High Potency API and Drug Product Services
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Siegfried offers the capability for early stage development, scale-up & commercial manufacture of both high potency drug substance and high potency oral solid dosage forms, with occupational exposure limits (OEL) ranging down to 1 μg/m³.

With continual investment in its containment technology, controls & the capability for safe handling of such materials and a breadth of operating experience since 2004, you can expect more with Siegfried as your preferred partner for high potency material needs.

For drug substances Siegfried offers in Zofingen, Switzerland a state of the art development & analytical building (opened 2009), using specific separate controlled areas for synthesis, process development & analysis. API scale-up and cGMP manufacturing is provided in its segregated production facilities for high potency materials.

Drug product formulation development and small scale cGMP manufacture is also provided at Zofingen in Siegfried’s purpose built containment facility opened in 2012. Coupled with existing high potency commercial manufacturing facilities at its Malta site, seamless scale up of your drug product from early development through to regular production is available.

The combination of both drug substance & drug product services when working with Siegfried means you can expect more value & synergies, offering you complete integration and continuity of supply for your high potency products throughout their lifecycle. Contact us for an informed and open discussion regarding how we can meet your requirements.
### Drug Substance

#### Overview

Zofingen (OEL to 1 μg/m³)
- Modern state of art development & analytical building (opened 2009), with specific separate controlled areas for synthesis, process & analytical development.
- Segregated cGMP production facility for high potency material process scale-up & API manufacture.
- Commercial scale cGMP production facility.

#### Development

Purpose built labs for handling high potency materials, both for synthetic chemistry and analytical services.
- Synthetic route investigation
- Process optimization
- Process implementation
- Salt screening / crystallization program
- Design of Experiment (DoE) approaches
- Developing 2nd generation processes

#### Small / Pilot Scale

**Production scale**
- Reactor configuration: 2 x 60 L glass lined
  - 60 L Hastelloy
  - 100 L glass lined
- Operating Range: -60 °C to 220 °C
- Pressure Range: up to 16 bar
- Product Isolation: 80 L Hastelloy Filter-dryer (incl. Glove box)
- Batch Sizes: 1–20 kg

**Pilot scale**
- Reactor configuration: 250 L glass lined
  - 400 L glass lined
  - 250 L stainless steel
- Operating Range: -60 °C to 220 °C
- Pressure Range: up to 2 bar
- Product Isolation: 40 L Hastelloy centrifuge
- Drying: 200 L Hastelloy spherical dryer
- Batch Sizes: 10–80 kg

#### Production

**Production scale**
- Reactor configuration: 1 x 1000 L stainless steel
  - 2 x 2500 L stainless steel
  - 2 x 2500 L glass-lined
  - 2 x 4000 L (stainless steel & glass-lined)
  - 1 x 5000 L stainless steel
- Operating Range: -20 °C to 160 °C
- Pressure Range: Up to 40 bar
- Product Isolation: Centrifuge (Halar/hastelloy)
- Drying: Spherical dryer
- Batch Sizes: 100 kg

### Drug Product

#### Overview

Zofingen (OEL to 1 μg/m³)
- Segregated cGMP high containment development area for formulation development & small-scale sample manufacture.
- Separate controlled area for analytical development and quality control.

Malta (OEL to 1 μg/m³)
- Segregated cGMP production areas for high potency material handling.
- 4 separate suites for granulation, tableting, coating & blister production.

#### Development

Wide range of pre-formulation and dosage form development services, including analytical development and stability studies.

**Operations:**
- Blending
- Mixing
- Granulation
- Compression
- Coating
- Encapsulation
- Bottling

#### Small scale

**Site:** Zofingen

**Scale:** Up to 3 kg

**Products:** granules, tablets, film-coated tablets, capsules

**Equipment:** Isolator, V-processor, sieve, tablet press, coater, capsule machine

**Service:** Initial formulation process development & cGMP clinical trial quantities

#### Siegfried substance classifications & handling

<table>
<thead>
<tr>
<th>OEL*</th>
<th>Exposure category</th>
<th>Hazard risk potential</th>
<th>Available at Siegfried</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1.0 μg/m³</td>
<td>4</td>
<td>Very High</td>
<td>No</td>
</tr>
<tr>
<td>10 – 1.0 μg/m³</td>
<td>3</td>
<td>High</td>
<td>Yes</td>
</tr>
<tr>
<td>50 – 10 μg/m³</td>
<td>2B</td>
<td>Substantial</td>
<td>Yes</td>
</tr>
<tr>
<td>500 – 50 μg/m³</td>
<td>2A</td>
<td>Enhanced</td>
<td>Yes</td>
</tr>
<tr>
<td>&gt; 500 μg/m³</td>
<td>1</td>
<td>Small</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Occupational Exposure Limit

**Note:** Cytotoxic and alkylating agents excluded

#### Production

**Site:** Malta

**Scale:** Up to 120 kg

**Products:** granules, tablets, film-coated tablets, blister

**Equipment:** Isolator, V-processor (one pot granulator), sieve (rotating), tablet press, coater, blister machine

**Service:** Scale-up and commercial manufacturing

### Other capabilities

#### Milling facilities

Hammer mill Micronisation (planned)