Analytical Services for all stages of Drug Development and Production

Amazing where you can go
Analytical services ...

### Increasing GMP requirements

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**Analytical Characterization**
Broad analytical information on purity and (physico) chemical properties

**Method Development and Validation**
Development and validation of robust and reliable analytical methods

**Quality Control Analysis / Routine Analysis**
Release testing to assess the quality of pharmaceutical products and chemicals

**Stability Studies**
Stability testing and stress tests on drug substances and drug products

**Highly Potent and Cytotoxic Substances, Controlled Substances and Genotoxic Impurities**
Analytical testing of highly potent and cytotoxic substances, and controlled substances

**Microbiology Services**
Microbiological testing of pharmaceuticals

**Specialties**
Reference substances, inhaler testing, extractables & leachables, troubleshooting, elemental impurities

**Our Technology Base/Our Method Portfolio**
Analytical Solutions
Solvias provides a wide range of analytical solutions for pharmaceutical and biotechnology companies for all stages of drug development and production.

We offer:
• State-of-the-art equipment
• Broad and in-depth know-how
• Extensive experience
• Flexible capacity to provide analytical services to meet your needs from a single measurement to large development projects.

Broad Portfolio of Methods
Our portfolio of analytical methods includes all the analytical techniques required for meeting the technical and quality standards for successful drug development:
• Latest separation technologies
• Hyphenated methods (e.g. with MS)
• Elemental analysis
• Spectroscopy, physical chemistry

Certified Quality
Solvias’ analytical department is certified to work according to GMP and has been FDA inspected on several occasions. The entire company is ISO 9001 certified.

Our Commitment | Your Benefit
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State-of-the-art equipment and scientific experts for all analytical requirements | Financial resources remain available for core activities

Flexibility | No bottlenecks, short lead-times

Confidentiality | Generated knowledge and intellectual property remains in your hands.

Dedicated teams | Responsive, reliable, and professional services

Efficient project management | Planning reliability, good communication across interfaces

Choice of quality standards | Fit for purpose and lower risk of failure

Overall

Broad range of analytical services | One service provider for all stages of drug development

... for all stages of drug development and production
Quality

We aim to fulfill all the contractual and project-specific requests from our clients according to the guidelines of the authorities. Through continuous quality management, we ensure the ongoing improvement of our processes, services and products, and continually increase the efficiency of our activities. Our Quality Management System and independent Quality Assurance Unit guarantee that you receive products and services of a permanently high standard of quality. Solvias undergoes regular customer audits – around 40 per year.

Certification to ISO 9001

Our Quality Management System is based on our business processes in compliance with ISO 9001:2008. The Swiss Association for Quality and Management Systems (SQS) has certified our system under the registry number 11237.

GMP Compliance

Solvias has been duly authorized by Swissmedic, the Swiss Agency for Therapeutic Products, to manufacture medical products. This authorization allows Solvias to perform pharmaceutical analyses and to manufacture active pharmaceutical ingredients (API) for use in clinical trials within the standard of Good Manufacturing Practice (GMP). Confarma France SAS is authorized by the ANSM (French Health Authority) for compliance to GMP.

FDA Inspections

The US Food and Drug Administration (FDA) successfully inspected Solvias AG and Confarma France SAS most recently in March 2014. Accordingly, both have been accepted and registered with the FDA as testing facilities for analyzing pharmaceutical products.

Project Management

Efficient and effective project management is key to successful service delivery. Our dedicated project managers take responsibility for the management and coordination of your project from kick-off to final delivery. They use their in-depth experience in development projects for the pharmaceuticals industry, best practice methodologies, and leadership to coordinate the specialists assigned to your project. We provide a clear structure for planning and carrying out your projects.

An important added-value is effective and timely communication, using for example frequently scheduled telephone conferences, personal discussions on site and regular reports.

Advantages of Solvias’ service-oriented project management:

- Dedicated project manager as direct contact for all project-related activities
- Supervision of timelines, budget, quality requirements and communication
- Diligent planning of projects based on our considerable experience
- Professional and client-oriented handling of unexpected results and issues within a project
- Advanced project management processes
Solvias offers characterization of new drug substances to meet the regulatory requirements for registration dossiers from physico-chemical parameter evaluation and preformulation to the setting up of complete analytical test programs. Typical services include, but are not limited to:

- Elemental composition and impurities
- Identification and quantification of impurities
- Spectroscopic and spectrometric characterization (MS, NMR, IR, UV)
- Particle size analysis
- Microscopy
- Solubility (aqueous and non-aqueous)
- pKa
- Partition coefficient
- Solid-state properties (DSC, DVS, TGA)
- Compatibility with typical excipients and packaging material

Many methods are available as micro-methods to reduce the required amount of precious samples. The details of each program are agreed with the client. Solvias can advise clients who wish to put together a specific characterization that will satisfy the requirements of the regulatory authorities.

Typical Techniques Used

AAS, classical elemental combustion analyzer, dissolution, GC-MS, gravimetric methods (LOD, sulfated ash), Headspace GC, HPLC, HPLC-MS, HR-LC-MS (Orbitrap), Headspace GC-MS, IC, ICP-OES, ICP-MS, IR, Karl-Fischer, laser diffraction, MALDI-MS/MS, MS, NMR, Raman, titration, UV, XRF, XRPD

Our Focus

- Meeting regulatory requirements
- From single analysis to complete test programs
- State-of-the-art equipment
Method Development
We have considerable experience in developing analytical methods for the complete range of our analytical portfolio, and for the entire lifecycle of a drug. Typical applications are:
- Quality control of APIs, raw materials, intermediates and finished products
- Stability testing
- Characterization of substances
- Cleaning validation
- Packaging material testing, extractables and leachables
- Safety, health and environment
- Occupational Hygiene Analysis
- Genotoxic impurities
- Specialized applications, troubleshooting

Complete Analytical Development Programs
- Expertise and know-how
- Capacity to perform comprehensive analytical development programs for a drug substance/API
- Access to a broad lab infrastructure matching the capability of a big-pharma environment
- Deliver the whole analytical package from pre-clinic to regulatory submission

Method Transfer
- Transfer methods to or from our clients or to third parties according to GMP quality standards
- Assist with your method transfer requirements, e.g. training of personnel at your site

Validation
- Full validation following ICH guidelines; specific designs like ANVISA or Kojima upon request
- Validation programs adapted to the development stage of the drug, based on your validation requirements beyond regulatory ones
- In line with your quality requirements
- Preparation of validation protocols and reports
- Cost-effective solutions

Our Focus
- Reliable and robust methods
- Methods validated according to the development stage
Analytical Packages or Single Methods

Based on full GMP compliance, we can take over the entire Quality Control testing program of a product. This option provides you with a cost-effective and trouble-free solution. Just send us a sample of your product, and we will deliver the results in a Certificate of Analysis or an analytical report that can be used to immediately release the product. Of course, Solvias is also pleased to perform selected methods of your monograph if this option better suits to your needs.

Quality Control analyses are routinely performed at Solvias according to ISO or GMP for:

- API starting materials
- Drug substances
- Drug products
- Enzymes
- Excipients
- Intermediates
- NGIs
- Raw materials

Analytical methods can be transferred to or from the client. Following ICH guidelines, GMP method transfer follows a formal process with transfer protocols and reports. Alternatively, the methods may have been developed and validated at Solvias previously, or they are simply compendial methods that are already in place at Solvias or require verification only.

Typical Techniques Used

AAS, CE, GC, GC-MS, gravimetric methods (LOD, sulfated ash), HPLC, Headspace GC-MS, IC, ICP-OES, ICP-MS, IR, Karl-Fischer, laser diffraction, LC-MS, particle size distribution, pharmacopeial tests, polarography, residue on ignition, titration, U(H)PLC, XRPD

Our Focus

- Cost effective solutions
- Quality
- Saving of time and resources for our clients
Solvias offers the complete bandwidth of stability studies according to ICH guidelines for drug development and follow-up stability studies. They cover all ICH standard storage conditions as well as low temperature storage. Furthermore, we can organize special storage upon request (e.g. special temperatures/relative humidity or various orientations of containers).

Based on your specific needs, stability protocols outlining all details of the study are written and approved prior to beginning a stability study. We have the know-how and experience to deal with unexpected situations during the stability study, such as the appearance of new degradation products, using our complete analytical portfolio and in-house expertise.

Interim reports, full stability reports or only analytical data will be provided upon request.

Our storage chambers are fully controlled with 24/7 monitoring and alert system. Furthermore, we monitor the air in the chambers to avoid cross contamination issues. In addition, we have back-up chambers for complete sample retrieval.

Our services include:
- Long-term stability testing
- Intermediate stability testing
- Accelerated stability testing
- Forced degradation studies/Stress tests
- Photostability testing
- In use testing
- Temperature cycle tests
- Comparative stability testing
- Compatibility studies

**Typical Techniques Used**
GC, GC-MS/MS, HR-LC-MS (Orbitrap), Karl-Fisher, LC, LC-MS/MS, LOD, titration

**Our Focus**
- Complete management of your stability studies
- Stability-indicating methods
- Comprehensive stability documentation protocol
Highly Potent and Cytotoxic Substances, Controlled Substances and Genotoxic Impurities

In recent years, the number of highly active and toxic substances in the pharmaceutical industry has greatly increased. This is mainly the result of intensified research in the anticancer drug field, which has yielded many cytotoxic substances. But other areas in the pharmaceutical world besides oncology generate substances that are cytotoxic or toxic in some way and this needs to be addressed.

Thanks to our experienced and specially trained staff and prerequisite protection measures, Solvias is now able to offer nearly all analytical services for highly hazardous substances. Furthermore, Solvias is authorized by Swissmedic for the analysis of controlled substances.

Our set-up:
- Fully operational systems
- Categorization of all substances according to potential safety risk
- All necessary safety precautions and technical safety measures according to category (e.g. laminar-flow safety benches with balances in ventilated enclosures)
- Staff training and protection
- SOPs and safety, health and environment manual
- Designated labs

Genotoxic Impurities
Genotoxic Impurities (GTI) must be detected, identified, and reported before clinical trial initiation to ensure patient safety and eventual drug approval, but every drug and process has a unique set of process impurities. To ensure drug approval, Solvias has the resources and the knowledge to address the GTI concerns from the analytical perspective. We can help you to stay compliant with limits of genotoxic and potential genotoxic impurities.

Our Focus
- Complete analytical package for highly potent and cytotoxic substances, and controlled substances
- No need for the client to implement own laboratory
- Safety for our employees
- Wide expertise and know-how for GTI issues
- Very sensitive methods (HPLC, HPLC-MS and GC-MS) and state-of-the-art instrumentation to measure genotoxic impurities
Solvias offers a widespread service for microbiological testing of pharmaceutical products, medical devices and cosmetics.

Our services include:
- Total aerobic count, yeasts and molds
- Exclusion of specific micro-organisms
- Microbial quality of pharmaceutical preparations (including harmonized methods)
- Antimicrobial conservation efficacy tests
- Endotoxins (LAL test)
- Microbial and physico-chemical testing of pharmaceutical water (e.g. water for injection or highly purified water)
- Identification of micro-organisms (Mini API®)
- Method development (product-specific)
- Method validation (product-specific)

Our Focus
- Microbiology services using harmonized methods
- Integrated services complement our microbiology
Specialties

Reference substances, inhaler testing, extractables & leachables, troubleshooting, elemental impurities

Reference Substances
Well-characterized reference substances make a crucial contribution to the accuracy of analyses in the pharmaceutical industry. Solvias provides a wide range of services for reference substances of small molecules and biopharmaceuticals:

- Synthesis of reference substances, including development of the synthesis route where necessary
- Isolation, purification or enrichment of by-products/impurities needed as reference substances, for example by crystallization, extraction, or preparative chromatography
- Characterization of reference substances (identity, purity and assay)
- Full certification, meeting GMP requirements
- Packaging, for example weighed quantities in vials, including certificate of analysis
- Storage and logistics
- Details of the analytical certification program will be agreed with you.

Inhaler Testing
Solvias is fully equipped to perform measurements according to USP <601> apparatus 5 and 6 and Ph. Eur. 2.9.18. apparatus E for dry powder inhaler (DPI) and pressurized metered dose inhaler pMDI for Delivered Dose (emitted Dose) and Particle Size (Aerodynamic Size Distribution) by using Next Generation Impactors (NGI). Different impactors e.g. Anderson cascade impactor can be implemented on request.

Typical Techniques Used
Using Next Generation Impactors
USP <601> & Ph. Eur. 2.9.18. for DPI & pMDI
- Delivered dose
- Particle size (aerodynamic size distribution)
Extractables & Leachables
Benefiting from its vast experience in analytical services, including trace analysis in numerous matrices, Solvias has the capability to provide a wide range of analytical technologies for investigating Extractables & Leachables in accordance with the guidelines of the EMEA and FDA for primary packaging materials. This is significantly improved by applying our proprietary database with >6000 compounds (all typical Extractables & Leachables) in addition to commercially available databases.

A typical program is made up in the following way:

Design and Perform an Extractable Study
Extract packaging material with defined solvents under defined conditions and analyze extract (for example using GC-MS, HR-LC-MS (Orbitrap), and for inorganics using ICP-OES, ICP-MS, AAS). If possible, identify the chemical structures.

Perform Risk Assessment
Evaluation of the hazard potential and maximum acceptable limits of each chemical detected by a toxicologist.

Develop Analytical Methods for the Drug Product Matrix
Make sure that all identified critical substances can be analyzed in the drug product with an LOQ at the maximum acceptance level or lower.

Perform Leachable Study
Put real samples into storage under normal and stress conditions (e.g. ICH conditions). Analyze the samples using the methods developed earlier. As each study is unique, and tailored to your specific needs, details of the program are agreed using a written protocol.

Our Focus
- Whole analytical capabilities for inorganic and organic Extractables & Leachables
- Reliable and fast identification of Extractables using realistic conditions
- Robust and sensitive quantification of Leachables
Troubleshooting

Solvias has been a specialist in troubleshooting for numerous years – analyzing irregularities is one of our core competencies. No matter what the problem or analytical method, you can expect to receive initial information or even the entire solution in just one to two days.

One example of how we can help in terms of troubleshooting is to identify unknown inorganic and organic contaminants, residues, impurities or foreign particles found in products.

- Unknown inorganic contaminants or residues can be identified by semi-quantitative X-ray fluorescence analysis
- All elements in the periodic table ranging from magnesium to uranium, including the halogens, silicon, phosphorus and sulfur, can be detected
- Foreign particles can be examined by microscopy. Elementary identification is accomplished using scanning electron microscopy (SEM) with energy dispersive X-ray analysis (EDX detector)
- Organic impurities can be analyzed using our spectroscopy and separation science knowledge maybe in combination with our sophisticated mass spectrometry equipment or other structure elucidation tools like NMR if needed.

These are the "usual suspects" we investigate on a routine basis:
- A white crystalline active substance/tablet contains dark particles. What do these particles consist of?
- A dark-brown residue was found in a reactor. Is it a reaction product?
- A synthesis step is no longer functioning as normal. Could metallic impurities be responsible for the malfunction?
- Sulfated ash levels exceed the maximum specification. Which inorganic components might be responsible for this?
- A new impurity is found in the API. What is it and at what concentration?

Our Focus

- Reliable characterization of unknowns and impurities
- Extensive know-how in separation science and spectroscopy/spectrometry
- Imaging of particles and surfaces
- Fast assistance to identify the origin and root cause of product complaints
Elemental Impurities
Solvias is future proofed for the continuously increasing requirements for sensitivity and repeatability in trace element analysis. Our ICP-MS screenings detect to the lowest level possible, and cover all limits listed in the “Guidelines for Elemental impurities” of ICH Q3D, which is in the alignment process with USP and Ph. Eur.

Metal-free sample preparation lab
For sample preparation, Solvias uses its dedicated metal-free lab, which has different compartments for better separation, containment and pressure regulation. A suspended ceiling, sealed walls and air filtering prevent as much external contamination as possible. Everything is optimized for working in trace metal analysis.

Typical Techniques Used
AAS, ICP-MS, ICP-OES, XRF

Our Focus
- Over 30 years of experience in ICP-MS
- Generally validated method available for screenings
- Metal-free sample preparation guarantees minimal false positives
- Latest technologies secures detection to the lowest possible level of element impurity
- Capacity to handle large volumes with a quick turnaround
Our Technology Base/Our Method Portfolio

The Solvias Portfolio of Analytical Solutions from Drug Development to Commercialization

**Separation Science**

CE  
- UV, FLD

GC, Headspace GC
- FID, TCD, NPD, MSD

IC

SEC / GPC
- UV, ELSD, MALSS
U(H)PLC
- DAD, FLD, RI, ELSD, CAD, ECD, MS, MS/MS

TLC

**Mass Spectrometry**

GC-MS/MS

HR-LC-MS (Orbitrap)

Headspace GC-MS

ICP-MS

Ion trap

MALDI TOF/TOF

Q-ToF, ESI-MSn

Single quadrupole

**Elemental & Microanalysis**

AAS
- FAAS, CVAAS, ETAAS

Classical elemental analysis
- e.g. combustion

Classical pharmacopeial analysis

Gravimetric tests

Heavy metal screening

ICP-MS, ICP-OES

Karl-Fischer

SEM with EDX

Titration

XRF

**Physical Chemistry**

Density
- liquid, solid, osmolality

Dissolution

Dynamic vapor sorption

Microscopy / imaging
- SEM, TEM, light, IR, Raman

Particle sizing
- laser diffraction, microscopy, sieving, DLS

Polarometry

Rheology / viscosity

Specific surface area
- BET

Thermal methods
- TG, DSC, TAM

X-ray powder diffraction (XRPD)

**Spectroscopy**

AAS
- FAAS, CVAAS, ETAAS

Circular Dichroism (CD)

Fluorescence

FTIR

ICP-MS

ICP-OES

Raman

UV/VIS