Arrhenius plot is constructed by plotting the natural log of the times required for the property under investigation to reach the specified threshold value $\ln t_{(x\%)}$ against the reciprocal of the absolute temperature. A typical plot is shown in figure B.2.



Key

E_A = 141,9 kJ/mol y = 17071 x – 47,71 R^2 = 0,9987

X 1/T in K^{-1} **Y** $\ln t_{(75\%)}$ in years

1 Extrapolation to 25˚C

Figure B.2 — Arrhenius plot for force at break assuming a threshold of 75%

NOTE The time estimated for the physical properties to fall to 75% from figure B.2 is 39 years at 25˚C. The activation energy is calculated as 142 kJ/mol.

In some cases the Arrhenius plot may not be linear. Several approaches to the analysis of non-linear Arrhenius plots have been explored and it is anticipated that as manufacturers and regulatory agencies accumulate real time data, a consensus method for the next revision of this European Standard will be developed. It must be emphasized that any attempt to extrapolate shelf life estimates from non-linear Arrhenius plots carries a high level of risk and manufacturers should be conservative about any estimates made under such conditions. Manufacturers should try to ensure that the physical properties change in a constant way over the temperature range used for the studies. In some circumstances it may not be possible to use the Arrhenius relationship at all.

Typically activation energies for many chemical reactions average 83 kJ/mol although the actual values found in practice vary widely. Published values for the activation energies associated with thermal and/or oxidative degradation of the material being used may be available in the scientific literature.

B.6 Application of the Time-Temperature Superposition Method on natural rubber latex gloves

B.6.1 Background to the Time-Temperature Superposition Method

An alternative method of presenting accelerated ageing data is to use the time-temperature superposition plot described by Barker [1, 2], Gillen [3] and others. This method is based on the Arrhenius equation and is widely used in the scientific literature to present accelerated ageing data on polymeric materials. In this procedure the time values at each temperature are transformed to equivalent times at a common reference temperature by multiplying them by the Arrhenius shift factor α_T, which is derived from the Arrhenius equation:

$$\alpha_T = e^{\frac{E_A}{R(T_{(ref)} - T_{(age)})}} \qquad \text{(B.5)}$$

where

E_A is the activation energy,

R is the gas constant (8,314 J · mol^{-1} · K^{-1}),

$T_{(ref)}$ and $T_{(age)}$ are the reference and ageing temperatures respectively in K .

The physical properties obtained at the various ageing temperatures are plotted against the respective transformed times on a common graph. If the ageing properties transform according to the Arrhenius equation and the correct value is used for the activation energy then a single master curve is obtained. The properties of the glove after any period of ageing at the reference temperature can be readily read off the resulting curve.

The activation energy for the specific material under consideration may be estimated as described in B.5 or obtained from the scientific literature.

In situations where the activation energy cannot be determined, for example because the Arrhenius plot is not linear, a Shift Factor for a specific temperature interval can often be calculated using the least squares method. For further information see ISO 11346.

B.6.2 Procedure for Constructing Time-Temperature Superposition Plots

Determine the activation energy for the specific material being used, preferably from an Arrhenius plot as described in B.5. Alternatively a literature value can be used. Calculate the shift factor values α_T from equation (B.5) for each ageing temperature using 25°C as the reference temperature.

a) For each set of ageing data, i.e. combination of time and temperature, calculate the transformed time by multiplying the time value by the shift factor α_T appropriate for that ageing temperature.

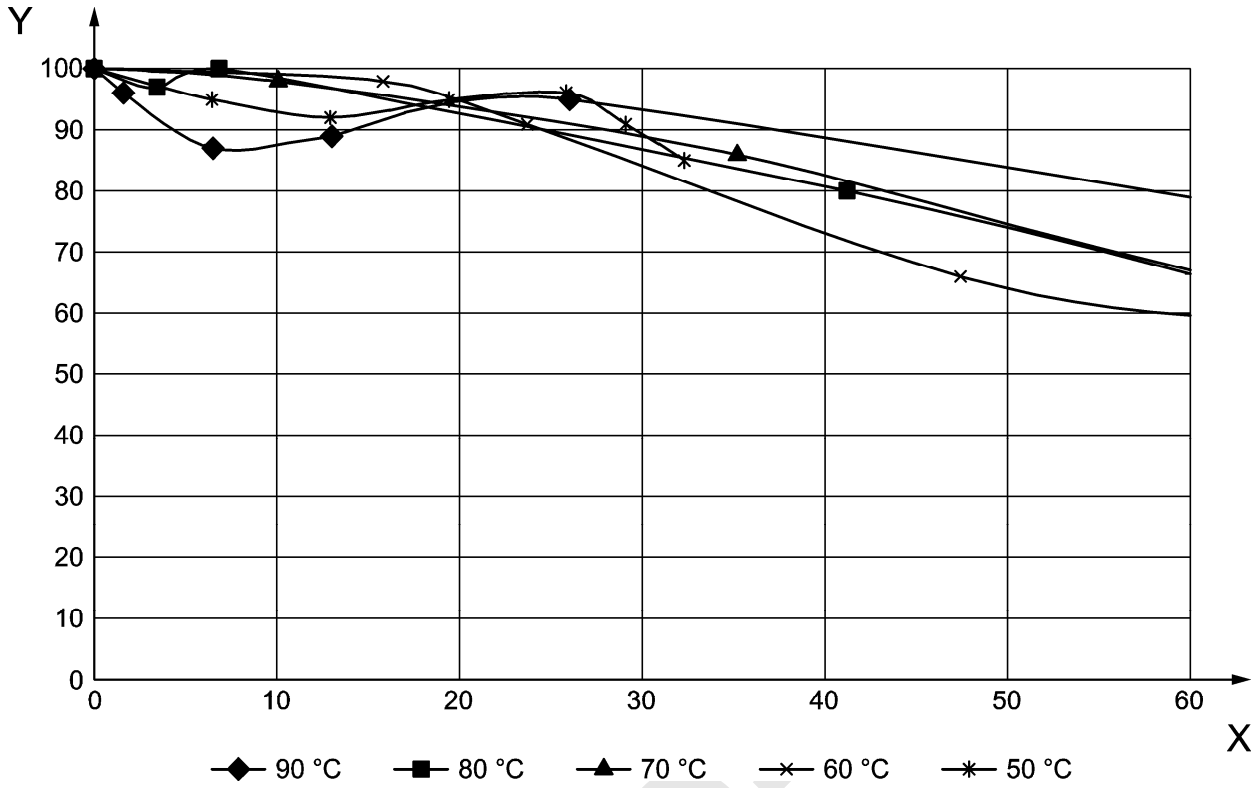
b) Plot the mean physical property (force at break or elongation at break) against the appropriate transformed times.

NOTE 1 Each property should be plotted on a separate graph.

c) To facilitate subsequent interpretation of the graphs, standard deviations can be included in the plots. Superposition plots showing the number of non-conforming gloves at each time point may also be informative.

d) Estimate the shelf life period from the graphs and knowledge of the variance or standard deviation of the sample populations. The shelf life period is the time required at 25°C for the physical property to fall to the limiting value where the gloves will still be in compliance with all parts of EN 455.

An example of a time-temperature superposition plot (based on the data given in figure B.1) is given in figure B.3.



Key

X t at 25°C in years **Y** Retained force at break in %

Figure B.3 — Time temperature superposition plot

NOTE 2 If a 20% decline in force at break can be tolerated before the product is at risk of failing the specified requirements then the shelf life will be in excess of 30 years. The maximum allowed shelf life claim of 3 years can therefore be justified.

Annex C
(informative)

Determination of the shelf life of a significantly modified product

C.1 Background

The following procedures may be used to estimate a provisional shelf life based when a significant change has been made to the formulation or manufacturing process for a product that could affect its shelf life. Prior to testing as described below, the gloves should be tested for compliance with the requirements of the EN 455 series of standards.

C.2 Principle

Pending completion of real time stability studies as required under Annex A, manufacturers may establish a provisional shelf life for a specified condition of storage and distribution by demonstrating that the modified product does not deteriorate to any greater extent than theoriginal product when conditioned as follows:

a) After storage at 70 °C for 7 days.

b) After storage for 90 days at 50 °C.

C.3 Procedure

Gloves packed in their consumer packaging or, in the case of sterile gloves, the peelpack, from three lots of the modified product and three lots of the original product shall be stored under the conditions described in Clause C.2 and tested for compliance with the requirements of the EN 455 series of standards including the following:

a) Force at Break according to EN 455-2,

b) freedom from holes according to EN 455-1,

c) that the glove is fit for the intended purpose, and

d) pack integrity (sterile gloves).

Providing the properties of the modified glove have not deteriorated to any greater extent than those for the original glove then the shelf life of the original design can be assumed pending verification through a real time ageing study according to Annex A.

C.4 Test report

The test report should be according to Clause 6 of this European Standard.

Annex ZA
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 93/42/EEC Medical Devices

This European Standard has been prepared under a mandate given to CEN by the European Commission to provide a means of conforming to Essential Requirements of the New Approach Directive 93/42/EEC Medical Devices.

Once this standard is cited in the Official Journal of the European Communities under that Directive and has been implemented as a national standard in at least one Member State, compliance with the clauses of this standard given in table ZA.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

Table ZA.1 — Correspondence between this European Standard and Directive 93/42/EEC Medical Devices

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
4.1	4, 5 , 9.2, 13.3e), 13.3i)	
4.2	4, 5, 13.3e), 13.3i)	
4.5	5, 8.3	
4.6	13.3i)	

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

Bibliography

[1] L R Barker. J. nat Rubb. Res., 2(4), 210 – 213 (1987)

[2] L R Barker. J. nat Rubb. Res., 5(4), 266 – 274 (1990)

[3] Gillen KT, Clough RL, Wise J., Extrapolating Accelerated Thermal-Aging Results: A Critical Look at the Arrhenius Method. Polymer Preprints 1993;34(2):185

[4] EN ISO 291, *Plastics - Standard atmospheres for conditioning and testing (ISO 291:2008)*

[5] EN ISO 2578, *Plastics - Determination of time-temperature limits after prolonged exposure to heat (ISO 2578:1993)*

[6] ISO 11346, *Rubber, vulcanized or thermoplastic – Estimation of life-time and maximum temperature of use*