



**BSI Standards Publication**

## **Specification and demonstration of system reliability of single-use drug delivery systems**

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## National foreword

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The UK participation in its preparation was entrusted to Technical Committee CH/84, Catheters and syringes.

A list of organizations represented on this committee can be obtained on request to its committee manager.

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Published by BSI Standards Limited 2025

ISBN 978 0 539 26029 8

ICS 11.040.01

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This Published Document was published under the authority of the Standards Policy and Strategy Committee on 30 November 2025.

### Amendments/corrigenda issued since publication

| Date  | Text affected |
|-------|---------------|
| <hr/> |               |



# Technical Specification

**ISO/TS 4452**

## **Specification and demonstration of system reliability of single-use drug delivery systems**

*Spécification et démonstration de la fiabilité des systèmes  
d'administration de médicaments non réutilisables*

**First edition  
2025-11**

Reference number  
ISO/TS 4452:2025(en)

Full document details: PD ISO/TS 4452:2025

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Published in Switzerland

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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. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see [www.iso.org/directives](http://www.iso.org/directives)).

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This document was prepared by Technical Committee ISO/TC 84, *Devices for administration of medicinal products and catheters*.

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](http://www.iso.org/members.html).

## Introduction

Current industry standards cover the quality of performance, e.g. dose accuracy or injection depth, of different types of drug delivery systems (DDS). These standards require the use of statistical tolerance intervals to quantify this quality of performance for each individual primary function.

The term “reliability” is commonly used to refer to such quantification, i.e. a tolerance interval based on a probability content and confidence level.

For at least two decades this approach has proven to be appropriate for many types of DDSs and continues to do so.

Today these DDSs are used across a broad range of therapeutic areas to deliver medicinal products treating chronic diseases of low immediate risk as well as potentially life-threatening acute illnesses.

Such DDSs not only need to meet the individual quality of performance for each primary function. They also need to successfully execute a sequence of functions necessary for delivery of the medicinal product.

In this document, the terms ‘capability’ and ‘system reliability’ are introduced to differentiate between the quality of performance of a primary function and the probability of each DDS to successfully deliver a medicinal product respectively.

Based on the severity of potential harm of not delivering the medicinal product this document suggests five reliability levels. Each of those is linked to minimum capability and system reliability values in line with current industry practice.

Due to the more severe consequences of some DDSs failing to deliver the medicinal product, requirements for demonstrating system reliability for the two highest reliability levels have also been added, as well as more stringent requirements for challenging the DDSs based on the environmental conditions they are intended to withstand and how these environmental conditions might need to be combined for testing purposes.

The document also emphasises that while both capability and system reliability must be demonstrated at the conclusion of development (as demonstrated by design verification), they also need to be maintained throughout manufacture of the DDS. In addition, the two highest reliability levels require additional effort to ensure these expectations are met.

The establishment of a system reliability is not intended to change the testing for devices that are already adequately addressed by the current standards (e.g. ISO 11608, ISO 20072 and ISO 21649). Specific detailed considerations for these standards are addressed in [Annex B](#).

Demonstration of system reliability is not limited to (verification) testing. The entire process of developing the product and the application of control strategies ensures the DDS continuously meets the system reliability requirements.

The concept of system reliability is a special case of reliability engineering that pertains to “out of box” failures for all disposable single use DDSs for which there is a single opportunity to deliver a single dose of a medicinal product. In contrast, reliability engineering is a collection of techniques to ensure performance of durable or reusable DDSs over a long period of time and through multiple, successive actuations to ensure consistent performance possibly over many years.

There can be examples of single-use devices which are built to have on-board a second (or “backup”) dose. This document can be helpful in the development of such devices, but the reader should be aware that multi-dose or reusable DDSs are outside the scope of this document (see [Annex B](#) for further details).

[Figure 1](#) illustrates the document structure and its relation to risk management.

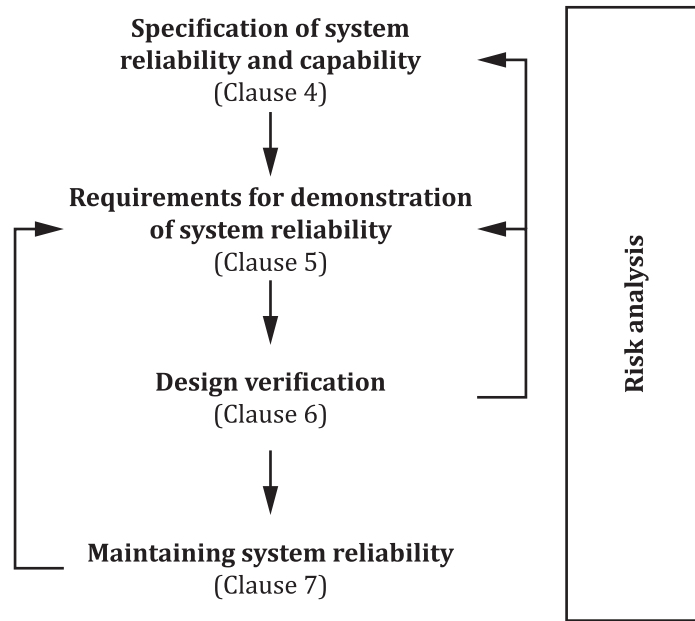


**Figure 1 — Structure of this document and its relation to risk management**