

# ISO/TR 21582:2021 (E)

## Pyrogenicity — Principles and methods for pyrogen testing of medical devices

---

### Contents

|       |   |
|-------|---|
|       | Foreword                                  |
|       | Introduction                              |
| 1     | Scope                                     |
| 2     | Normative references                      |
| 3     | Terms and definitions                     |
| 4     | Abbreviated terms                         |
| 5     | Characterization of pyrogen               |
| 5.1   | General                                   |
| 5.2   | Bacterial endotoxin                       |
| 5.3   | Microbial components other than endotoxin |
| 5.4   | Pro-inflammatory cytokines                |
| 5.5   | Chemical agents and other pyrogens        |
| 5.6   | Principle of febrile reaction             |
| 6     | Assessment of pyrogenicity                |
| 6.1   | General                                   |
| 6.2   | Bacterial endotoxin test (BET)            |
| 6.2.1 | General                                   |
| 6.2.2 | Principle of LAL reaction                 |
| 6.2.3 | General procedure of BET                  |
| 6.2.4 | Properties of the BET                     |
| 6.3   | Rabbit pyrogen test                       |
| 6.3.1 | General                                   |
| 6.3.2 | Principle of the rabbit test              |
| 6.3.3 | Procedure of the rabbit test              |
| 6.3.4 | Characteristic of the rabbit test         |
| 6.4   | Human cell-based pyrogen test (HCPT)      |
| 6.4.1 | General                                   |
| 6.4.2 | Principle of the HCPT                     |
| 6.4.3 | Selection of human cells                  |
| 6.4.4 | Selection of marker cytokine              |
| 6.4.5 | Procedure of HCPT                         |
| 6.4.6 | Characteristic of the HCPT                |
| 6.4.7 | Validation study                          |
| 7     | Conclusion                                |

Page count: 16