Bonded in Science, LLC.

Fit for Purpose Chemical Characterization Studies for Medical Devices

A Practical Approach

Sandi Schaible · Bonded in Science LLC · Biocompatibility Insights 2026, Copenhagen

The house on Riverside Drive

A SHORT STORY



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WHAT THIS TALK IS ABOUT

Marcus was not insufficiently rigorous.

He was precisely rigorous about the wrong layer.

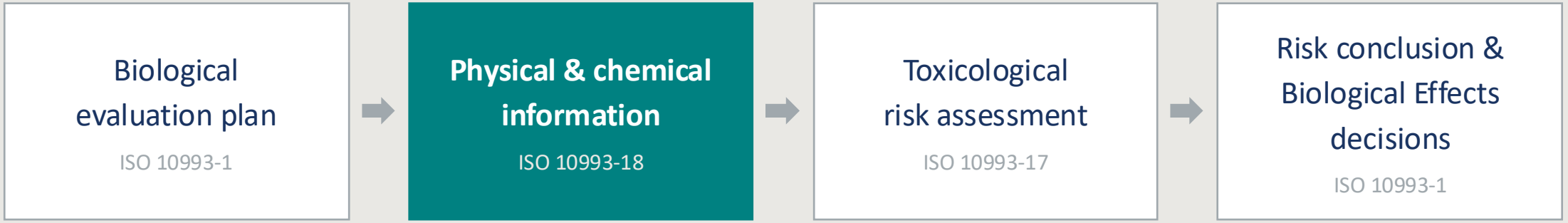
Rigor in chemical characterization is assumed to scale in one direction — toward more testing and tighter analytical precision.

That assumption does not make the conclusion safer. It moves effort away from the questions that decide it.

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FRAMING

Where chemical characterization sits



Chemistry is an input to a risk conclusion — not a deliverable in a table.

Every question that follows is really the same question: does this piece of work change what the risk assessment concludes?

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THE ARGUMENT

Three questions

1 Does this device need an E&L study at all?

2 What analytical precision is actually fit for purpose?

3 Which biological effects can the chemistry already answer?

One principle underneath all three: effort belongs where it changes the risk conclusion.

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QUESTION ONE

Does this device need a E&L study?

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WHETHER TO TEST

What ISO 10993-1 and ISO 10993-18 actually ask for

- They describes a risk-based process for obtaining chemical information — not a requirement to run a study on every device.
- The question it poses is what information the biological risk assessment still needs, and whether that information already exists.
- Characterization testing is triggered by an information gap, not by a device category.
- The common misreading: “10993-18 applies” becomes “an E&L study is required.” Those are not the same statement.

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The information you may already have

Sources of existing information

- Material master files and supplier data
- Compendial data (USP, Ph. Eur.)
- Predicate and legacy device characterization
- Prior toxicological risk assessments
- Manufacturing, sterilization and process records

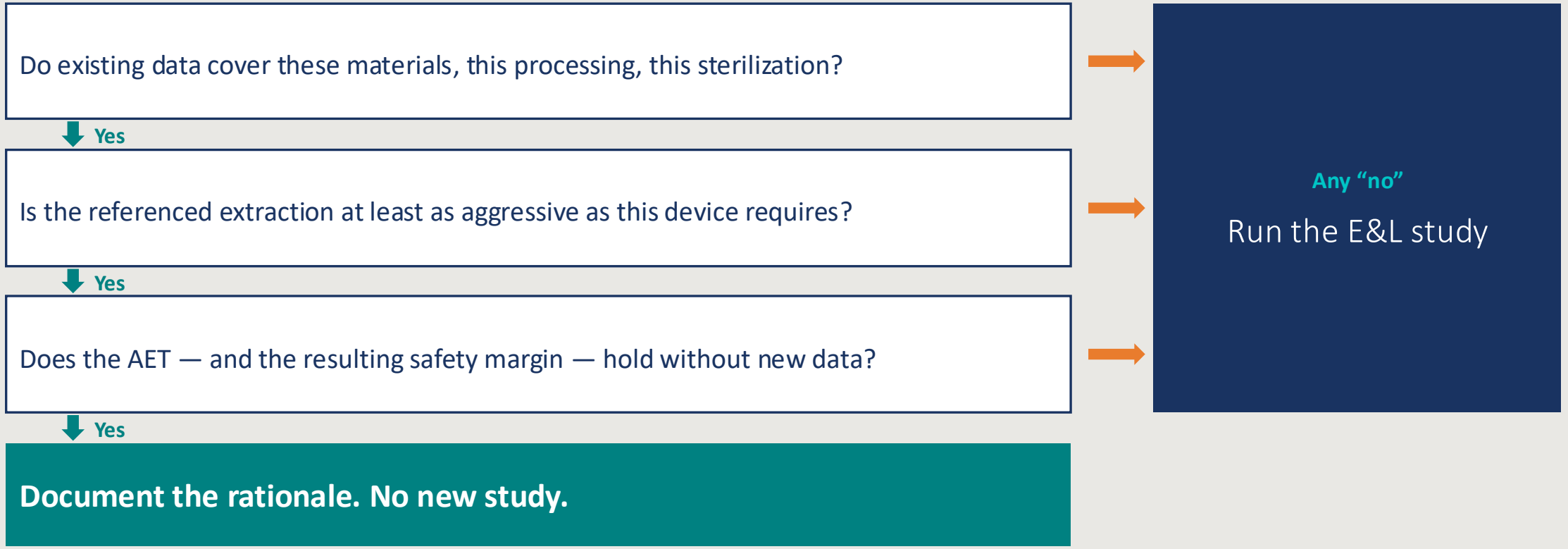
What each must still establish

- Same materials, processing and sterilization
- Contact category and duration at least as severe
- Extraction at least as aggressive as would apply now
- An AET at least as conservative as this device requires
- Documentation that is traceable and retrievable

WITH ENOUGH SPECIFICITY TO CLOSE THE GAPS

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Gap analysis: the decision logic



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WHETHER TO TEST

Anatomy of a defensible rationale

- **Scope** — device, materials, contact category, duration
- **Equivalence** — why the referenced data represents this device
- **Worst case** — why the referenced conditions are at least as severe
- **AET derivation** — dose-based, with the conservatism stated explicitly
- **Residual gaps** — what is not covered, and why it does not change the conclusion
- **Sign-off** — experienced toxicologist, quality report, dated and traceable

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QUESTION TWO

How precise does the chemistry data need to be?

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HOW PRECISELY

The workflow 80–120% was written for

Assumed by the criterion

- A known analyte with a matched reference standard
- Volumetric glassware, Class A (+/- .0X mL)
- A controlled, well-characterized matrix
- A single measurement step (minimally processed)
- Optimized instrument methods and instruments

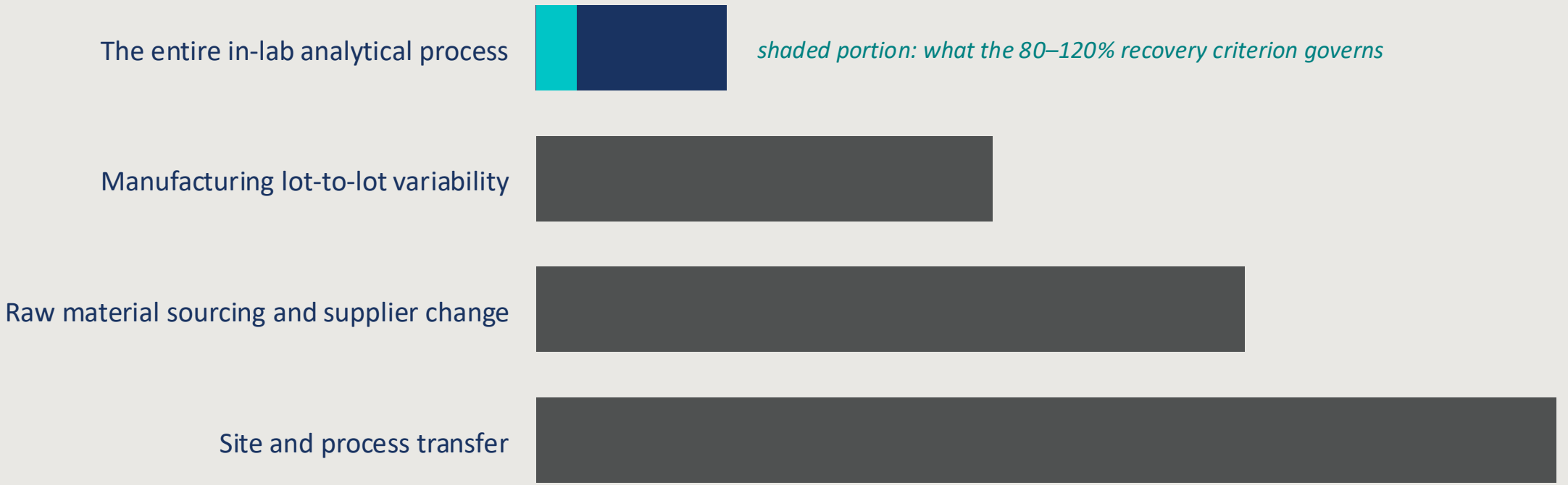
What actually happens in an E&L study

- **Surface area & extraction ratio** accepted within 10% before anything is measured (ISO 10993-12)
- **Graduated cylinders, beakers, containers** not volumetric glassware
- **Evaporation during extraction** known, accepted, grossly corrected
- **Solvent exchange and concentration** losses that differ by compound
- **Methods optimized for screening** to detect everything
- **Instrument sensitivity and cleanliness** drifting across the sequence
- **Quantitation on surrogate standards** against identifications that may be tentative

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HOW PRECISELY

Where the uncertainty actually lives



Relative ordering, illustrative — not measured magnitudes.

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HOW PRECISELY

Refine the study to the risk

TODAY — one study asked to do everything at once

Worst-case extraction, identification of every compound above the AET, and the most accurate concentration obtainable for all of them — including compounds that will never appear under clinical conditions, and never at that concentration.

STAGE 1

Extractables, first pass

Worst-case extraction. Identification is the deliverable. Concentration only to the resolution needed to sort compounds against the AET.

STAGE 2

Qualitative Risk assessment

Which identified compounds could plausibly reach the patient in clinical use — and at what order of magnitude? Most will not.

STAGE 3

Simulated use, targeted

Targeted analysis of the few compounds that survived. This is where concentration accuracy earns the effort spent on it.

STAGE 4

Quantitative risk assessment

Measured concentrations feed a margin of safety per ISO 10993-17 — and the mitigation decisions that follow from it.

Uncertainty enters long before the sample reaches the lab, and again before the extract reaches final interpretation. Precision spread evenly across every compound is precision spent where it cannot change the conclusion.

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Three weeks on the crown molding.

Quantitation inherits everything above it.

Including the identification.

80–120% level recovery is an expectation— for the final step, against a surrogate standard, for a compound we believe we have identified with a range of certainty. It does not consider an extraction ratio accepted within 10%, a volume read from a beaker, an evaporation correction estimated, or an identification that was only ever tentative. It also does not address the variation in chemical makeup of device, material changes, manufacturing changes, lot to lot differences.

A precise concentration assigned to an unconfirmed compound is a confident description of the wrong thing.

ISO/TS 25364-1 (identification) is finalized and expected to publish. Part 2 (quantification) is still in development — and can only be as sound as the foundation Part 1 sits on.

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QUESTION THREE

What can chemistry already answer?

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DOWNSTREAM VALUE

What chemistry data and a 10993-17 assessment can carry

Where chemistry + TRA has carried the argument

- Systemic toxicity — acute, subacute, subchronic, chronic
- Genotoxicity, where extractables are identified and assessed
- Irritation, where compound-specific potency data support it
- Carcinogenicity, Neurotoxicity, Repro/Developmental Toxicity
- Material-mediated pyrogenicity, in some submissions

Where chemistry alone has not been sufficient

- Sensitization without compound-specific potency data
- Implantation and local tissue response
- Hemocompatibility — driven by surface and flow, not extractables alone
- Anything governed by physical form, topography or degradation over time
- Absorbable devices

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DOWNSTREAM VALUE

Animal reduction and regulatory acceptance

- ISO 10993-1 already places biological testing after existing information and risk assessment. Chemistry-led evaluation is the intended order, not an exception to it.
- ISO 10993-17 provides the framework for turning identified extractables into a margin of safety.
- Chemistry-led justification has been accepted where the data package is complete and the reasoning is explicit.
- The 3Rs case and the regulatory case point the same direction: fewer animals, better-supported conclusions.
- The constraint is rarely the concept. It is the quality of the chemistry underneath it.

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DOWNSTREAM VALUE

Why chemistry-led arguments succeed — or fail

Why they succeed

- AET derived from a documented dose, conservatism stated
- Extraction demonstrably at least as aggressive as clinical use
- Identifications confirmed for anything near the AET
- Every compound accounted for — including those not assessed
- Written as an argument a reviewer can follow

Why they fail

- AET asserted rather than derived
- Extraction never shown to be worst-case
- Unidentified or tentative peaks above the AET
- Silent gaps — compounds detected but never addressed
- A chemistry report submitted in place of an argument

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“Nobody ever asks how good the soil test was.”

Scientific effort belongs where it impacts the risk conclusion.

Patient safety — not analytical performance — is the measure of success.

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MONDAY MORNING

Three questions to take back

1 Before commissioning an E&L study, ask what existing information already establishes — and write the rationale either way.

2 Before tightening a concentration value, ask what change in the number would change the conclusion.

3 Before defaulting to biological testing, ask which biological effects the chemistry and the TRA can already answer.

The answer to all three may still be "do the work." The point is that it becomes a decision rather than a default.

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