

## Custom organic synthesis

Selvita understands the need for its customers to conduct chemical research, development and synthesis of drug candidates in a cost effective approach. A carefully designed compound synthesis allows for minimal use of reagents and solvents, as well as reducing the time needed for obtaining desired compound. This allows for often significant reductions in the overall costs of the whole R&D process.

The range of services offered by Selvita covers:

- consulting
- Computer-Aided Synthesis Design
- toxicity and metabolite prediction
- combinatorial libraries
- solid phase synthesis
- custom synthesis
- analytical chemistry
- crystallography


## Consulting services – from synthesis design to process optimization

Selvita has developed expertise in supporting its customers and offers consulting services throughout the various phases of:

- process optimization:
  - evaluation of alternative and innovative manufacturing pathways
  - by-passing undesired reaction steps, improving inefficient reactions
- patent intelligence:
  - verification of reaction routes
  - information for generic manufacturers
  - market studies (such as data about existing developments, description of medicines targeted at particular disease, market analysis, clinical trials)

## First step of the synthesis – computer aided synthesis design

Using the latest tools for in silico retrosynthetic analysis, including some of the most effective software as well as reaction databases comprising of hundreds of thousand carefully selected reactions, in exceptionally complex cases by applying quantum chemistry calculations (reaction energy barrier, transition state location etc.). Selvita's chemists are able to perform standard retrosynthetic analysis within approximately 5 working days (in case of compounds with a more complicated structure, designing the synthetic route may take a little longer not exceeding two weeks).



This service can be used to modify existing synthetic routes in order for instance to:

- increase yields
- reduce impurities
- replace hazardous chemicals
- improve inefficient reaction steps or by-pass undesired chemical reactions
- comply with more stringent environment protection regulations

As a unique service, Selvita also offers to design of synthetic routes based on both a target molecule and starting materials defined by the customer.

In most cases, Selvita will propose several alternative reaction routes for which the yield of each particular reaction step is estimated, in order to calculate a potential cost of goods.

As for its consulting services, Selvita warrants the freedom of IP hurdles of its synthetic route by extensive search of data in a weekly updated patent databases and scientific publications.

## Toxicity and metabolites prediction

With algorithm from LHASA LLC software or Accelrys, scientists at Selvita are able to predict toxophores responsible for:

- carcinogenicity, mutagenicity and teratogenicity
- respiratory and skin sensitization
- neurotoxicity cardiotoxicity and thyroid toxicity
- lachrymation and irritancy

Using GeneGo solutions the team is able to predict most likely metabolic routes and metabolic products.

## Combinatorial libraries

As properly designed library increases probability of finding the desired molecule, Selvita's teams are experienced in designing and synthesizing combinatorial libraries. Right from the beginning Selvita prepares compound safety assessment, including identification of potential toxophores and metabolites, thus helping partners to select only the most likely compounds for synthesis with regards to toxicity, therefore saving time and money.

Selvita's scientists are also experienced in pharmacophore modeling and lead optimization process.

In addition to the above in-silico services, assessment of synthetic accessibility of chemical compounds is performed (Molecular Networks software). Using this approach, Selvita is able to provide library of more than 90% synthesizable compounds.





## Solid-phase synthesis

Following combinatorial library design, or independent of it, Selvita's scientists are able to synthesize 50–100 compounds per month through solid-phase synthesis using state of the art equipment. Typical sample is 10–25 mg and is provided with its certificate of analysis, including a mass spectrum.

## Custom synthesis

Selvita's experienced team focuses on producing structurally complex, toxic or hazardous, difficult to synthesize molecules or time consuming and multi-step reactions.

Commissioned compound can be synthesized, scaled-up or optimized according to the route provided by the customer or developed in Selvita's laboratory. Selvita can synthesize from milligrams to hundreds of grams of high purity (purity > 99%, chiral purity 98–99%; determined by HPLC) and if required, through a preferential partner Selvita can synthesize batches of up to 5 kg.

Turn-around time for custom synthesis is 6–9 weeks (it very seldom takes longer, and only in case of structurally very complex molecules or when a specific reagent has to be acquired).

Selvita also prepares reference substances (such as impurities for impurity profiling of API) and synthesizes peptides (using peptide synthesizer).

## Analytical chemistry

Selvita offers a very broad range of analytical chemistry services:

- isolation and identification of side-products using the latest products reaction prediction software
- analytical methods validation:
  - liquid chromatography: measurements in typical solvents, serum and blood (human and rat blood available)
  - mass spectrometry (ion trap with electrospray ionization and spectrometer with MALDI-TOF for protein studies)
  - development chromatography for LC-MS (Bruker HCT Ultra + Dionex UltiMate 3000 RSLC)
  - analytical and semi-preparative chromatography
  - detection of heavy metals – atomic absorption spectrometry and atomic emission spectrometry (ICP-AES)
- measurements and interpretation of NMR (500MHz and 700MHz; measurements of time consuming two-dimensional spectra), IR, UV-VIS and Raman spectra
- measurements using X-ray diffractometer
- elemental analysis

Selvita's analytical chemists are supported by a theoretical chemist. Selvita's computer capabilities are sized up for high-level quantum calculations for the interpretation of very complicated spectra or in case of insufficient experimental data.

## Crystallography

Selvita offers the following crystallography services:

- crystal structure analysis (using monocrystal diffractometer – measurements for chemistry and structural biology)
- powder diffractometry (polymorphic structure determination)
- developing and improving purification methods (elaboration of best conditions for crystallization such as solvent or temperature gradient)

## Protection of Intellectual Property

Selvita understands the concerns of confidentiality and intellectual property. All information supplied is treated as strictly confidential and safe data flow and storage is ensured (compliance with ISO 27000 standard data storage security (encryption, archiving, secure communication channels). Selvita's cost-effective solutions coupled with Poland's high level of science, political and economical stability, strong IP protection and near-shore logistics make Selvita a great outsourcing partner for a company which intends to improve their R&D productivity.

## Our strengths:

- high scientific level of our specialists
- competitive prices
- fully equipped laboratory with modern equipment
- professional project management with remote access to data possible
- strong protection of intellectual property
- near shore logistics
- economical and legal stability of Poland



**Selvita sp. z o.o.**

e-mail: [selvita@selvita.com](mailto:selvita@selvita.com)

[www.selvita.com](http://www.selvita.com)

### **Office Kraków North**

ul. Ostatnia 1c  
31-444 Kraków, Poland  
tel. +48 12 410 73 80  
fax +48 12 410 73 82

### **Office Kraków South**

ul. Gronostajowa 7  
30-387 Kraków, Poland  
tel. +48 12 664 62 87 (88)  
fax +48 12 664 53 93