Highly Potent APIs
The right platform, people and procedures for successful development and manufacturing
Highly potent active pharmaceutical ingredients (HPAPIs) represent a significant change in the way pharmaceutical innovators are using small molecules to deliver new patient therapies. This shift toward highly potent APIs has not only led to a pipeline of more effective medicines that require lower doses and lead to fewer side effects, but also to new manufacturing challenges.

With 15 years of experience and over 10 products taken from early development to late development or commercialization, Lonza understands the challenges that come with producing such high potency APIs, and we look forward to tackling them with you. Together – your in-depth product knowledge and our development and manufacturing experience, technical know-how, reliable procedures, and cutting-edge facilities – we can safely take your highly potent compound to the next level.

For more information, or to tour our facilities, please feel free to contact one of our experts at highlypotents@lonza.com
Overview

- Chemical, microreactor, peptide, fermentation and antibody drug conjugate capabilities
- 15-year, multi-product track record
- Dedicated safety, health and environmental (SHE) experts to assess compound potency, evaluate production and monitor procedures
- State-of-the-art Equipment: R&D and QC laboratories, production facilities, equipment, engineering control
- Trusted Procedures: Maintenance, experience and training, specifically designed for handling of HPAPIs
- Waste management in place
- SafeBridge® certified: Visp, Switzerland, ADC facilities, laboratory and quality control

Customer Benefits

Cost Reduction: A wide range of production scales, from lab scale to 10 m³, means we can take your product from early development to launch to in-market supply without additional technology transfer costs.

Time Savings: A valuable track record with scores of highly potent APIs and over 10 products scaled up, experience with a wide variety of compounds, and the right process, plants and highly trained people can minimize errors, reduce rework and improve time to market.

Peace of Mind: Our cutting-edge facilities, extensive product experience, and expert evaluation and training procedures help you rest assured that your highly potent API is in safe hands.
The Right Capabilities

The successful and safe manufacture of high potency APIs requires a highly skilled team, the proper evaluation and training procedures, state-of-the-art facilities, and the right experience. Collectively, these attributes offer our customers a unique platform for safe and effective high potency API production.

A Unique Platform

<table>
<thead>
<tr>
<th>Technology</th>
<th>Infrastructure</th>
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<tbody>
<tr>
<td>Complex chemistry tool box</td>
<td>Hazardous waste handling and disposal with on-site incineration</td>
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<tr>
<td>Biotechnology</td>
<td>Existing infrastructure</td>
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<tr>
<td>Backwards integration of Biopharmaceutical and Small Molecule product groups</td>
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<tr>
<th>Plant Set-up</th>
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<tr>
<td>Multi-purpose / product</td>
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<tr>
<td>Clean-in-place set-up / decontamination</td>
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<tr>
<td>Containment / Environment</td>
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<tr>
<th>Resources</th>
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<tr>
<td>Handling of toxic substances</td>
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<tr>
<td>cGMP experience</td>
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<tr>
<td>In-house design capabilities</td>
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<tr>
<td>Highly skilled personnel</td>
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### Manufacturing Capabilities

**Chemical Synthesis**  
[Visp, Switzerland]  
- All standard chemical reactions  
- Lab to 10 m³ scale  
- Target OEL 0.1 – 1 µg/m³

**MicroReactor Technology**  
[Visp, Switzerland]

**Microbial Fermentation**  
[Kouřim, Czech Republic and Visp, Switzerland]  
- up to 15 m³

**Peptides**  
[Braine, Belgium and Visp, Switzerland]

**Antibody Drug Conjugates**  
[Visp, Switzerland]  
- OEL down to 40 ng/m³ of air  
- Lab to 600 L scale

**Other Specifics**  
- Dedicated and Specialized labs in R&D and Analytical  
- Clean room facility  
- Air classified clean rooms

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### Experience You Can Trust

Lonza has over 110 years of chemistry know-how and an API development and production track record few contract manufacturers can match. Our experience in producing highly potent APIs goes back over 15 years. Over the past decade we’ve invested $150 million to build cutting-edge facilities for highly potent API success. Today, we are able to offer a wide range of advance capabilities, from process development to large-scale manufacturing, with the potential for expansion and improvements to meet customer demand.

At the heart of our high potency capabilities is our Visp, Switzerland, site. Here a dedicated high potency team is able to leverage all of Lonza’s resources for highly potent API manufacturing success.
Extensive Track Record

– Historical expertise in handling hazardous compounds
– Over 15 years of experience of HPAPI manufacturing at various production scales (laboratory to 10 m³ scale)
– First peptide project in 2008 with Class 5 OEL
– Antibody drug conjugates unit with lab to plant scale experience since 2004 (OEL down to 40 ng/m³ of air)
– Currently, active projects with OEL ranging from 5 to 0.04 mg/m³
  – oncology
  – immuno-suppression
  – veterinary

Production Facilities

– Several multi-purpose trains
  – 250L, 630L, 2 500L, 10 m³
  – target OEL 0.1 – 1 µg/m³
– Scale up from lab to > 500 kg per batch
– Hydrogenation capabilities
– Highly motivated and well trained operators – permanent training
– Concept
  – Isolators
  – Big bags handling
  – Dedicated clean room
  – Cleaning in Place
  – Cleaning based on MAC concept
  – Validated cleaning procedures
  – Effective cross-contamination prevention
– Potential Expansion Reserve (lead time 12 – 18 months)

R&D Laboratories

– 4 separate labs for chemical synthesis
– 4 separate labs for peptides and antibody drug conjugates
– Lab-scale production up to 10L
– Class 4 and 5 (down to OEL 30 ng/m³)
– SafeBridge® certification
– Operating under cGMP
– Concept
  – Glove box
  – Dedicated HVAC system
  – a1-safetech hoods
  – Laminar flow type work benches equipped with HEPA filters enabling efficient lab work
– Preparatory HPLC/chromatography
– Lyophilization
– Experienced chemists with track record in scale-up and tech transfer from lab to 10 m³ scale
– Dedicated, specialized training program
QC Laboratories

- 2 dedicated and fully equipped laboratories
- Class 4 and 5 analysis, solid handling
- OEL minimal 40 ng/m³
- Methods available
  - HPLC/GC
  - CE/IEF
  - ELISA
  - Cell-Based Assays
  - UV
  - TDC
  - Endotoxin
  - Bioburden
  - Osmolality
  - Moisture by KF
  - Turbidity
  - Particle Testing
  - Ion Mobility Spectroscopy / LC/MS/MS
  - Solid state: PSD, TGA, NIR (up to Class 4)
- SafeBridge® Certified

Quality Assurance

- Fully cGMP-certified sites
- Regular inspections from authorities (FDA, Swissmedic, etc.)
- Frequent customer audits

Safety Health Environment (SHE) Compliance

- SHE assessment made by experts in occupational hygiene and toxicology and pharmacology
- Extensive infrastructure for Waste Management on site
- SafeBridge® certification (2008)

Lonza classification system compared to SafeBridge®

<table>
<thead>
<tr>
<th>Lonza Class 1–6</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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<tbody>
<tr>
<td>OEL (mg, µg/m³)</td>
<td>10 mg</td>
<td>1 mg</td>
<td>100 µg</td>
<td>10 µg</td>
<td>1 ng</td>
<td>1 ng</td>
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<tr>
<td>Manufacturing</td>
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<td>Standard trains</td>
<td>HPAPI trains</td>
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<td>R&amp;D and QC labs</td>
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<td>Standard Hoods/Labs</td>
<td>Specialty Hoods/Labs</td>
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<tr>
<td>Specialty Hoods/Labs</td>
<td>Isolators</td>
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SafeBridge® Categories 1–4

* antibody drug conjugate
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