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Chemical Characterization for Medical Devices

Core concepts, key standards, and the questions professionals ask most — explained by an active ISO TC194 expert.

- What chemical characterization is, and when it's required
- Key analytical thresholds, explained in plain language
- How ISO 10993-18 and ISO 10993-17 work together
- How characterization data feeds biological evaluation
- The most common gaps — and how to avoid them

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SECTION 1

What Chemical Characterization Is — and When It's Required

A quick orientation

Chemical characterization is the process of obtaining chemical information, accomplished either by information gathering or by information generation — for example, by literature review or chemical testing. In practice, that testing route most often means extractables and leachables (E&L) testing: identifying and quantifying what a device or its materials can release into a patient. It is the evidentiary backbone of a biological evaluation: rather than relying solely on animal testing, characterization data lets you understand *what* a device might expose a patient to, so exposure can be weighed against known toxicological limits.

Regulators increasingly expect this approach. It sits at the center of the ISO 10993 series, and reviewers at FDA, in the EU, and elsewhere now routinely ask for it as a first line of biological evaluation, ahead of — or instead of — biological effects (previously known as biological endpoint) testing.

> **WHY IT MATTERS**
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> A well-designed characterization study can reduce or eliminate the need for certain animal-based biocompatibility tests, shortening timelines and strengthening your submission — but only if the study is scoped correctly from the start.

When is it required?

Chemical characterization is expected whenever a device has any patient-contacting material, but the depth and rigor scale with risk. Regulators and ISO 10993-1 both frame the decision around contact duration and contact type, not device complexity alone.

CONTACT CATEGORY	TYPICAL EXPECTATION
Limited contact (≤24 hrs)	Often paper assessment or exaggerated extractions (72 hours or less).
Prolonged contact (24 hrs–30 days)	Exhaustive extractions
Permanent contact (>30 days), or implant	Exhaustive extractions

For devices with intermittent use, consider cumulative contact time — changes in ISO 10993:2025 now require accounting for bioaccumulation, which can move a device from limited to prolonged or even permanent contact.

New materials, new suppliers, formulation changes, sterilization method changes, and color or additive changes are the most common triggers for re-characterization — even on an otherwise "unchanged" device.

SECTION 2

Key Analytical Thresholds, Explained Plainly

Thresholds are where chemistry meets regulatory decision-making. Below are the concepts that come up in almost every characterization conversation — described conceptually rather than as a how-to calculation guide.

Analytical Evaluation Threshold (AET)

The AET is the concentration above which an extracted substance must be identified and evaluated toxicologically. Below it, a peak can generally be reported without full identification. Think of the AET as a "worth worrying about" line — it's derived from a target toxicological safety concern and back-calculated into an instrument response, so it's specific to the device, the extraction conditions, and the patient population.

Threshold of Toxicological Concern (TTC)

The TTC is a generic, conservative exposure limit used when a substance-specific toxicological value isn't available. It lets an assessment proceed without a compound-specific study for every trace-level finding, based on established chemical structure categories (the Cramer classification) and duration of exposure.

Estimated Exposure Dose (EED)

The EED translates an analytical concentration into a patient-relevant dose — accounting for device size, contact duration, extraction efficiency, and use pattern. This is the number that actually gets compared against a toxicological limit; concentration alone never tells the full story.

> **COMMON MISCONCEPTION**
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> A "high" concentration in an extract is not automatically a safety signal, and a "low" one isn't automatically safe. Everything depends on how that concentration converts to a patient exposure dose and how that dose compares to the compound's specific toxicological limit — this is precisely the judgment a qualified toxicologist and chemist apply together.

SECTION 3

How ISO 10993-18 and ISO 10993-17 Work Together

These two standards are often discussed separately, but they are designed to function as a pair. Treating them as independent checkboxes is one of the most common — and most costly — strategic mistakes companies make.

10993-18		10993-17
Chemical Characterization of Materials	↠ Extraction, analytical identification & quantification	Toxicological Risk Assessment

The division of labor

ISO 10993-18 governs the analytical side: how extracts are generated, how they're analyzed (typically via GC-MS, LC-MS, and ICP-MS), and how identified substances are reported with appropriate confidence and quantification. This is *hazard identification* — figuring out what's present.

ISO 10993-17 governs what happens next: taking each identified substance, estimating patient exposure (the Estimated Exposure Dose, or EED), and comparing it against a toxicological threshold to establish whether the exposure represents an acceptable risk. This is *exposure and risk estimation* — figuring out whether what's present actually matters.

> **THE CORE RELATIONSHIP**
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> ISO 10993-17 frames this as Hazard × Exposure = Risk. A substance can be present (a hazard) without posing meaningful risk, if the exposure dose is low enough relative to its toxicological threshold. Characterization data is only useful when it's carried all the way through this second step. Having the chemist and the toxicologist communicating upfront is the best way to ensure an extractables/leachables study will be suitable for a proper risk assessment.

Where this goes wrong

In practice, the most common failure is that the wrong AET gets applied. That usually traces back to one of three root causes: the device's actual clinical use wasn't communicated accurately to the lab (contact time, number of devices used per patient, or surface area was misstated or estimated rather than confirmed). Other common pitfalls include: the analytical techniques used weren't appropriate for the material or compound classes involved; or substances were detected above threshold but never carried through to full identification. Any one of these breaks the chain between -18 and -17 — the AET may be technically correct but built on the wrong inputs, or compounds that should have driven a toxicological assessment are left unidentified and effectively invisible to the risk assessment.

SECTION 4

How Characterization Data Feeds Biological Evaluation

Under ISO 10993-1, chemical characterization isn't a stand-alone deliverable — it's an input into a broader biological evaluation plan (BEP) and biological evaluation report (BER). Understanding this flow helps teams avoid generating data that ultimately can't be used.

- ✓ **Step 1 — Material and device information gathering.** Formulation, processing aids, supplier data, and prior use history are reviewed before any extraction begins.
- ✓ **Step 2 — Extraction and analytical testing (10993-18).** Simulated-use and/or exaggerated extraction conditions generate an extractables profile.
- ✓ **Step 3 — Toxicological risk assessment (10993-17).** Each relevant substance is carried through exposure and risk estimation.
- ✓ **Step 4 — Gap analysis against the biological evaluation plan.** The toxicologist and biological safety team determine whether chemical data adequately addresses each biological effect (cytotoxicity, sensitization, irritation, systemic toxicity, etc.) or whether supplemental biological testing is still needed.
- ✓ **Step 5 — Integration into the BER.** Chemical and biological data are presented together as a cohesive rationale, not as two disconnected reports.

> **A FREQUENT DISCONNECT**
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> Chemistry, toxicology, and biocompatibility functions often work in sequence rather than in parallel — meaning a characterization study gets finalized before anyone confirms it will actually satisfy the biological effects it's meant to address. Cross-functional alignment early in study design prevents costly rework later.

SECTION 5

The Most Common Gaps — and How to Avoid Them

1 Extraction conditions that don't match clinical use

Using generic extraction solvents or durations without justifying them against the device's actual use conditions is a frequent reviewer question. Extraction design should be defensible on its own, not just borrowed from a similar submission.

2 Treating –18 and –17 as separate workstreams

As covered in Section 3, analytical and toxicological work needs to be planned together from the outset, with the AET and TTC decisions made jointly — not handed off after the fact.

3 Under-scoping supplier and material-change tracking

A resin supplier's minor formulation change, a color additive swap, or a sterilization method shift can invalidate prior characterization data. Change control processes often don't flag these as chemistry-relevant events.

4 Incomplete or inconsistent analytical method coverage

Relying on a single analytical technique (e.g., GC-MS only) can miss non-volatile or polar substances that require LC-MS or ICP-MS. Comprehensive characterization typically requires a multi-technique approach appropriate to the material class.

5 Reports that don't connect back to the biological evaluation plan

A chemistry report that reads as a stand-alone document — without a toxicological risk assessment and an explicit tie to the biological effects it's meant to support — invites additional reviewer questions and delays.

SECTION 6

Questions Professionals Ask Most

Does chemical characterization replace biocompatibility testing entirely?

Not automatically. It can address, and often reduce the need for, certain biological effects — but the biological evaluation plan determines what's ultimately required for a given device and risk profile.

How often does characterization data need to be refreshed?

There's no universal calendar interval. It's triggered by material, process, supplier, or sterilization changes, and periodically revisited as standards and toxicological data evolve.

Is a paper assessment (information gathering) ever enough on its own?

Sometimes, for lower-risk, limited-contact devices with well-characterized materials — but this is a risk-based judgment made deliberately, not a default shortcut.

What's the difference between a qualitative and quantitative extractables study?

Qualitative work identifies what's present; quantitative work measures how much. Both are typically needed to complete the exposure and risk assessment under 10993-17.

Do I need a toxicologist and an analytical chemist, or can one person do both?

The disciplines are distinct, and reviewers generally expect to see both perspectives represented — whether through one cross-trained expert or a coordinated team. In either case, be sure to assess their professional credentials carefully.

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Where to Go From Here

Understanding the framework is the first step. Applying it correctly to your specific device, materials, and regulatory strategy is where most teams need support.

1:1 REGULATORY SCIENCE CONSULTING

Work directly with an active ISO TC194 expert to scope, review, or defend your chemical characterization and biological evaluation strategy — from study design through submission response.

THE ACADEMY — SELF-PACED ONLINE COURSES

Go deeper on biocompatibility and extractables & leachables with structured, self-paced courses built for working professionals. Learn the frameworks behind this guide in full detail, with practical application exercises.

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