EXTRACTABLES & LEACHABLES
CHEMICAL CHARACTERIZATION

INSTITUT FRESENIUS

PRODUCTS

- Primary packaging for pharmaceuticals (Solid, semi-solid and liquid drug forms)
  e. g. bottles, tubes, bags
- Secondary packaging
  e. g. labels, packaging made from cardboards, plastic, metals and laminates of all sorts
- Delivery-Systems
  e. g. syringes, transdermal patches, all sorts of dosage systems
- Active pharmaceutical Ingredients and finished drug formulations
  e. g. traditional drug applications (small molecules) and biopharmaceuticals (large molecules)
- Single use systems (SUS)
  e. g. Filter systems, tubes, connectors, storage bags, seals, membranes
- Component parts from medical devices
  e. g. Mostly higher risk class devices (Article IX of the EU Council Directive 93/42/EEC), Transfer Sets, Implants, prostheses (stents, joints, bone replacement material) components that are used in dialysis systems, contact lenses
- Kind of materials
  e. g. Plastic, ceramics, elastomers, coatings, metals and alloys, varnished parts

PRINCIPAL TESTS

TESTS ACCORDING INTERNATIONAL STANDARDS

- Physico-chemical testing according compendium monographs
  - e. g. Ph.Eur 3.X und 3.2, USP <661.X>, JP 7 and customized methods
  - organic and inorganic residues, ICH Q3
- Extractables & Leachables assessments for finished packaging
  - EMA, US-FDA, USP <1663>, <1664>; recommendations of PQRI
  - Sound scientific research Leachables-screening studies
  - Migrations-/simulated use studies
  - Leachables shelf life studies (GMP/cGMP studies)
- Extractables&Leachables Assessments for single use systems (SUS) that are used in pharmaceutical production
  - EMA, US-FDA, USP <665>, <1665>; current recommendations of ASTM, ISPE, BPSA, BPOG, PDA can be taken in account
- Quantitative and qualitative determinations of plastic additives and related substances (impurities/breakdowns)
- Chemical characterization studies according to ISO 10993
- Biocompatibility studies (inVivo, inVitro on special request) for medical devices and system-componentse according to ISO 10993, USP <87> and <88>
- Aging studies under accelerated conditions according to ASTM F 1980-07

PRINCIPAL ANALYTICAL TECHNIQUES

- Extraction: Reflux, Soxhlet, static extraction and under agitation, pump assisted extraction, chemical digestion of polymers
- HS-GC/MS (EI), GC-FID/MS (EI), GC-QTof (CI), HPLC-DAD/QTof (ESI, APCI), ICP-MS, ICP-OES, IC-CD, Specific trace analytical methods, targeted analysis: e.g. low mass aldehydes, perfluorinated carbonic acids (PFCA), nitrosamines (GC-TEA)
- Wet chemical methods: pH, TOC, conductivity, NVR and others
- Structural elucidation by high resolution mass spectrometry, fraction collection by HPLC, NMR-analysis (requires sufficient amounts of analyte)

CONSULTANCY SUPPLEMENTARY SERVICES

- Method development and validation of analytical leachables methods GMP/cGMP
- Toxicological assessments of extractables/ leachables studies for medicinal products (USP <661.2>)
  - Derivation of health-based thresholds like PDE values („Permitted Daily Exposure“) as needed for validation of packaging materials.
  - In silico toxicology for the assessment of substances without sufficient data by using TTC-concept or other QSAR tools.
  - Assessment of genotoxic/carcinogenic substances according to ICH-M7 or ICH S9.
  - Toxicological assessments of extractable/ leachable studies of medical devices according to ISO 10993-17
- Determination of the AET (Analytical Evaluation Threshold)
- Consultancy to find the best customized study design to met regulatory requirements
- Support in developing risk mitigation strategies for packaging and single use systems to avoid non-compliance with regard to E&L

ADDITIONAL SERVICES

- Impurity profiling in any starter material for pharmaceutical use, solutions, bulk or others
- Particle identification and particle distribution
- Cleanness of surfaces
- Material failures and damage analysis by analytical methods

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