RESOLIAN
ANALYTICAL SCIENCES

Extractables and Leachables Testing

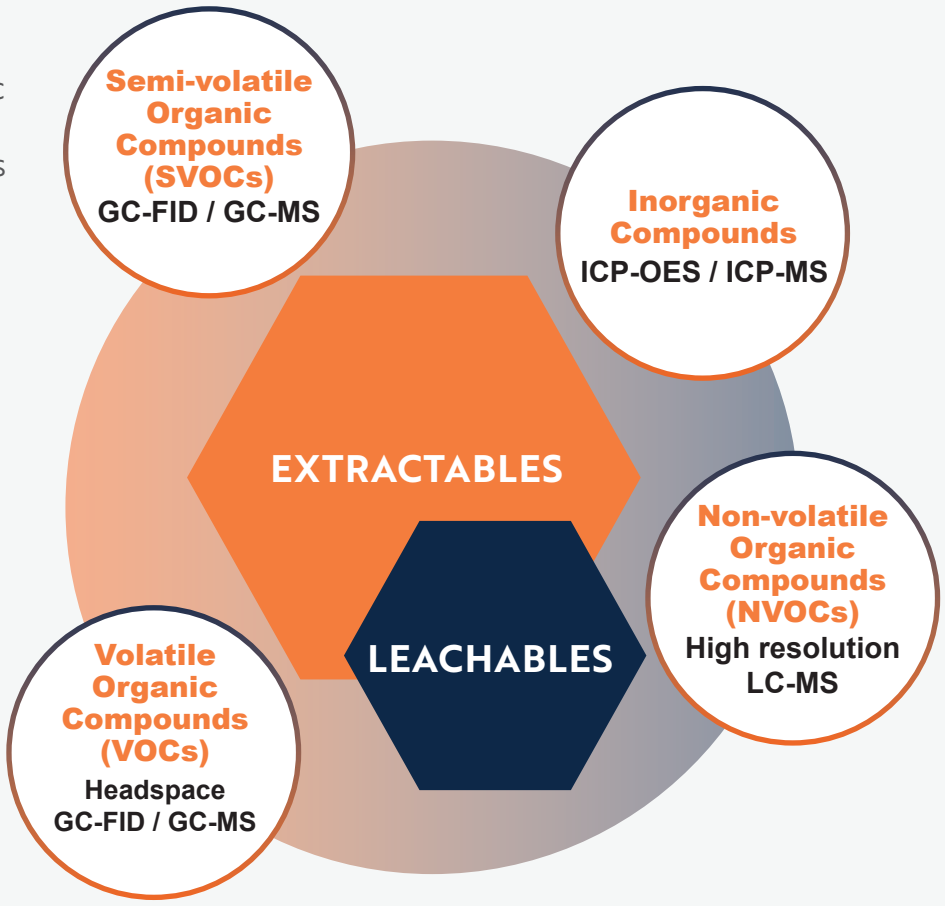
Extractables and leachables (E&L) testing provides vital information concerning the potential for impurities deriving from container closure systems, drug delivery devices and manufacturing processes.

E&L studies utilise organic and inorganic screening methods to profile extractables from polymeric componentry, see the table below for examples, and target leachables in final drug product formulations.

Our expert team designs bespoke study protocols in accordance with the latest regulatory guidelines to ensure drug product safety and compatibility with storage and delivery devices.

- Extraction under exaggerated or simulated use conditions
- Accelerated leachable studies
- Screening and compound specific validated assay methods
- Characterisation of unknowns
- Toxicological assessment (using our partner provider)

All testing is performed at our UK cGMP facilities.



Drug container / delivery devices
pMDI
Vials, ampoules and bottles
Blister packaging
Syringes
Process components and consumables

Extractable and simulated leachable assessments

» Standard or bespoke protocols
» Accelerated extractions of components following contact with control solvents to provide information on potential leachable compounds
» Accelerated extractions of components following contact with product formulation to provide information on potential leachable compounds (simulated leachable)
» Screening methodology for the assessment of volatile, semi-volatile, non-volatile and inorganic compounds
» Further structural elucidation capabilities for unknown components (high resolution accurate mass-spectrometry (HRAM-MS) and nuclear magnetic resonance (NMR))
» All work is carried out according to FDA, EMA and PQRI guidance

Leachable assessments

» Assessment of actual leachable compounds in the product following stability storage
» Screening and compound specific validated methodologies
» Storage of samples and leachable assessment in parallel with stability testing as part of a larger CMC package

Change of packaging and product/packaging interaction assessments

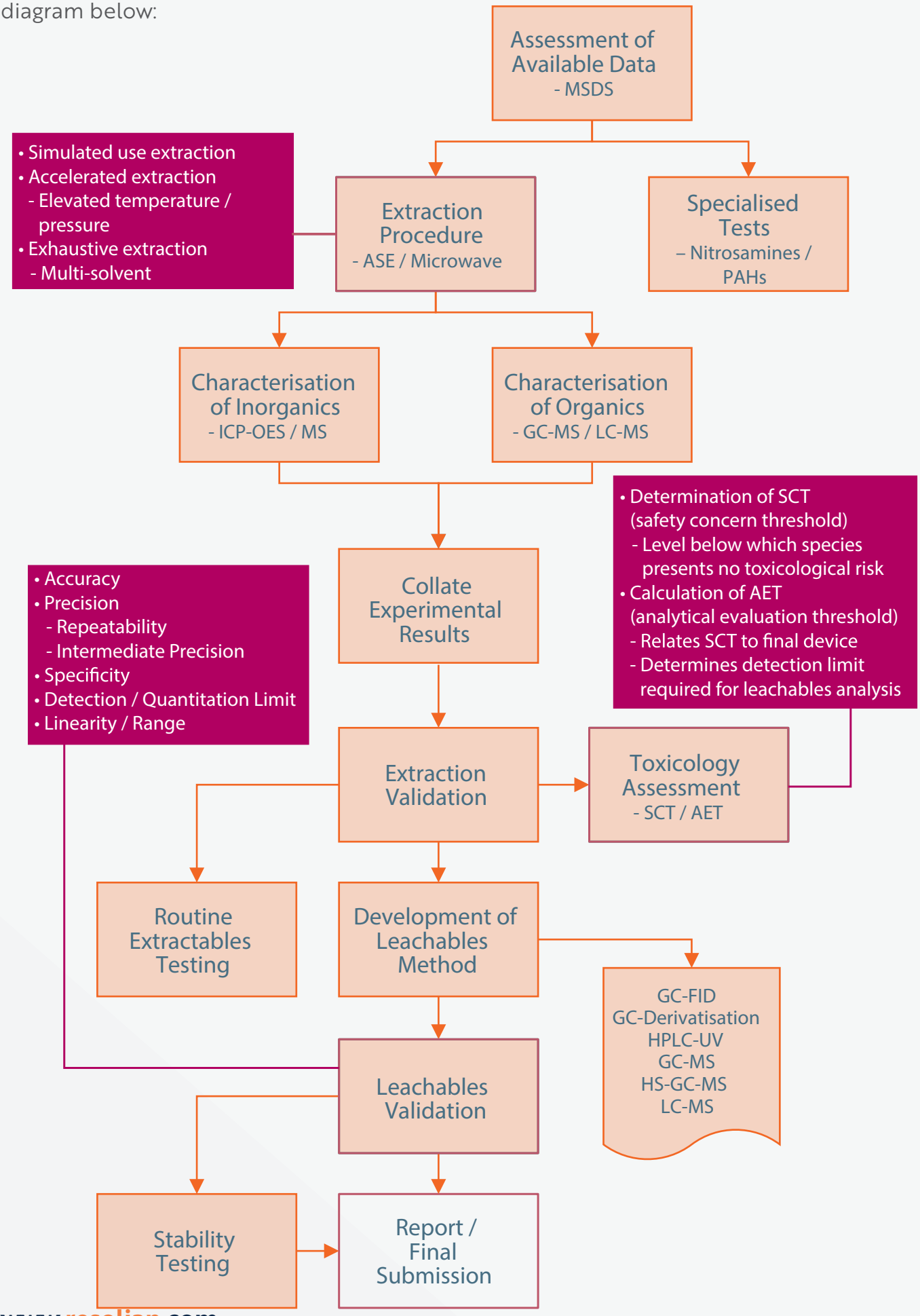
For Consumer Healthcare products Drug Development Solutions has designed bespoke fit for purpose protocols to assess a change in contact material, to provide you with confidence that your product is safe within its new packaging material. Using expert knowledge in the field of E&L, we will work with you to minimise the risk associated with change in components.

Degree of Concern Associated with the Route of Administration	Likelihood of Packaging Component – Dosage Form Interaction		
	High	Medium	Low
Highest	Inhalation Aerosols and Sprays	Injections and Injectable Suspensions; Inhalation Solutions	Sterile Powders and Powders for Injection; Inhalation Powders
High	Transdermal Ointments and Patches	Ophthalmic Solutions and Suspensions; Nasal Aerosols and Sprays	
Low	Topical Solutions and Suspensions; Topical and Lingual Aerosols; Oral Solutions and Suspensions		Oral Tablets and Oral (Hard and Soft Gelatine) Capsules; Topical Powders; Oral Powders

Table 1: Examples of regulatory concerns for common classes of drug products

Overview of a typical extractables and leachables programme

The key stages involved in an extractables and leachables programme are shown in the diagram below:



Applications

» Screening studies to aid single use manufacturing component, container closure system component, transfer system component or medical device component selection
» E&L studies for regulatory submission
» Managing forced or elective changes in single use manufacturing components, container closure system components, transfer system components or medical device components
» Method development, validation and technology transfer of analytical methods for product testing and quality control

Techniques

» Solvent extraction including ultrasonication, microwave, ASE (Automated Solvent Extraction), Soxhlet and Soxtect
» Headspace GC-MS (Volatile Organic Compounds)
» GC-MS and GC-FID (Semi-Volatile Organic Compounds)
» HPLCDAD- MS/MS (Non-Volatile Organic Compounds)
» ICP-MS (Inorganic Compounds)
» Gel Permeation Chromatography (GPC)
» FT-IR, GC-ToF-MS, HRAM-MS and NMR (structural elucidation and unknown ID)

Toxicological risk assessment

The data generated by Resolian's E&L studies can be used for toxicological assessment of any specific compounds as part of a human health risk assessment package. We partner with one of Europe's leading chemical hazard and toxicology risk consultants to provide this service to our customers.

Our expertise

Resolian has a wealth of experience in assessing extractables and leachables for a wide range of products, including:

Pharmaceuticals and Biopharmaceuticals

» Container closure systems (plastic/glass bottles, stoppers, blow seal vials, labels etc.)
» Pre-filled syringes
» Transfer systems (tubing, iv bags, connectors etc.)
» Single use systems/process contact materials (tubing, gaskets, filters, bags, o-rings etc.)
» Parenteral, ophthalmic, dermal, topical, orally inhaled and nasal drug products, metered dose inhalers

Consumer Healthcare

» Container closure systems (plastic/glass bottles, stoppers, laminated tubing, labels etc.)
» Creams, ointments, toothpaste, shampoo

Medical Devices

» Whole or component parts according to ISO-10993 (biocompatibility)

Animal Healthcare

» Container closure systems (plastic/glass bottles, stoppers, blow seal vials, labels etc.)
» Tags, implants

Electronic Nicotine Delivery Systems (ENDS)

» Device components
» E-liquid container closure systems

With an array of modern technologies, knowledge of regulatory issues and complimentary CMC analytical capabilities, this makes Resolian your ideal partner for E&L studies.

Learn more about our services

www.resolian.com