Nelson Labs®
A Sotera Health company

Chemical Characterization of Medical devices

Meet our Unmatched Experience!

Quality
Nelson Labs Europe offers a high-quality technical service by adhering to quality assurance and regulatory control requirements.

Flexible
Nelson Labs Europe is adaptable, flexible and working to meet your needs.

Customer-centric
Nelson Labs Europe so values its customers that it commits to quality first.

World-wide
Nelson Labs Europe is a world-wide provider of support services for the pharmaceutical, biotech and medical device sectors.

Expertise
Nelson Labs Europe has an extensive knowledge base and diverse capabilities. It continuously improves and advances its testing and product development technology. Nelson Labs Europe has special expertise in several areas: drug products, container/closure systems, medical devices and combination products.

EXPERTISE

We know materials.

We know materials, we know additives, anti-oxidants, processing aids, plasticizers, degradation compounds, monomers, oligomers, catalysts, curing agents, accelerators, colorants, processing and washing impurities...

We can identify them, we know their analytics, we know their physicochemical behavior, we know their migration potential and we know their toxicity.

This knowledge has allowed us to design optimized scientific procedures (eg. Nelson Labs Compounds Screener Database), tailored and customized protocols, smooth state-of-the art analytical testing (eg through our accurate mass analytical platforms), and comprehensive reporting, in line with the global regulatory requirements.

Indeed, we know materials. But most of all, we understand the needs of our customers!

GENERAL SERVICES

Recently, updated guidances, standards and regulations for medical devices have driven the device industry to take a more **risk based approach** in the safety evaluation of their products.

ISO10993 - Part 1 now considers **chemical characterization** of the materials of construction as a crucial first step in the biological evaluation process of a medical device, where possible. The extent of chemical characterization may depend on different variables, such as the nature and duration of body contact, any existing material safety or toxicological data, etc... However, a characterization study should – at a minimum – be able to identify the chemical compounds potentially released from a device, as well as to quantify the potential exposure to the patient.

ISO 10993 – Part 18 provides a more generic framework on how a chemical characterization could be performed.

ISO 10993 – Part 12 describes in more detail how the test articles should be prepared prior to analytical testing.

DEVELOPMENT AND OPTIMIZING STUDY PROTOCOLS

Over the last 15 years, Nelson Labs Europe has been working on chemical characterization according to the FDA, EMA and ISO guidelines for:

- Medical devices
- Combination products
- Colorants

CUSTOMIZED STUDY DESIGNS

Most chemical characterization projects will require an expert study design, which is optimized or customized for the medical device under investigation, taken into account a series of parameters such as:

- Type/Class of device
- Contact conditions with the patients and/or drug products
  - Nature of contact
  - Final exposure to the patient
  - Contact time
- Mode of action
- Type of medicinal product
- Packaging material of the device
- Process parameters (cleaning steps, sterilization steps)
- Composition of the device and its compatibility with the selected extraction solvents

We are your partner in providing tailored protocols, specifically designed for your requirements or needs.

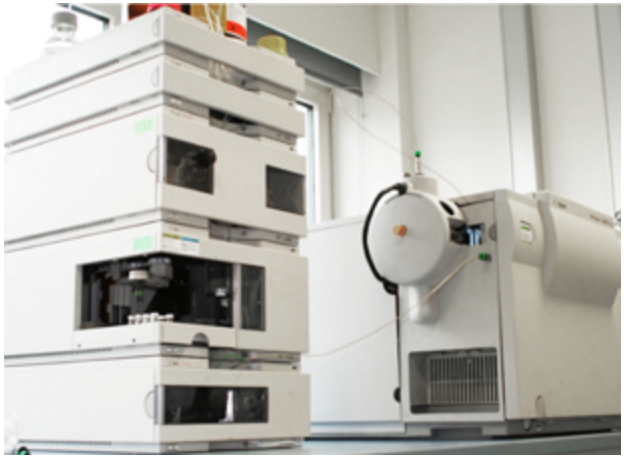
STATE-OF-THE-ART-EQUIPMENT

We use state-of-the-art analytical equipment to study the impurities, present in polymers, plastics, rubbers and alloys that might be introduced from the medical device either into the patient or into the medicinal product during its shelf life. All instruments are fully qualified (IQ/OQ/PQ).

Typical techniques, available at Nelson Labs Europe:

- Headspace GC/MS (volatile organic compounds)
- GC/MS (semi-volatile organic compounds)
- LC/MS (Triple Quad technology and HRAM (High Resolution Accurate Mass)) (non-volatile organic compounds)
- ICP (Element / metals analysis)
- Ion chromatography (anions)
- Total organic carbon
- Non Volatile Residue
- FTIR
- LC/UV/VIS
- GF/AAS (silicon oil)

In addition, we have invested in hyphenated chromatography – accurate mass instruments (GC-ToF-MS; UPLC-ams (AMS: accurate mass spectrometry) which allows identifying compounds at an elemental composition level on a routine basis.



NELSON LABS COMPOUNDS SCREENER DATABASE

Nelson Labs Europe has developed a unique compounds screener database of thousands of extractable compounds including colorants, which allows a broad compound identification based upon a double identity confirmation (retention time and mass spectrum) in “first pass” testing. All analytical standards, used in the development of the database, were either purchased from qualified vendors or synthesized through the in-house synthesis services. The documentation and use of the database is fully GMP-compliant.

Solvent residues

Polymer residues (e.g. monomers)

Glue adhesive residues

Polymer oligomers & degradation compounds

Polymer additives & degradation compounds

Impurities in Polymer additives

Filter residues rubber ingredients and impurities

Plasticizers Tubing residues

Colorants

STRUCTURAL ELUCIDATION OF UNKNOWNS **"SECOND PASS TESTING"**

In order to perform an adequate risk and safety evaluation of your Medical Device based upon Material Characterization data, it is of the utmost importance to broadly identify all detected compounds detected in the **combined chromatographic methods**.

Although it is evident that Nelson Labs' unique Screener Database will assist tremendously in compound identification, still some compounds may remain unidentified.

"Second Pass Testing" is then the ideal way of addressing the safety assessment of these unknowns: using the high-end state-of-the-art analytical techniques like GC-Q-ToF or UPLC-HRAM (Q-Exactive) will assist in elucidating their structure which further allows an in depth risk assessment.

Our analytical expert team is renowned for their ability to elucidate the structure of unidentified compounds in a broad set of materials via the above mentioned accurate mass platforms.

CHEMICAL CHARACTERIZATION

Chemical characterization studies can result in long lists of compounds shown to be present as an impurity on the medical device.

A toxicological assessment may be very cumbersome, even for experienced toxicologists, because of the lack of accurate toxicological information on the reported compounds.

With our approach, every single extractable, reported in an extraction study, is evaluated based upon a Structure Activity Relationship (SAR) Assessment (combined Cramer Classification and Derek Nexus Assessment). As a result, **extractable compounds of concern will be picked-up immediately and can facilitate the full toxicological assessment**.

WE'RE HERE TO HELP EVERY STEP OF THE WAY

Nelson Labs' Technical Consulting Group provides Sponsors with dedicated resources to develop solutions that advance your product innovation. Our network of scientists, engineers, and regulatory experts will collaborate with you to maximize efficiency, reduce risk, and accelerate your time to market.

We can provide you access to our experience of assessing over 6 000 different materials each year, our interaction with regulatory agencies, and first-hand participation in setting standards such as ISO 10993, AAMI, and USP. This extends our expertise into your team, enabling you to bring your product to market successfully.

Once a project is completed, it is often necessary to further evaluate the obtained analytical data in the light of a subsequent safety assessment of the medical device or combination product. Therefore, we offer in-depth guidance on how to evaluate the data and how to prepare for a submission.

COMBINATION PRODUCTS

When combination products are being investigated at Nelson Labs Europe according to the FDA requirement 21 CFR Part 4 “Current good manufacturing practice requirements for combination products”, a combined tailored approach is provided. Both drug product quality/ stability and chemical characterization (extractables and leachables) are evaluated, based on the classification of the combination product.

In use stability testing evaluates if the quality of the drug product is not negatively affected by the combination of the drug product-device. These investigations may cover both analytical and micro-biological testing.

Chemical characterization includes the evaluation of the potential migration behavior of chemical compounds, leaching from the medical device into the drug product.

PHARMACOPOEIA TESTING

Pharmacopoeial testing comprises all the analytical testing required to prove the identity, efficacy and safety of raw materials intended for medical device use. These testings are relevant to assess the biocompatibility of the materials because they try to determine the release of toxic compounds under standard conditions in a direct or indirect way.

Pharmacopoeial monographs such as the USP/NF, EP and JP provide standardized methods and specifications for raw materials and finished products.

USP – PHARMACOPOEIA TESTING

<87> In-Vitro Biological Reactivity – Cytotoxicity Testing
<88> In-Vivo Biological Reactivity – Class I-VI Testing
<381> Elastomers
<661> Containers

E.P. – PHARMACOPOEIA TESTING

3.1 Series; materials used in the manufacture of Pharmaceutical containers
3.2 Series; Containers

J.P. – PHARMACOPOEIA TESTING

JPXVII, 7.02 Test for plastic containers – physico-chemical testing
JPXVII, 7.03 Test for rubber closure for aqueous infusions – physicochemical testing

BIOCOMPATIBILITY TESTING

For medical devices, appropriate biological testing according to the ISO 10993 standard series may also need to be considered. Nelson Labs Europe has a 35 year long history and a vast experience in biocompatibility testing for the medical device industry.

Nelson Labs Europe offers a broad range of biological tests, such as:

- ISO 10993 – Part 3: Tests for Genotoxicity, Carcinogenicity, Reproductive Toxicity
- ISO 10993 – Part 4: Selection of Tests for Interactions with Blood
- ISO 10993 – Part 5: Tests for In-Vitro Cytotoxicity
- ISO 10993 – Part 6: Tests for local Effects after Implantation
- ISO 10993 – Part 10: Tests for Irritation and delayed-type Hypersensitivity
- ISO 10993 – Part 11: Tests for Systemic Toxicity
- OECD 471: AMES testing (Mutagenicity)

QUALITY

Nelson Labs Europe obtained the **ISO 17025** (BELAC) accreditation in 2003. In order to offer the highest level of quality data, Nelson Labs Europe has also received the **GLP** certification (2010) and the **GMP** accreditation (FaGG/aFmPs, Federal agency for medicinal and Health Products) for the release of medicinal products.

Nelson Labs Europe is **FDA registered.**

NELSON LABS OFFERS

Complete confidence

Your test is done right every time. Our track record and reputation for quality and reliability sets us apart.

Industry-leading experts

We understand your business and the challenges you face. Thanks to our active monitoring of the regulatory landscape and working with industry groups we give a full perspective on critical topics and changes.

Exceptional Service

95% of all first-time customers partner with Nelson Labs for future testing. We serve our customers from a worldwide network of labs and facilities.

End-to-end solutions

We are the only comprehensive provider of mission-critical services. Our experts can guide you along the entire product development life cycle.

Nelson Labs®
A Sotera Health company

Safeguarding Global Health®
with every test we complete

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About Nelson Labs

Nelson Labs, A Sotera Health company, is the leading, global provider of lab testing and expert consulting services. We perform microbiological and analytical laboratory tests across the medical device, pharmaceutical, and tissue industries. The company is regarded as a best-in-class partner with a strong track record of collaborating with customers to solve complex problems. We have over 700 scientists, technicians, and service specialists who diligently perform more than 400 rigorous tests in 11 global laboratory locations.

Based in Belgium, Nelson Labs Europe specializes in providing premium Extractables & Leachables testing services to the pharmaceutical and medical device industries. We also support pharmaceutical companies across the globle in developing worldwide compliance testing strategies to qualify container/closure applications and pharmaceutical production equipment from an Extractables & Leachables perspective.

With decades of expertise, we stand behind the quality of our results and the strength or our customer partnerships. Along with sister companies Sterigenics and Nordion, we are part of Sotera Health, the world's leading, fully-integrated protector of global health.

www.nelsonlabs.com