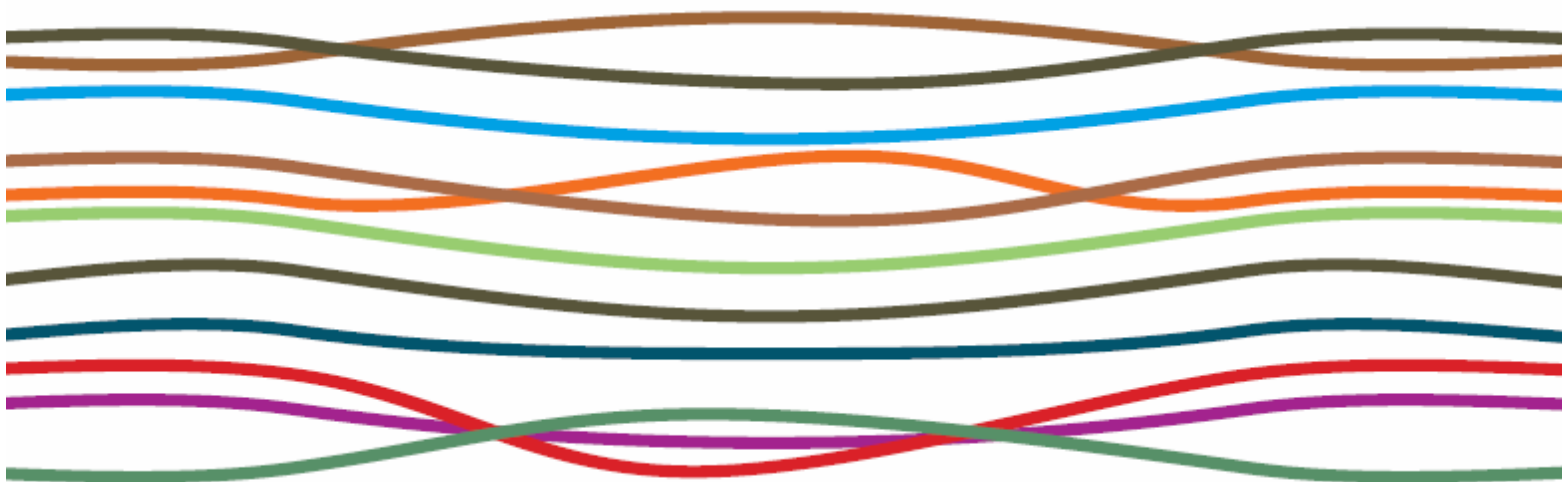




**International Standards
Organisation**
Practical Guide to ISO 10993



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David Eldridge - PRW

What is ISO 10993?

The International Standards Organisation (ISO, *from the Greek word; isos, meaning equal*) was established to determine uniform worldwide standards. ISO developed a standard for biological evaluation of medical devices – ISO 10993 in 1995 which is a 20 part standard used to evaluate the effects of medical devices and their component materials on the body.

The most influential guideline for biocompatibility is the first part of this standard, "ISO 10993- Part 1: Evaluation and Testing," which provides a methodology for choosing the proper biological evaluation test programme. From here it is possible to determine also which test program to utilise depending on the device category of which there are three: Surface, External Communicating and Implant, and the exposure period of the material: Limited (<24 hours), Prolonged (24 hours to 30 days) and Permanent (>30 days).

The ISO 10993 structure is set up as follows:

ISO Part	Title
1	Evaluation and testing
2	Animal welfare requirements
3	Tests for genotoxicity, carcinogenicity and reproductive toxicity
4	Selection of tests for interactions with blood
5	Tests for in vitro cytotoxicity
6	Tests for local effects after implantation
7	Ethylene oxide sterilisation residuals
8	Clinical investigation of medical devices
9	Framework for identification and quantification of potential degradation products
10	Tests for irritation and delayed type hypersensitivity
11	Tests for systemic toxicity
12	Sample preparation and reference materials
13	Identification and quantification of degradation products from polymeric medical devices
14	Identification and quantification of degradation products from ceramics
15	Identification and quantification of degradation products from metals and alloys
16	Toxicokinetic study design for degradation products and leachables
17	Establishment of allowable limits for leachable substances
18	Chemical characterisation of materials
19	Physico-chemical, morphological and topographical characterisation of materials
20	Principles and methods for immunotoxicology testing of medical devices

ISO 10993 Device Categories

Device Categories	Body Contact	Examples
<p align="center">Surface Devices</p>	Skin	Electrodes, external prostheses, fixation tapes, compression bandages, monitors of various types
	Mucous Membrane	Contact lenses, urinary catheters, intravaginal and intrainestinal devices (stomach tubes, sigmoid scopes, colonoscopies, gastroscopies), endotracheal tubes, bronchoscopes, dental prostheses, orthodontic devices, IUDs
	Breached or Compromised Surfaces	Ulcer, burn and granulation tissue dressings or healing devices, occlusive patches
<p align="center">External Communication Devices</p>	Blood Path Indirect	Solution administration sets, extension sets, transfer sets, blood administration sets
	Tissue/Bone/Dentine Communicating	Laparoscopes, arthroscopes, draining systems, dental cements, dental filling materials, skin staples
	Circulation	Intravascular catheters, temporary pacemaker electrodes, oxygenators, extracorporeal oxygenator tubing and accessories, dialysers, dialysis tubing and accessories, hemoadsorbents and immunoabsorbents
<p align="center">Implant Devices</p>	Tissue/Bone Implant Devices	Orthopaedic pins, plates, replacement joints, bone prostheses, cement and intraosseous devices, pacemakers, drug supply devices, neuromuscular sensors and simulators, replacement tendons, breast implants, artificial larynxes, subperiostealimplants, ligation clips
	Blood	Pacemaker electrodes, artificial arteriovenous fistulae, heart valves, vascular grafts, internal drug delivery catheters, ventricular assist devices

Benefits of cytotoxicity testing

Cytotoxicity testing is a rapid, standardised, sensitive, and inexpensive means to determine whether a material contains significant quantities of biologically harmful extractables. The high sensitivity of the tests is due to the isolation of the test cells in cultures and the absence of the protective mechanisms that assist cells within the body. A mammalian cell culture medium is the preferred extractant because it is a physiological solution capable of extracting a wide range of chemical structures, not just those soluble in water. Antibiotics can be added to the medium to eliminate potential interference from microbial contamination that may be present on the test material and control samples. Results of cytotoxicity tests correlate reasonably well with short-term implant studies. However, they do not necessarily correlate well with other standard tests of biocompatibility that are designed to examine specific end points (such as sensitisation) or that use extracts prepared under more rigorous conditions (for example, at 121°C in saline or cottonseed oil).

Cytotoxicity test methods are useful for screening materials that may be used in medical devices because they serve to separate reactive from non reactive materials, providing predictive evidence of material biocompatibility. The ISO 10993-1 standard, "Guidance on the Selection of Tests," considers these tests so important that they are prescribed for every type of medical device, along with sensitisation and irritation testing. Cytotoxicity test methods are also useful for lot-to-lot comparison of materials, for determining whether a potential replacement material is equivalent to that currently being used, and for troubleshooting and exploring the significance of changes in manufacturing processes.