DIN EN ISO 10993-23:2021-10 (E)

Biological evaluation of medical devices - Part 23: Tests for irritation (ISO 10993-23:2021)

Contents

Page

European foreword ... **4**

Annex ZA (informative) **Relationship between this European Standard and the essential requirements of Directive 93/42/EEC [OJ L 169] aimed to be covered** ... **6**

Annex ZB (informative) **Relationship between this European Standard and the essential requirements of Directive 90/385/EEC [OJ L 189] aimed to be covered** ... **8**

Annex ZC (informative) **Relationship between this European standard and the General Safety and Performance Requirements of Regulation (EU) 2017/745 aimed to be covered** ... **10**

Foreword ... **12**

Introduction ... **13**

1 Scope ... **14**

2 Normative references ... **14**

3 Terms and definitions ... **15**

4 General principles — Step-wise approach ... **16**

5 Pre-test considerations ... **17**
5.1 General ... 17
5.2 Types of material ... 18
5.2.1 Initial considerations ... 18
5.2.2 Ceramics, metals and alloys ... 18
5.2.3 Polymers ... 18
5.2.4 Biologically derived materials ... 18
5.3 Information on chemical composition ... 18
5.3.1 General ... 18
5.3.2 Existing data sources ... 18

6 *In vitro* irritation tests ... **19**
6.1 General ... 19
6.2 ***In vitro*** reconstructed human epidermis model ... 19
6.2.1 Test system — Reconstructed human epidermis model ... 19
6.2.2 Principle of the method ... 19
6.2.3 Prediction model ... 20
6.3 Materials ... 21
6.3.1 Reconstructed human epidermis models — Product description ... 21
6.3.2 Preparation of medical device extracts ... 21
6.4 Methods ... 22
6.4.1 General ... 22
6.4.2 Test procedure ... 22
6.4.3 Media and end point solutions ... 23
6.4.4 Test sample and control preparation ... 23
6.5 Considerations for test performance ... 24
6.5.1 Receipt of the reconstructed human epidermis tissues ... 24
6.5.2 Preparation and pre-incubation ... 24
6.6 Application of the test sample and rinsing ... 24
6.6.1 General ... 24

6.6.2 Preparation ... 25
6.6.3 Test extract and controls exposure ... 25
6.7 MTT test for determination of RhE tissue viability after the exposure period ... 26
6.7.1 MTT incubation and Isopropanol extraction ... 26
6.7.2 Absorbance measurements ... 26
6.8 Test acceptance criteria ... 27
6.9 Data calculation steps ... 27
6.9.1 General ... 27
6.9.2 Isopropanol background control for OD in RhE assay ... 27
6.9.3 Negative DPBS or PBS treated controls ... 27
6.9.4 Positive control ... 27
6.9.5 Tested extract and VC samples (TTs) ... 28
6.10 Data interpretation — Prediction model ... 28
6.11 Method documentation sheet ... 28
6.12 Test report ... 29

7 *In vivo* irritation tests ... 29
7.1 General ... 29
7.2 Animal irritation test by skin exposure ... 30
7.2.1 Principle ... 30
7.2.2 Test materials ... 30
7.2.3 Animals and husbandry ... 30
7.2.4 Test procedure ... 30
7.2.5 Observation of animals ... 32
7.2.6 Evaluation of results ... 32
7.2.7 Test report ... 34
7.3 Animal irritation test by intracutaneous (intradermal) administration ... 34
7.3.1 Introduction ... 34
7.3.2 Exclusion from test ... 34
7.3.3 Test sample ... 34
7.3.4 Animals and husbandry ... 35
7.3.5 Test procedure ... 35
7.3.6 Observation of animals ... 36
7.3.7 Evaluation of results ... 36
7.3.8 Test report ... 36

8 Human skin irritation test ... 37
8.1 Introduction ... 37
8.2 Initial considerations ... 37

Annex A (normative) **Preparation of materials for irritation testing ... 39**

Annex B (informative) **Test method check list for *in vitro* irritation testing using reconstructed human epidermis models ... 41**

Annex C (informative) **Example of method documentation sheet for reconstructed human epidermis models ... 43**

Annex D (normative) **Special irritation tests ... 48**

Annex E (normative) **Human skin irritation test ... 64**

Annex F (informative) **Background information on irritation tests ... 68**

Bibliography ... 70