



We specialise in the Development, Launch and Manufacture of complex and difficult APIs, including your requirements for High Containment and Particle Characterisation



GSK Cork, Ireland: your development and manufacturing partner of choice

GSK Cork, Ireland: A History of World-Class Operational Excellence in API Development & Manufacturing

GlaxoSmithKline Cork has been the sole producer of GSK's major active pharmaceutical ingredients at its Cork site for over 35 years. With a total capital investment of €600m since it began operations, the facility has been a new product introduction site for the past 10 years. Our team of highly skilled people supports €4 billion of GSK sales annually.

GSK has made a strategic decision to provide development, launch & supply services to the pharmaceutical industry. Due to our long history of improvements in development, launch & supply we have created significant capability & capacity which is now being made available.

GSK Cork's business partnering proposition for R&D, scale-up and manufacturing is unique. Our internal linkages with our on-site R&D Pilot Plant and sister Drug Product sites provide the wider context for all your needs, while our on-site facilities, our successful new product introduction record and ten years of Phase 2/3 clinical manufacture and scale-up are at your disposal.

We are looking to establish long-term partnerships with development and manufacturing organisations that require the best-in-class practice in the industry.



Best-in-class
compliance performance

Able to predict how
your API performs
in secondary
formulation

Access to one of the
best physical property
characterisation
laboratories in
the industry

A unique network of
industry/government/
academic professionals
coupled with access to
resources located within
the world's largest
pharmaceutical cluster

**MANUFACTURING
YOUR PRODUCTS
LIKE OUR OWN**

A scale for
development &
manufacturing of
compounds from < 1kg to
400 kg coupled with
seamless two-way
knowledge transfer

High scientific and
engineering capability
that will drive down
your cost of goods

To build smarter, simpler
and sustainable
processes and ways
of working

Reduce process
variation, eliminate
waste and improve
process efficiencies

A total
commitment to
minimising your
impact on the
environment



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Do you need...

- Proven experience in enhancing and accelerating new product development and launch activities
- Seamless two-way knowledge transfer
- Delivery of optimum process design and environmental efficiencies
- High process capability
- Continuous development and optimisation of the process



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ON-SITE R&D AND NEW PRODUCT DEVELOPMENT CAPABILITIES

Activities

- The development and supply of Phase 1, 2 and 3 clinical trial intermediates and APIs for new compounds
- The manufacture of validation, launch and commercial material
- 35 multi-stage products transferred and validated since 2000, including 3 products (7 stages) in 2010

Equipment

- A fully flexible Chemical Development Pilot Plant facility with 2 production modules
- Each module comprising of 6 reactors (up to 2500 litres), with multiple connectivity
- Extensive application of Process Analytical Technologies and data logging systems
- A fully dedicated Development Laboratory with extensive analytical capability, including NMR and full physical property testing services
- A pilot / commercial scale Pharmaceutical Development Wet Bead Milling facility which includes spray drying capabilities for volumes up to 20MT - licensed by the Irish Medicines Board for clinical supply of Drug Product Intermediates



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Do you need...

- To be able to predict how your API performs in secondary formulation
- To ensure your API and secondary processes are dovetailed and provide consistent right first time performance
- To know you have developed the optimum process and maximised product efficiency



INNOVATION AND A HISTORY OF FLEXIBILITY

- Unique use of statistical tools to link API processing and physical properties data to predict the performance of the product in secondary manufacturing
- Ability to rapidly identify and introduce new technologies such as PAT, wet bead milling, containment technology
- Excellent use of real time and off-line data to provide rapid troubleshooting capability and the ability to identify opportunities to deliver improved yield, quality and cycle time
- Strong track record of significant cost of goods reduction through chemistry, engineering and operational improvements
- 6 APIs (19 stages) positively impacted in recent years (>25% COGs reduction)



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Do you need...

- A scale for development and manufacturing of compounds from < 1kg to 400kg
- High containment facilities
- GMP Pilot Plant
- Coupled with process analytical technology
- A business partner that manufactures your product like its own



EXTENSIVE STATE OF THE ART PLANT & TECHNOLOGIES

Equipment

8 production buildings
 19 production modules
 269,297 litres capacity
 61 reactors (30 - 16,000 litres)

42 glass lined vessels, 16 Hastelloy vessels & 3 stainless vessels
 2 hydrogenation vessels

Large range of isolation and drying equipment -
 23 isolation devices (filter dryers & centrifuges)
 1 offline dryer

High Containment

High containment facilities for highly potent compounds (including cytotoxic). Pioneers in glovebox technology. Experienced at manufacturing APIs with exposure limits <30 nanograms/m³.

Milling / Size Reduction

Central milling facility including wet bead milling and spray drying.

Supporting Technology

- Fully automated sequence control with Delta V batch software control, including the eBR system to generate electronic batch reports
- Infoplus 21 data logging system and application of statistical packages for trending and correlation analysis
- Modern, recently upgraded laboratory information system

The production plant is designed for quick changeover between products by allowing each vessel in the processing train to be cleaned independently.

Supporting Technology

- Reaction monitoring (solution spectroscopies IR, NIR, UV)
- Crystallisation monitoring (in slurry: Lasentech, turbidity)
- Distillation monitoring (solution spectroscopies in the vessel, mass spec and NIR for distillate lines)
- Isolation and drying monitoring (mass spec and NIR for vent gas)



Do you need...

- Access to one of the best physical property characterisation laboratories in the industry
- Product characterisation
- Product release
- Process understanding
- A predictable crystallisation profile
- Your regulatory submission prepared and reviewed



LABORATORIES

Physical Property Laboratory

Dedicated, modern laboratory with all of the instruments necessary for assessing suitability of API for drug product formulation staffed with physical property scientists and supported by a full time statistician.

Equipment

- PSA - Particle size analysis
- SEM - Scanning electron microscopy
- XRPD - X-ray powder diffraction
- DSC - Differential scanning calorimetry (TA Instruments Q1000)
- TGA - Thermogravimetric analysis
- GVS - Gravimetric vapour sorption
- OM - Optical microscopy
- SSA - Specific surface area
- TBD - Tap bulk density
- AJS - Air jet sieve
- Sonic Sifter - Classification/sizing
- Viscometry

Development Laboratory

- Providing process and analytical technical support for technical development group priorities
- Ensuring that annual validation programs are complete
- Providing analytical technical support/troubleshooting for established and new products
- Giving analytical support for regulatory questions, such as demonstrating equivalency with pharmacopoeial methods
- Supporting the analytical activities for new products, i.e. participate in analytical technical transfers with R&D

Quality Control Laboratory

The quality control laboratory is responsible for testing and approving raw materials, Intermediate stages and active pharmaceutical ingredients (APIs).



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Do you need...

- A partner with best-in-class compliance performance - 12 successful FDA inspections since 1978 (11 with zero findings on form 483)
- One of the best Quality Management Systems in the industry



COMPLIANCE RECORD

- 12 successful FDA inspections since 1978 (11 with zero findings on form 483)
- Irish Medicines Board (IMB) GMP certificate at Cork site since 1976
- IMP Licence since 2004
- Site GMP certificate (renewed in January 2009)
- Investigational Medicinal Products Licence for wet bead milling and spray drying (renewed January 2009)

Recent External Inspections and Agencies

US FDA September 2009	No findings
IMB GMP certificate January 2009	No major findings
IMB (IMP Licence) January 2009	No findings
Japan PMDA May 2008	No findings
Mexican COFEPRIS November 2007	No findings
Korean FDA April 2005	No findings

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Do you need...

- To partner with one of the top global pharmaceutical companies with direct access to the company's scientific expertise in our chemical and pharmaceutical development groups
- Use of the company's global distribution and supply chain management processes in developed as well as emerging markets



COMPREHENSIVE CORPORATE RESOURCES

- Links to sister drug product facilities
 - Biopharmaceuticals
 - API
 - Steriles
 - Solid Dose
 - Cephalosporins and Penicillins
 - Liquids
- 102,000 employees in 119 countries
- Total sales of over €34.6 billion
- Global market share of 6.1%
- Products sold in over 160 countries
- 77 production sites in 37 countries
- 4 billion packs sold annually
- 14.9% of total annual sales invested in research
- 5 Nobel Prizes
- 15,000 researchers operating in approximately 20 research centres in 9 countries worldwide



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Do you need...

- To be in the best business location for the healthcare industry, proactively supported by government and state agencies e.g. IDA Ireland (Industrial Development Agency)
- A gateway to Europe



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DOING BUSINESS IN IRELAND

Ireland has developed a highly attractive tax system designed to support continued economic development whilst providing investors with significant advantages. 13 of the world's top 15 pharmaceutical companies have substantial operations in Ireland.

- Ireland's corporation tax rate of 12.5% is amongst the lowest in the world and compares very favourably with other countries
- Ireland also has a favourable holding company regime and is an attractive location to establish corporate support / hub activities
- A 25% tax credit can be claimed for R&D expenditure. Ireland also has a network of double taxation treaties
- Government support is available for capital projects, employment grants and research and development activities
- Ireland is the only English speaking member of both the EU and Euro Zone
- GSK Cork is located 15 minutes from Cork International Airport

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Do you need...

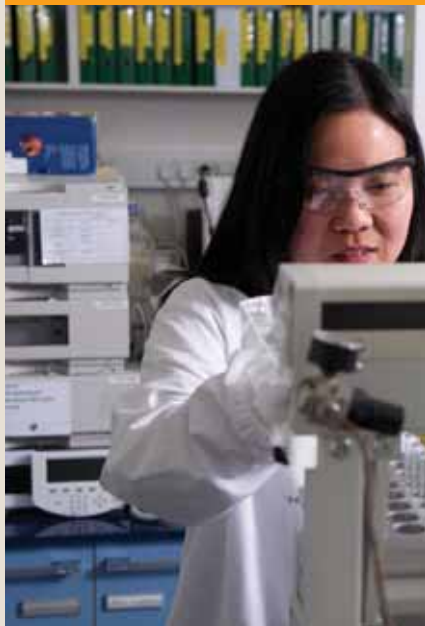
- Access to resources located within the world's largest pharmaceutical cluster
- Links to some of the best pharma aligned universities in the world
- A unique network of industry / government / academic professionals

HIGHLY EXPERIENCED PROFESSIONALS

GSK Cork's employees come from an excellent educational system with the following qualifications:

• PhD	14%
• 3rd Level Qualifications	52%
• Process Operators	25%
• Craft persons	9%

Access to ~ 3000 scientific professionals from within GSK.





Do you need...

- A total commitment to minimising your impact on the environment
- Solvent recovery capability to reduce your COGs



ENVIRONMENTAL OPERATIONS

Equipment Incineration

- There are two high temperature waste incinerators on site
- Each unit is designed to burn liquids and vapours from chemical processes
- Each unit operates at 1100°C and destroys the waste to > 99.99% removal
- Continuous measurement & recording of all stack emissions

Waste Water Treatment / Chemical Treatment

- The waste water treatment plant is used for treatment of sewage as well as certain liquid wastes from processes
- Bacteria in the plant sludge remove ~ 95% of chemical / toxic compounds from the input streams
- Capacity to treat a volume of 360m³/day / 4,000kg of COD
- Treated wastes are pumped to the harbour twice a day
- Chemical treatment of some wastes

Solvent Recovery

- Two large solvent recovery plants - 1 Multi Purpose Unit & 1 Batch Recovery Unit
- Solvents (e.g. Toluene, IPA, Methanol, Ethyl Acetate, Acetone, Heptane, Methylene Dichloride) contaminated with chemicals are generated from plant operations and distilled in the plants
- The clean distillates are reused in the processes
- Capacity of the Multi Purpose Solvent Recovery unit is 25,000MT of foul material a year

Storage of Chemicals

- Liquid and solid raw materials and wastes are stored on site
- The liquids are stored in large steel tanks contained in a bund
- All solids are stored in a special drum park, designed to control spillages



CORK PERFORMANCE MANAGEMENT



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Do you need...

- Operational Excellence (OE) at the heart of everything you do
- To build smarter, simpler and sustainable processes and ways of working
- To reduce variation, eliminate waste and improve process efficiencies



THE WAY WE WORK

OE certified personnel across all areas of the GSK Cork's business:

- 152 Yellow Belts
- 78 Green Belts
- 5 Black Belts
- 2 Master Black Belts

Performance Management

- 5S - organised workplace is a critical necessity to progress Visual Controls. It also helps to develop the disciplined work habits that are required
- Visual Controls - to contrast actual versus target performance at a glance
- Tiered accountability process - the systematic management processes. Performance reviews replace meetings and they happen on the shop floor at the Visual Control Boards
- Standard Work - the identified and agreed 'single best way' to perform activities and organise teams
- Problem Solving Root Cause Analysis - remove the problems not manage the symptoms
- GEMBA - go see, coach, mentor critical part of the tiered accountability
- Leaders Standard Work- explicit expectations for each management level

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