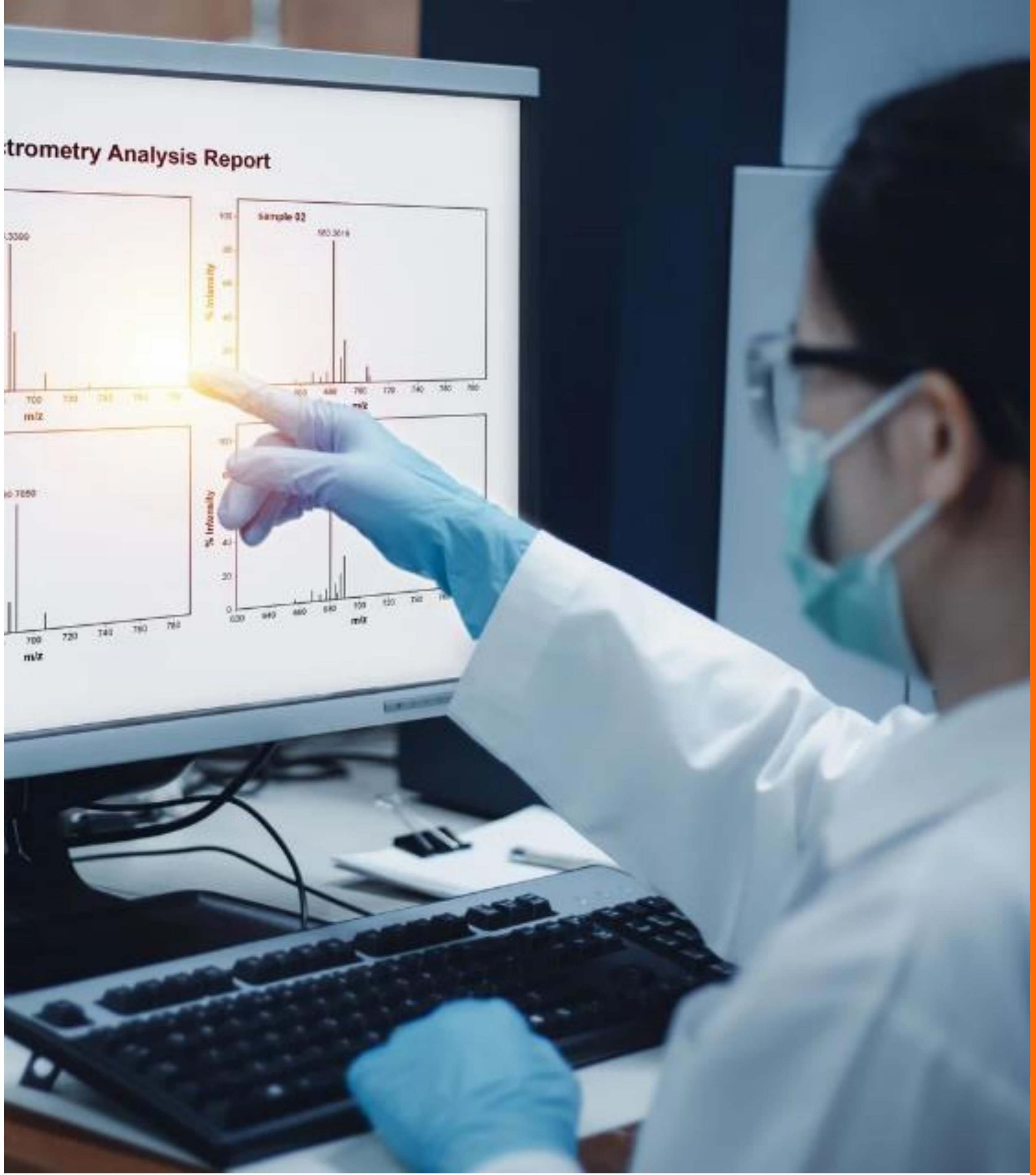
Webinar

Chemical Analysis

The Essential Tool for Controlling Toxicological Risks

- January 21st, 2026
- **Marilys Blanchy – Emilie Danel**



Introduction of the speakers

Marilys Blanchy

Technical expertise in materials

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Laboratory analysis manager

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Applus+ Group

Applus+ is a global leader in inspection, testing and certification. Driven by our passion for progress and technological development, we'll keep moving towards a more sustainable future alongside our customers; re-enforcing our mission and company motto: **Together beyond standards.**

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People in 2024

€2,209M
Revenue in 2024

+65
Countries in all continents

Accredited
By main international entities

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€ 1,137M revenue

16,000+ personnel

Laboratories Division

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2,857 personnel

Automotive Division

€ 429M revenue

5037 personnel

IDIADA Division

€ 356M revenue

3466 personnel

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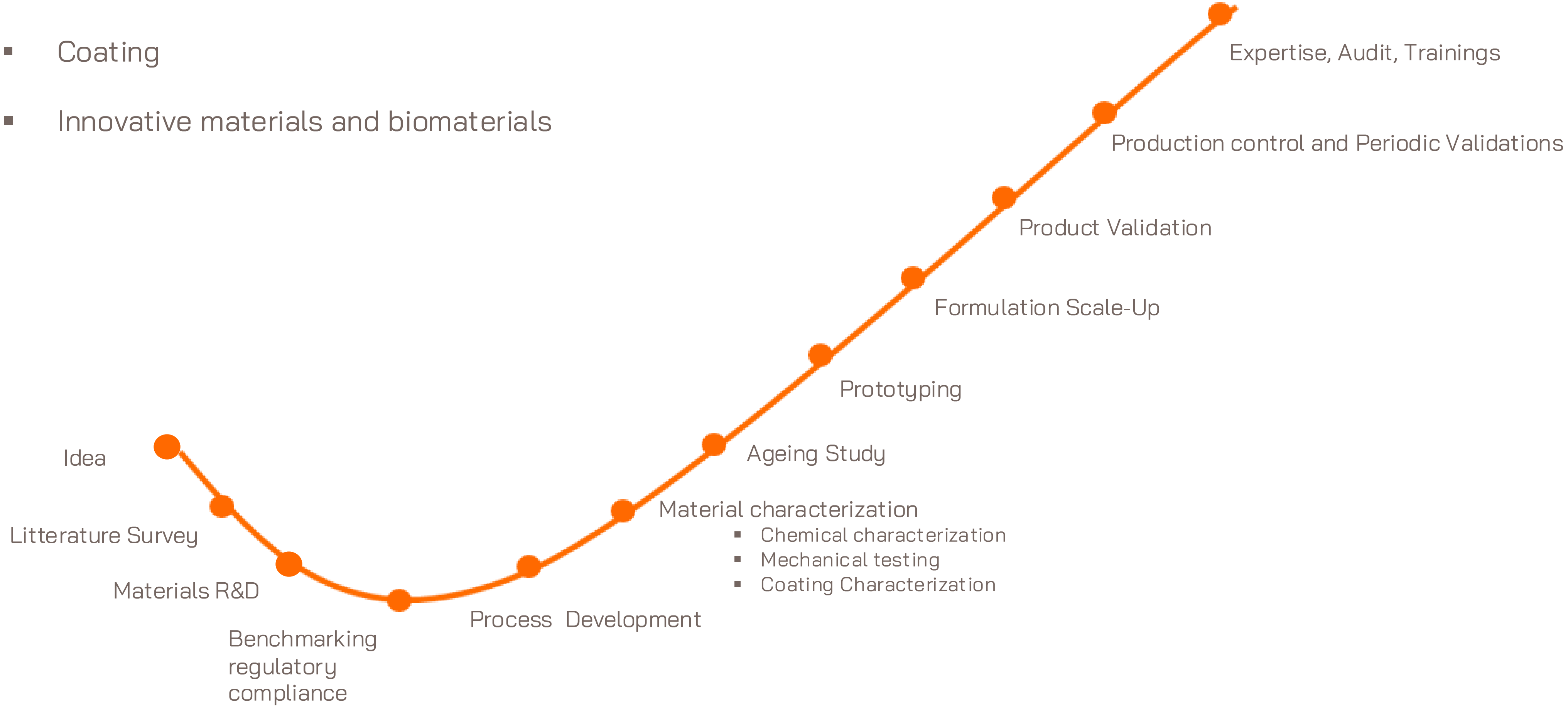
- Coating
- Innovative materials and biomaterials



Range of Services

Offer in Applus+ Laboratories

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THERMAL ANALYSIS

ENDURANCE TEST

MICROSCOPIC AND SURFACE ANALYSIS

VALIDATION

CLEANING

BIOCOMPATIBILITY (-13/14/15/18/19)

PACKAGING

TRANSPORT

STABILITY

TYPICAL SERVICES

CHEMICAL IDENTIFICATION OF RAW MATERIALS AND FINISHED PRODUCTS

QUALITY CONTROL

CONTAMINATION CONTROL

MATERIAL PROPERTIES

REVERSE ENGINEERING

RE-FORMULATION

SELECTION OF RAW MATERIALS

DEFINITION OF IMPLEMENTATION RANGE

Introduction

The biocompatibility of a medical device ensures its safety

It must be considered from the design stage and validated at every step of development

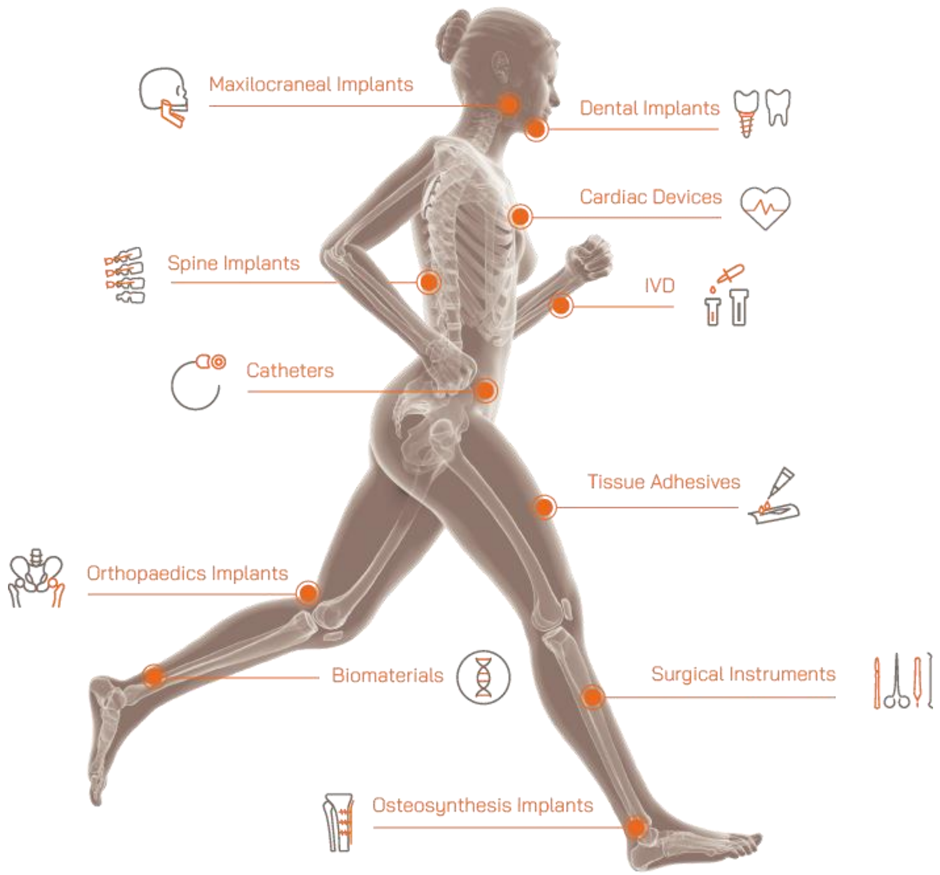
Definition of a medical device

Biocompatibility and regulatory requirement

Definition of a medical device

A medical device… A very wide variety of products
but they all have in common that

They should be sure and performant and do not present any unacceptable risk while used in its intended use. GRSP cover these aspects design, risk management, biompatibility and available data



The concept of biocompatibility/biological safety is fundamental in the design of a medical device

'The ability of a device to be in contact with living organisms without causing unacceptable adverse effects'

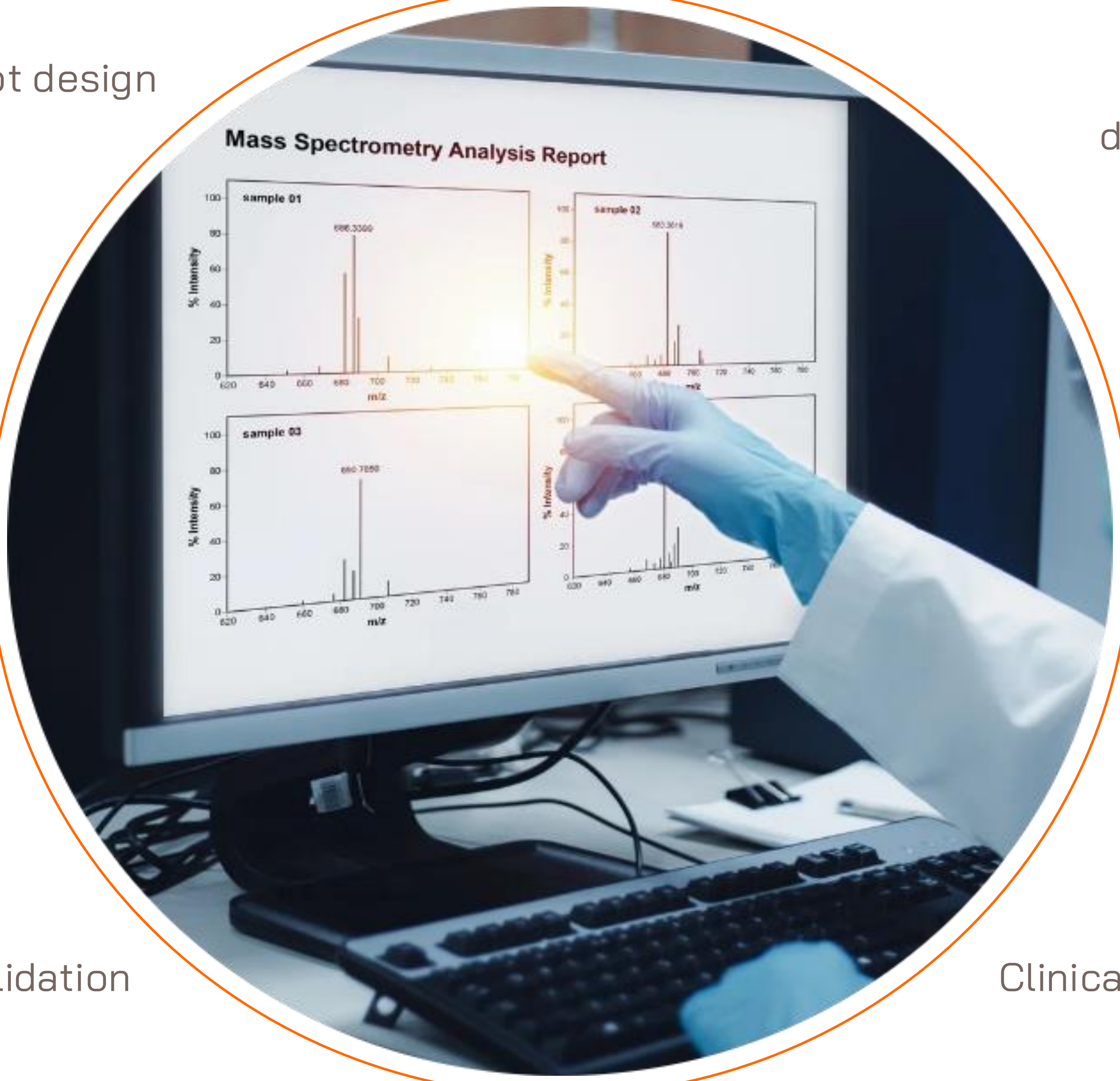
AND risk management

When taking into account biocompatibility and regulatory requirement ?

Ideation/Concept design

Product design/Prototyping

Technical documentation



Pre clinical evaluation

Manufacturing validation

Clinical evaluation

Regulatory overview

Ensuring material compatibility and regulatory compliance is essential for the safety and performance of medical devices.

Strategy for biological safety

According to MDR 2017/745 GRSP – General requirements

Medical device should be sure and performant

- During all its life cycle
- In normal conditions of use
- Without adverse effect on patient or users

Material compatibility with its environment

Material interaction between componant

Material properties before and after production storage and transport

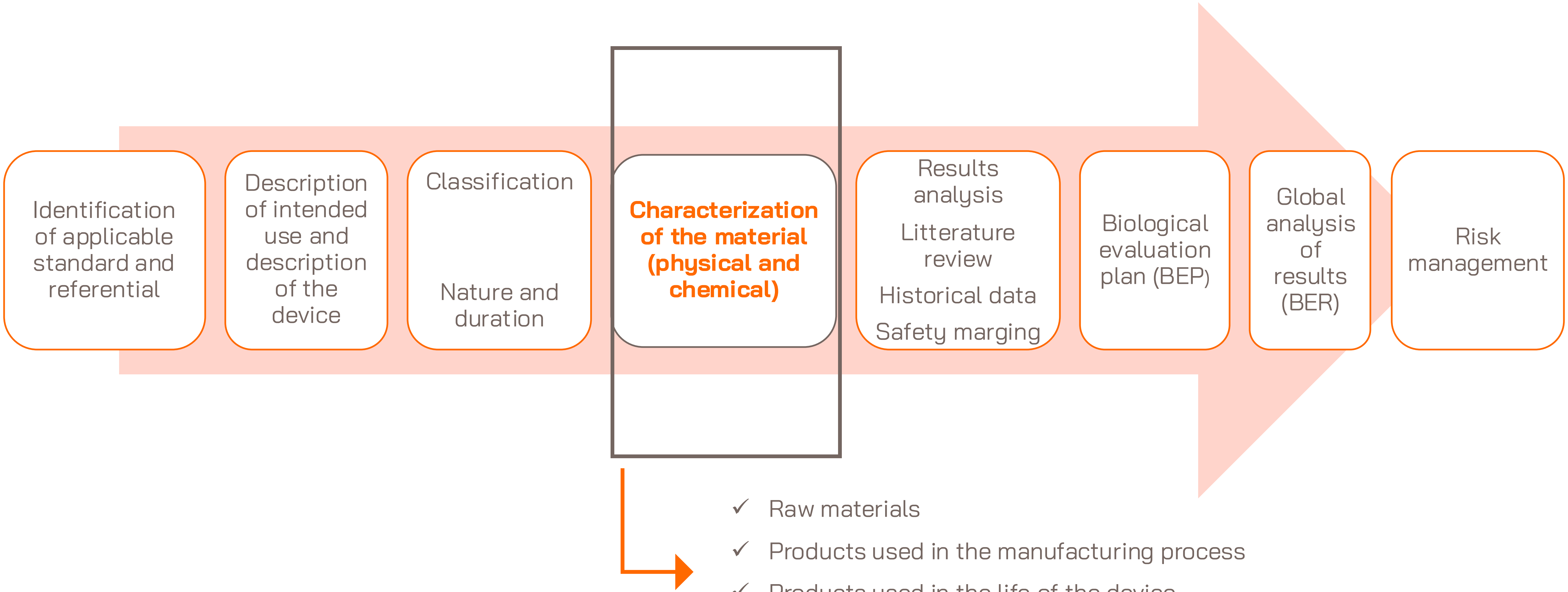
Compliant to Current chemical regulation

Strategy of evaluation

ISO 10993-1 sets the international standard for evaluating the biological safety of medical devices

ISO 10 993-1 for biological safety

Strategy for biological safety assessment according to ISO 10993-1



- ✓ Raw materials
- ✓ Products used in the manufacturing process
- ✓ Products used in the life of the device

BUT also, constraints that may alter material characteristics: process, use, etc.

- ✓ Degradation products
- ✓ Release and leachable products

Strategy for biological safety assessment according to ISO 10993-1

Step 1 : Collection of existing information

- Collection and categorization of DM
- Collection of already available chemical and biological data
- Identification of biological hazards relevant to the nature and duration of contact over time
- Definition of adaptability criteria

Step 2 A : Gap analysis

Step 2 B : Conducting tests on missing informations about material

- Physical characterization tests
- Chemical characterization tests
- Biological tests

Step 3 : Risk assessment

Step 4 : Risk control

Step 5 : Biological assessment report

Step 6 : Estimation of the benefit/risk ratio and collection of post-production information

The new version of ISO 10993-1 2025 focus on:

- Alignment with ISO 14971 and risk management philosophy → iterative process with available data and generated data
- Concept of bioaccumulation Better consideration of all life cycle of the MD
- A strong importance of scientific argumentation and therefore control on product/process

Main changes

- Terminology clarification
- The notion of reasonably foreseeable misuse
- Reorganisation of Biological endpoints
- Equivalence definition
- Integration of chemical and physical analysis in biological risks

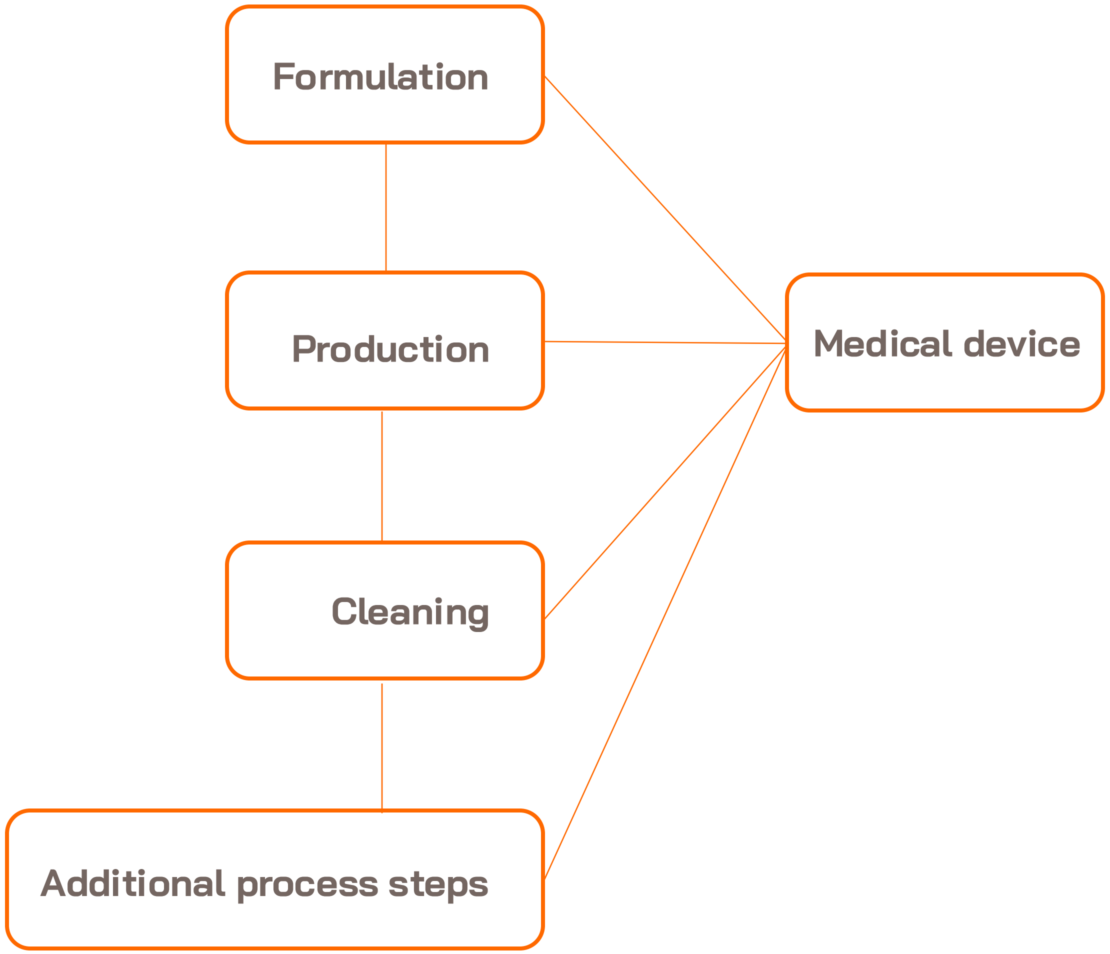
Chemical analyses

Chemical analyses help identify and control toxicological risks to ensure the biocompatibility of medical devices

Product substances requirements

Chemical analyses in biocompatibility evaluation

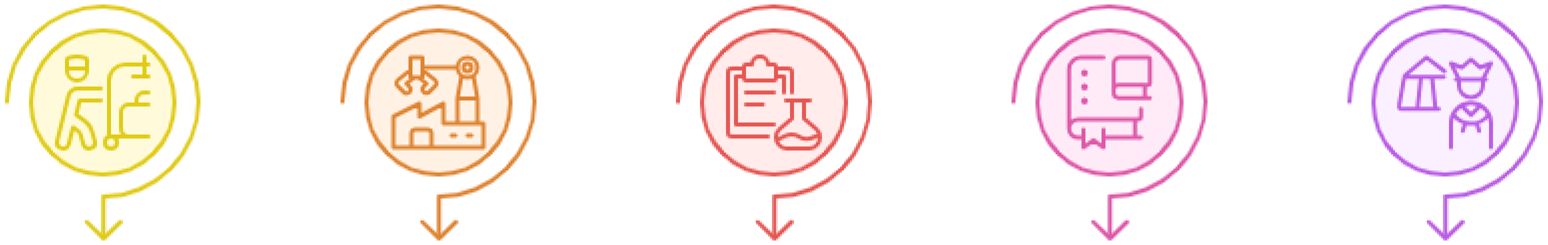
Main steps of chemical analysis



Collected information

Chemical nature (metallic, ceramic, polymer, adhesive, …)
Additives, processing and cleaning agents

Information sources



Supplier
Information obtained from the supplier of a product.

Manufacturer
Information obtained from the manufacturer of a product.

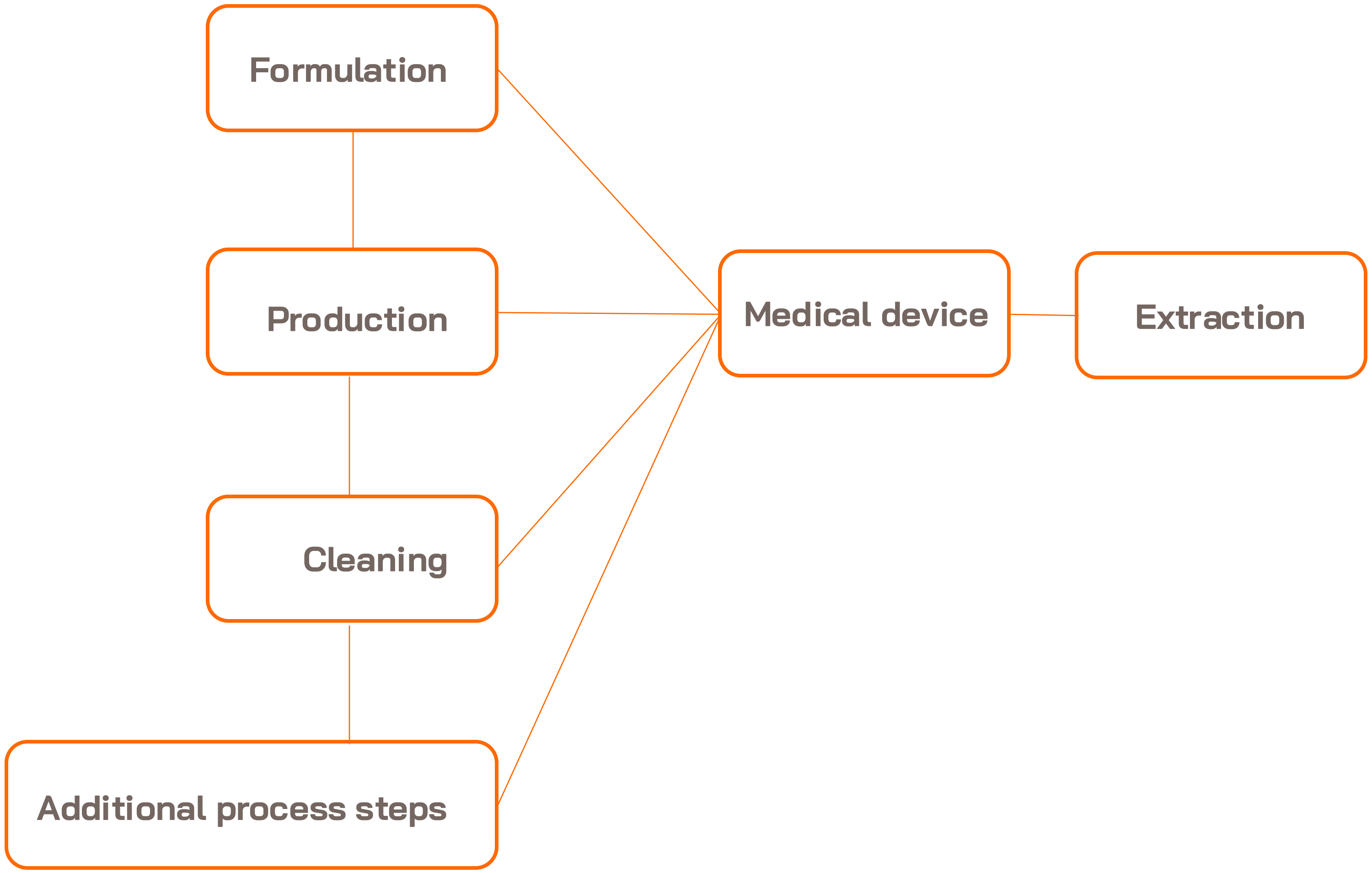
R&D studies
Information obtained from research and development studies.

Litterature review
Information obtained from a review of existing literature.

History
Information obtained from historical records.

If the amount of available data are not sufficient for the biological evaluation, the next step is to generate these data

Main steps of chemical analysis



Extraction: first and main step of chemical analysis

Objectives :

1) Simulate the final use (type of contact, duration of contact, …)

2) Extraction of compounds coming from the medical device by several solvents

- Polar
- Semi-polar
- Non-polar

Medical device manufacturer

- Complete description of the device and its use
- Dimensions
- Process details
- Chemical composition

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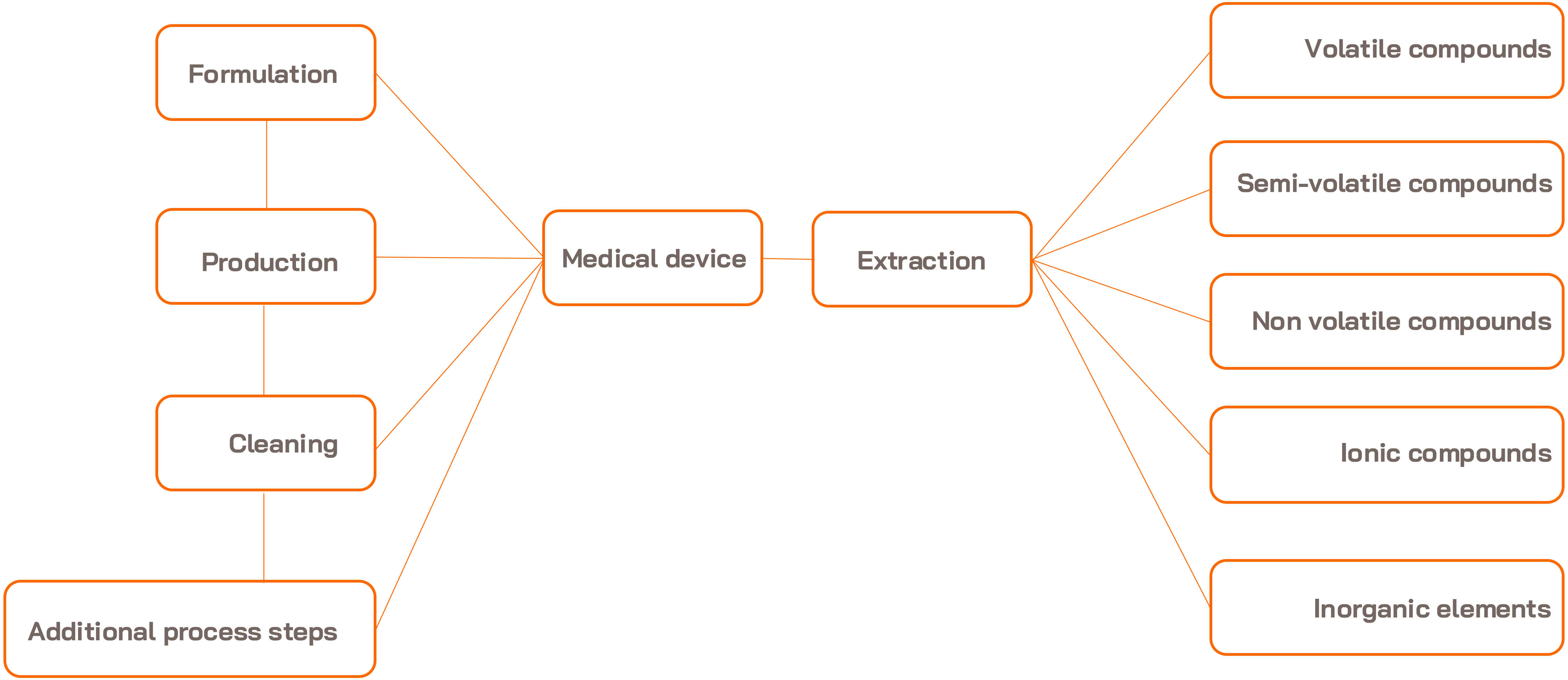
Expertise and support

- Solvent choice → no degradation
- Temperature of extraction → chemical nature

Main steps of chemical analysis



Chemical analyses

- Anions using ion chromatography – quantitative analysis
- Inorganic elements using ICP – quantitative analysis (ICH Q3D)
- Organic compounds using gas and liquid chromatography coupled with mass spectrometry detection – semi-quantitative analysis

→ Semi-quantitative analyses require additional interpretation

Understand GC/MS and LC/MS results

Screening = identification of all quantified compounds without preconceptions

Why GC/MS and LC/MS instead of GC/FID and HPLC/UV?

➔ Mass spectrometry = sensitive detector allowing identification

GC/MS identification

- NIST library (universal)
- Near 350 000 compounds
- Based on mass spectrum
- Some families of compounds have very similar mass spectra

LC/MS identification

- Internal library (specific to the equipment and the method of each lab)
- Based on exact mass
- Calculations to determine chemical formula
- Difficult to distinguish between molecules with the same formula
  - For example, $C_{12}H_{24}O$ corresponds to more than 4000 molecules on PubChem

Expertise in the interpretation using knowledges on polymer, materials, medical devices, chemistry, cleaning processes, manufacturing processes, formulation … based on information given by the manufacturer

The product

Chemical analyses are essential for assessing and ensuring the biological safety of medical devices.

A better knowledge of the final product

Arplus laboratories

In addition to chemical analyses results…

Sources of extractables

Chemical composition

- Monomers
- Additives

Process additives

- Mineral oil
- Demoulding agent

Cleaning process

- Solvent
- Detergent

Decomposition / Degradation compounds

Impurities from compounds

Sterilization

Final conditionning

MSDS and Certificates of Analyses

Compliance with REACH and CLP regulations

Presence of CMR, SVHC, PFAS, ED, PMB, PBT

The strategy of the testing laboratory

Additional chemistry for less toxicology

For compounds higher than AET, toxicological study must be performed based on the approximate amount

Laboratory work :

- **Check of the coherence with medical device composition and type**
- **Evaluation of the potential source**
- **Evaluation of the process**
- **Evaluation of degradation mechanisms**

Not so easy to determine CAS number or exact chemical nature of extractable compounds

→ **Need additional investigation**

Atopic skin cream analysis

Complex galenic formulation comprising numerous components (12 raw materials with thickeners, lubricants, etc.)

Step 1 : Exhaustive extraction using two solvents and SVOC, NVOC and VOC analysis.

59 molecules extracted

- Verification of consistency with components.
  - For example, the presence of a biocide is not consistent
- 15 molecules clearly not identified other than by their chemical formula

Ingrédient	Main function
Glycerol	Humectants
White Soft Paraffin (Petrolatum)	Emollient
Liquid Paraffin	Lubricants
Fatty Acids	Emulsifier
Glyceryl Monostearate	Emulsifier
PEG	Humectant & solvent
Ethylhexylglycerin & Pentylene Glycol	Preservatives
Polysorbate	Thickener

Results unusable for advanced toxicological analysis further investigation required

Atopic skin cream analysis

Step 2: Additional analysis

For each raw material, review the literature on potential degradation, MSDSs and technical data sheets, presence of additives

- Association of each raw formula with a **raw material** in the formulation.
  ➔ Presence of triglycerides ➔ typical fatty acid **decomposition product** commonly found in the formulation

- Discuss with the customer to detail the **manufacturing processes** (steps, time, temperature)
  ➔ Identification of a step inducing a **chemical reaction** of one of the compounds that is expected

At the end only 4 left unidentified molecules

Possible to go further in the evaluation

- By studying fragmentation of molecules during chemical analyses, and their degradation product
- By correlating specific molecules analysis based on specific raw material

Specific analysis : additional chemistry for less toxicology

Screening study = semi-quantification

Why specific molecule analysis?

- Confirmation of the molecule with the analysis of a standard (retention time)
- External calibration using specific standard ➔ true concentration
- Less time for toxicological study
- Better argumentation for notified bodies

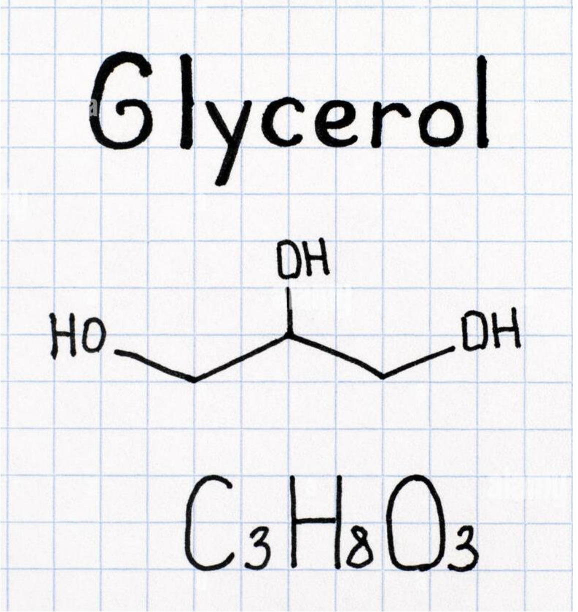
Specific analysis : additional chemistry for less toxicology

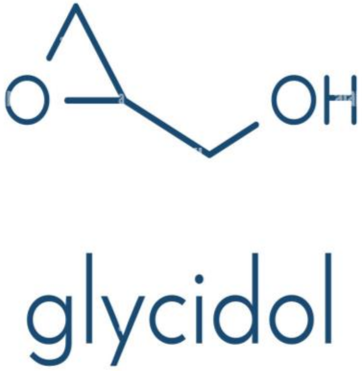
Example: Glycidol analysis

Medical device contains **glycerol** in a high amount
Chemical characterization leads to the detection of glycidol (toxicological risk)

- Kinetic study
- Specific quantification
- Test on the most representative solvent for final use

Conclusion: Glycidol can be formed in the medical device when adding solvent. However, in ethanol 50% (simulating blood), glycidol hydrolyses and is not detected anymore. Risk is then negligible





Conclusion

To remember

- **Chemical analyses** are **increasingly challenged** by regulation evolution illustrating the need for exact identification of extractables ➔ Teamwork between manufacturer and laboratories is the key solution

- **Anticipate the formulation** early in the device conception helps to **minimize the risks** and **improve biocompatibility**

- The more the **device is known,** the more the **chemical results are precise** and the more the **conclusions are reliable**

- Keep in mind that **extractables** can be **non-intentionally added substances**

Thanks!

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New FDA Guideline

Chemical Analysis (#Vi)

- In general, FDA recommends profiling of extractables through a non-targeted analysis with susbsequent use of targeted analysis to identify and quantify appropriate extractables, as necessary.

- FDA recommends initiating the analyses as soon as is practically possible after performing the extraction to avoid deterioration of the extracts (e.g., within 24 hours)

- For each solvent, identified and quantified/semi-quantified extractables above the AET should be tabulated, including :

  - RT
  - Chemical name (e.g., International Union of Pure and Applied Chemistry (IUPAC) name)
  - Chemical Abstracts Service Registry Number (CASRN), when available.
  - Structural descriptor (e.g., international chemical identifier (InChl), simplified molecular-input line-entry system (SMILESS))or image of chemical/compound molecular structure, particularly if a CASRN is not available.
  - Major icons observes (m/z).
  - Type(s) of data used to establish analyte identity 'e.g., library match, RT, manual spectral interpretation)
  - Identification confidence level (i.e., unknown, tentative, confident, or confirmed).
  - Amount in units of µg/device.
  - Quantification method and reference standard
  - Extraction iteration (if not all extracts are pooled for analysis)