QMS Standard ISO 13485

ISO 13485:2003 Medical devices — Quality management systems — Requirements for regulatory purposes.

ISO 13485:1996 Section 4.4 Design Controls. **Intent very similar to that of 21 CFR 820.30**

DESIGN CONTROL GUIDANCE

FOR

MEDICAL DEVICE MANUFACTURERS

This Guidance relates to
FDA 21 CFR 820.30 and Sub-clause 4.4 of ISO 9001

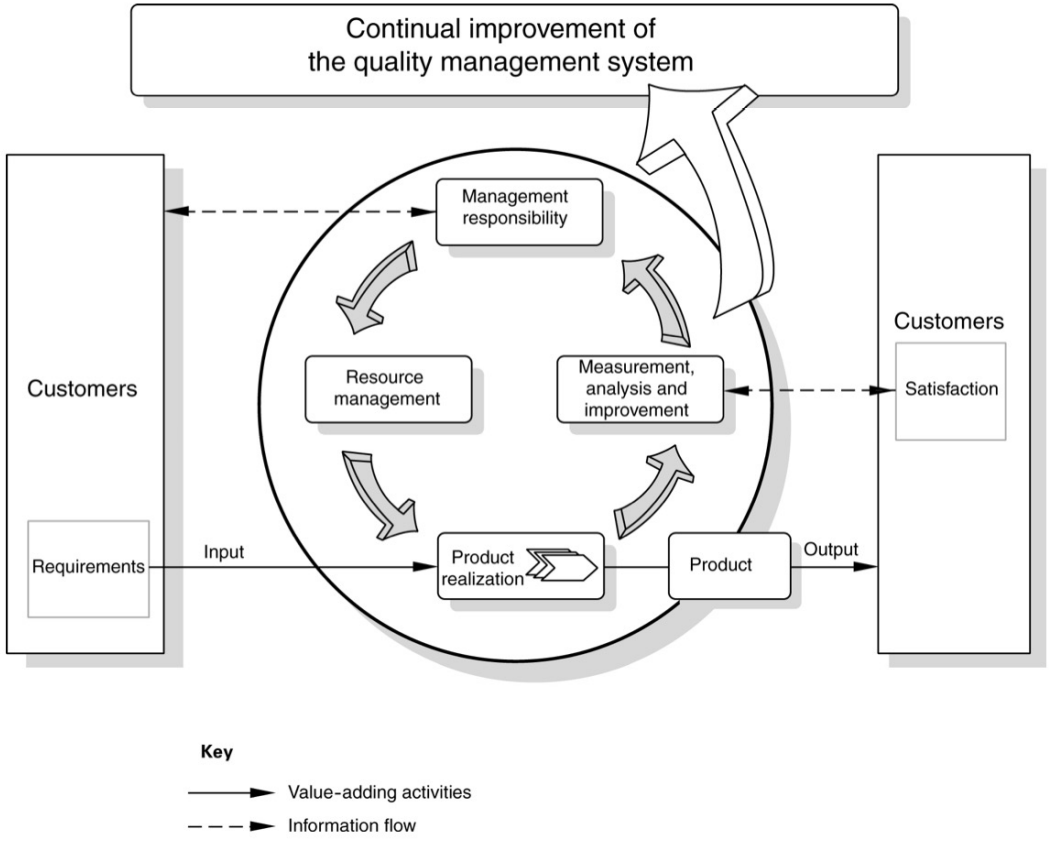


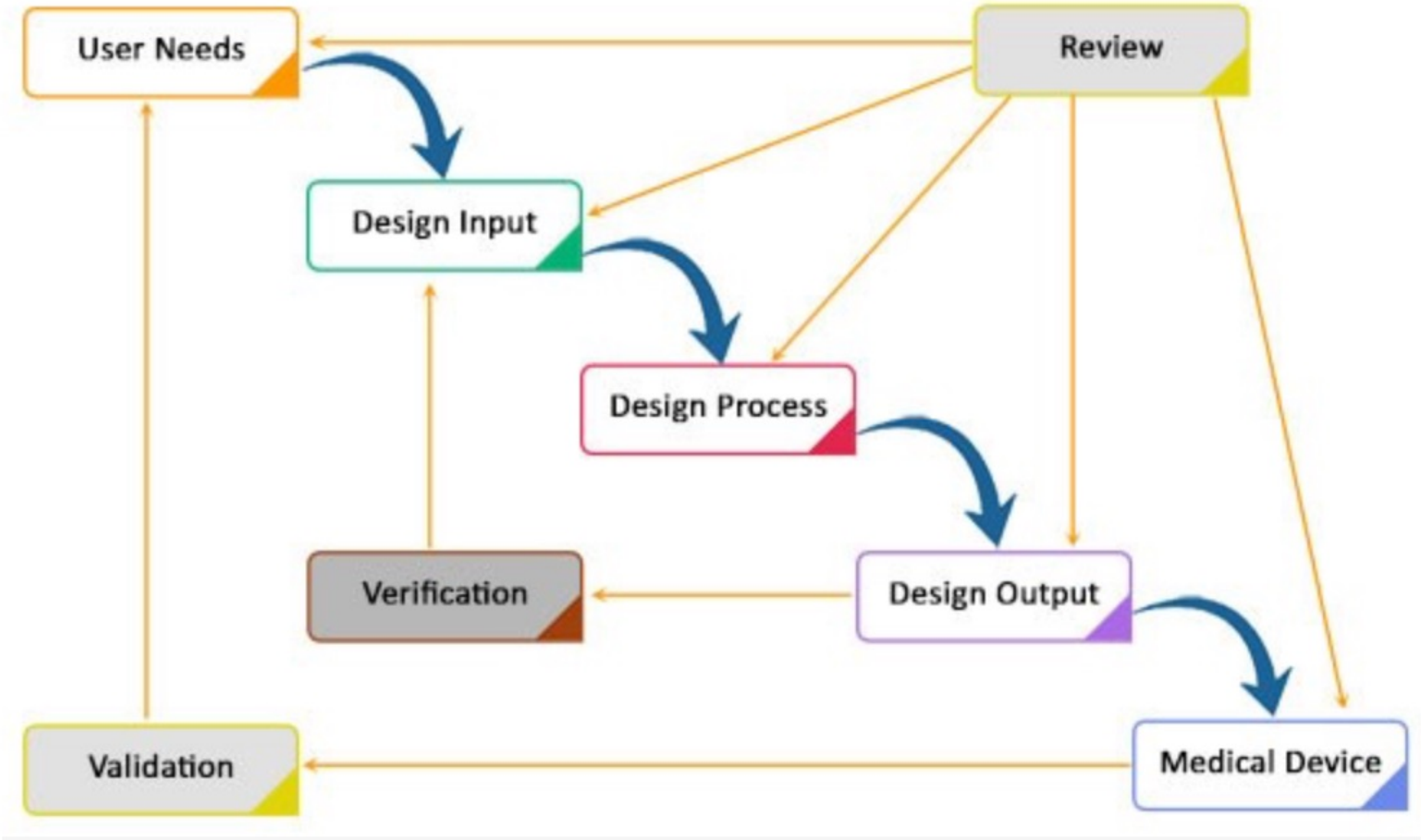
Figure 1 — Model of a process-based quality management system

21 CFR 820.30

"All manufacturers (including specification developers) of Class II and III devices and select Class I devices are required to follow **DESIGN CONTROLS** [§ 820.30] during the development of their device."

"The **DESIGN CONTROL** requirements are basic controls needed to ensure that the device being designed will perform as intended when produced for commercial distribution."

“Waterfall” Design Process



Two Feedback Loops

Verification loop from Design Output to Design Input

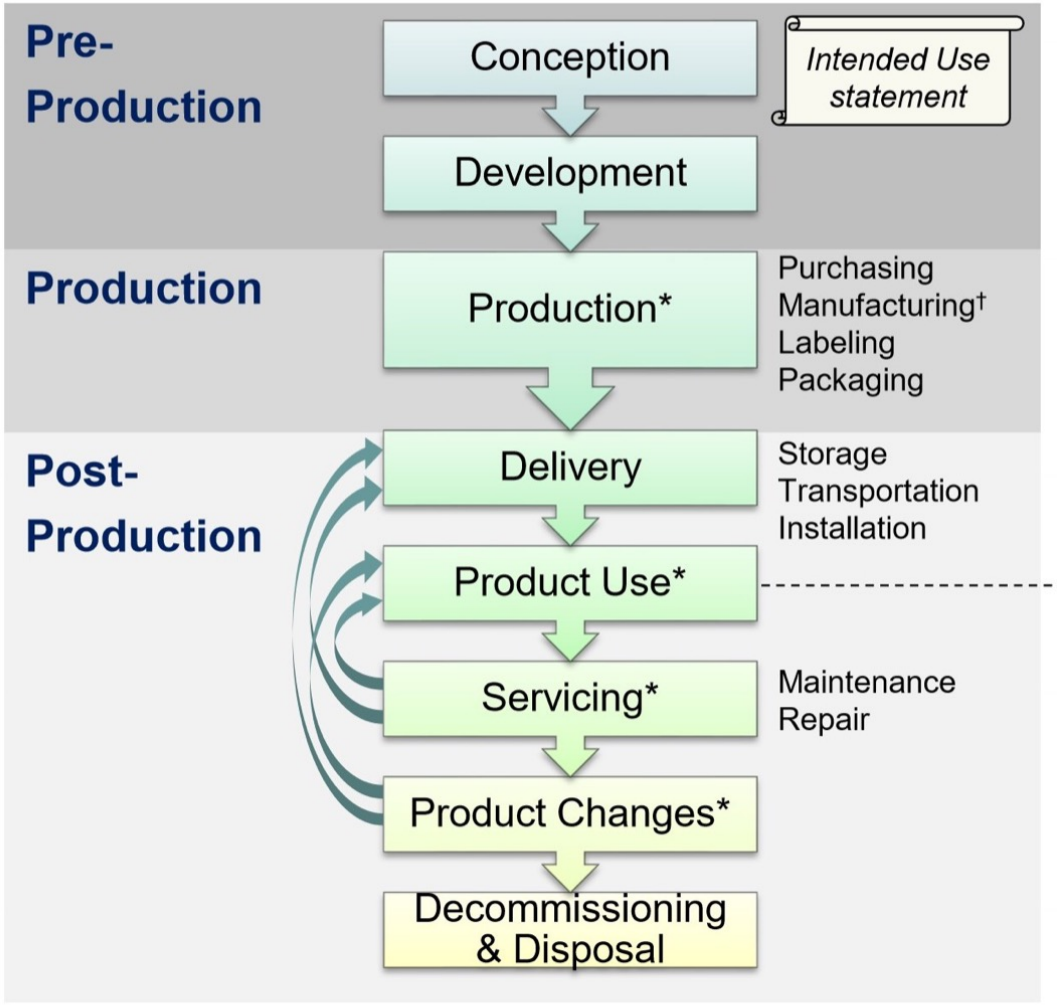
Validation loop that demonstrates that the medical device satisfies user needs

Verification and Validation

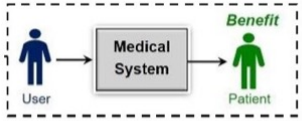
Design **Verification** – Evidence that the manufacturer **made the product right**

Design **Validation** – Evidence that the manufacturer **made the right product**

Product Life-Cycle



Note 1: Every individual medical device undergoes some or all of the life-cycle stages shown here.



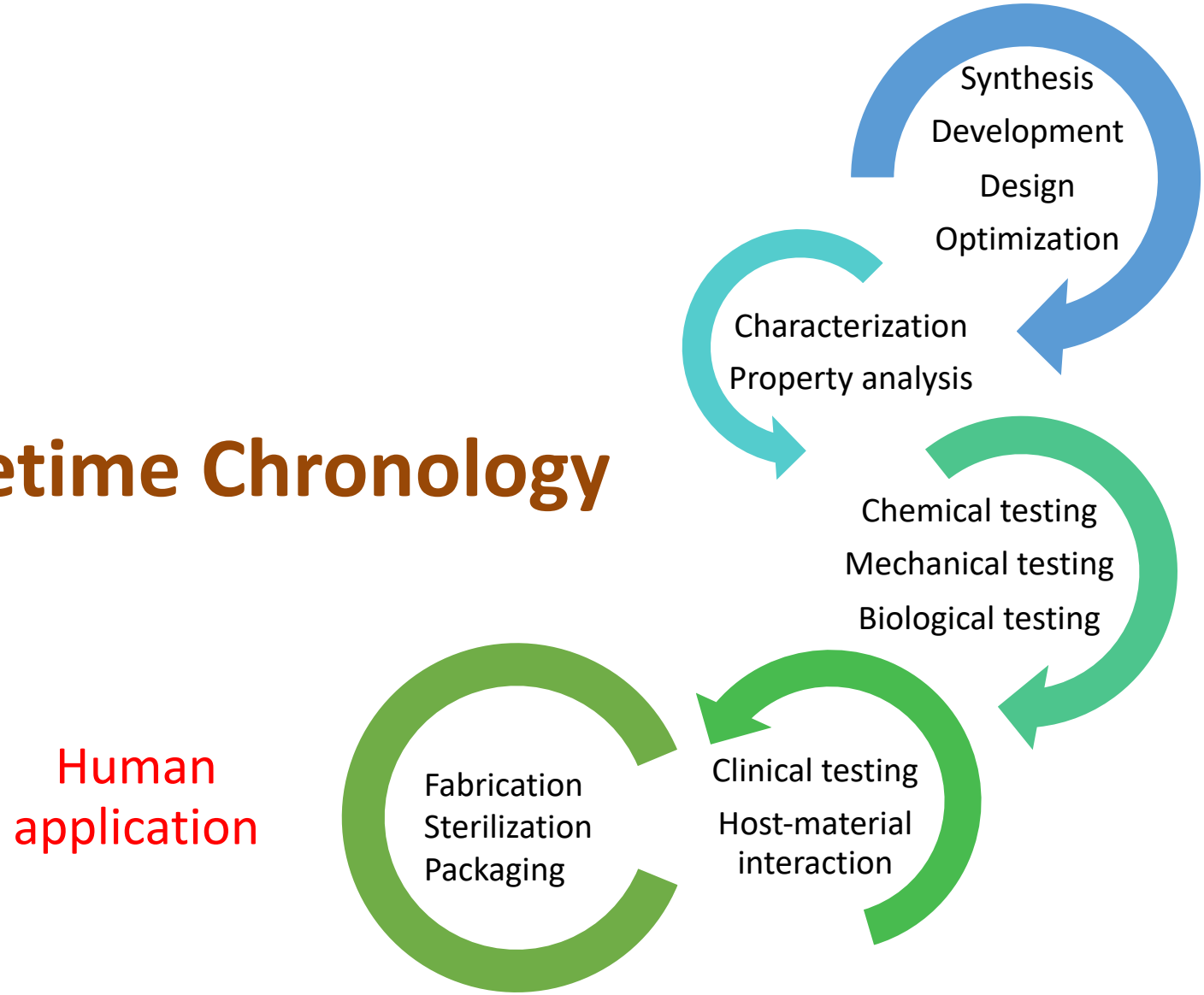
Intended Use

Note 2: The first four post-production life-cycle stages may sometimes occur in a different order.

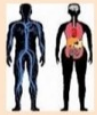
** may include Cleaning, Disinfection, Sterilization*

† may entail Remanufacturing (Reprocessing, Fully refurbishing)

Lifetime Chronology



Product Development Process Functions

Product Development Process Function	Product Design	Operations	Risk Management	Clinical Performance	Regulatory Compliance	Finance & Marketing
						
Description	Design of the medical device (including labeling and packaging)	Design and execution of production, delivery, and servicing processes	Systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating, controlling and monitoring risk	Activities necessary to confirm clinical performance and clinical safety in intended markets	Activities necessary to obtain regulatory clearance in intended markets	Activities focused on financial & market success
Main Goal	Establish a product design that fully specifies a medical device that meets the Intended Use and user needs	Produce and deliver a medical device that meets its product design specifications	Ensure risks are acceptable	Confirm clinical performance and clinical safety in intended markets	Obtain regulatory clearance in intended markets	Achieve financial and market success
Typical Process Owner(s)	**R&D:** Design Engineering	**Operations:** Purchasing (Supplier Management), Manufacturing Engineering, Distribution, Customer Service, Service Engineering	**Quality Assurance (QA):** Quality Engineering	**Clinical Affairs (CA)**	**Regulatory Affairs (RA),** Compliance officer	**Finance, Marketing**

Note: There is inherent overlap between these process functions requiring frequent communication and collaboration during product development.

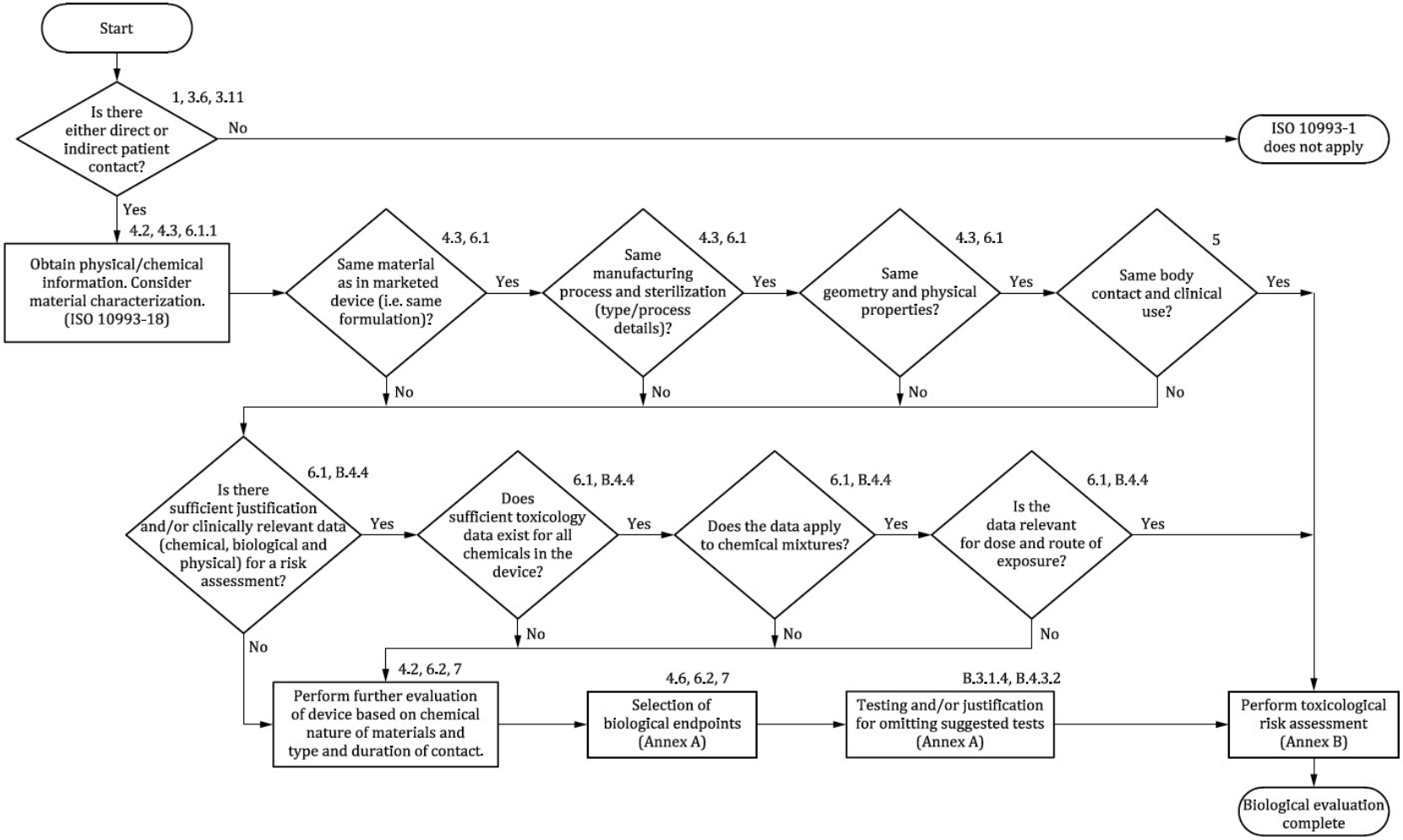


Figure 1 — Summary of the systematic approach to a biological evaluation of medical devices as part of a risk management process

Biological Compatibility ISO 10993

ISO 10993-1:2018, Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process
ISO 10993-2:2006, Biological evaluation of medical devices — Part 2: Animal welfare requirements
ISO 10993-3, Biological evaluation of medical devices — Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
ISO 10993-4, Biological evaluation of medical devices — Part 4: Selection of tests for interactions with blood
ISO 10993-5, Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity
ISO 10993-6, Biological evaluation of medical devices — Part 6: Tests for local effects after implantation
ISO 10993-7, Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals
ISO 10993-9, Biological evaluation of medical devices — Part 9: Framework for identification and quantification of potential degradation products
ISO 10993-10, Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization
ISO 10993-11:2017, Biological evaluation of medical devices — Part 11: Tests for systemic toxicity
ISO 10993-12, Biological evaluation of medical devices — Part 12: Sample preparation and reference materials
ISO 10993-13, Biological evaluation of medical devices — Part 13: Identification and quantification of degradation products from polymeric medical devices
ISO 10993-14, Biological evaluation of medical devices — Part 14: Identification and quantification of degradation products from ceramics
ISO 10993-15, Biological evaluation of medical devices — Part 15: Identification and quantification of degradation products from metals and alloys
ISO 10993-16, Biological evaluation of medical devices — Part 16: Toxicokinetic study design for degradation products and leachables
ISO 10993-17, Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances
ISO 10993-18, Biological evaluation of medical devices — Part 18: Chemical characterization of materials within a risk management process
ISO 10993-19: Biological evaluation of medical devices — Part 19: Physico-chemical, morphological and topographical characterization of materials
ISO/TS 10993-20, Biological evaluation of medical devices — Part 20: Principles and methods for immunotoxicology testing of medical devices
ISO 14971:2007, Medical devices — Application of risk management to medical devices

Biological Testing: Testing for evaluation

The physico-chemical characterization (within the bulk or surface structure) and the other specific properties (i.e. electrical, mechanical, and eventually of biodegradation) **must be carried out on the raw materials.**

The *in vitro* characterization (with live tissues) of the materials and performances of the biomedical device prototype is necessary preliminary to the evaluation of their biocompatibility.

These data should be compared with the results at the end of each phase of the productive process (manufacturing, sterilization, packaging, stockage) that can affect the stability of the device and compromise its safety and its effectiveness of use.

The biocompatibility check is performed only on devices that have passed these preliminary tests. The main advantages of in vitro tests are related to low costs, the small size of the equipment required and the relative speed of execution that allows to quickly evaluate, and compare, many materials and many devices.

In vitro tests are currently considered effective for **a preliminary assessment** of the biocompatibility of materials. As with any other model, also in this case a lot of attention must be paid in interpreting the results, avoiding risky extrapolations.