ThermoFisher SCIENTIFIC

Summary of capabilities

Linz, Austria

Facility Facts:

Regulatory Approval:	US FDA, EMA, PMDA, Austrian Federal Office for Safety in Health Care (BASG)
Potency Capability:	Up to Cat HPC 3a
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Unique Offering:

- Process development and chemical production of intermediates and APIs for clinical and commercial supply under cGMP and ISO conditions, combined with the ability to solve complex challenges for our customers.
- Experience with a wide range of chemical reactions on a kg to ton scale
- Safe handling of highly reactive (intermediate) products
- Experience in development and scale-up of continuous manufacturing processes

Offerings:

- Small molecule and polymer API production for clinical and commercial materials (cGMP, Halal, Kosher)
- Production scales ranging from 100 kg to hundreds of metric tons
- Optimization and upscaling of chemical processes, QbD approach (Quality by Design)
- Process development from early clinical phase up to commercial production
- Analytical method development and phase appropriate method validations
- Proven Acceptable Range (PAR), Process safety studies, Stability studies and Solid state investigations
- Control Strategy/Fate of impurities
- Micro reactors/flow chemistry for developmental quantities and commercial productions
- Process transfers / Tech transfers
- Raw material sourcing and outsourcing, external manufacturing
- Registration, validation, product launch
- Support customer in filing strategy and filing activities (CMC, DMF) — FDA, EMA, PMDA, etc.
- Regulatory support (Audits of any regulatory authorities, registration/validation, ICH stability studies, etc.)
- Project management

Technical Capabilities: > 95% of all Commercially-used Chemical Transformations

Esterification / Saponification / Amide-formation (various methods)	Cycloaddition
Li / Hal-ex (n-/sec-BuLi); ultralow cryo conditions	Cyclopropanation reaction
Grignard and other metalorganic reactions	Friedel-Crafts reaction
Hydrogenation (Pd, Pt) up to 90 bar (1,305 psi) @ 350 L and 50 bar (725 psi) up to 12,500 L scale	Mitsunobu reaction
Carbonylation (Pd)	Knoevenagel condensation, Swern oxidation, POCl3
Reduction (boranes, silanes, hydrides), reductive amination	Metal catalyzed Cross Coupling Reactions (e.g. Suzuki, Ullmann, …)
Radical reaction (e.g. radical bromination)	Biocatalysis, chemical and enzymatic racemic resolution
Hetero- and Homogeneous Catalysis; asymmetric hydrogenation	Polymerisation reaction
(De-)protection of diverse functionalities	Flow Chemistry
Nitration, Diazo chemistry, Hazardous compound handling	

Linz Key Equipment List by Lifecycle:

Item			Size / Details	Early Development			Late Dev		Commercial Supply		
				Process Development	Analytical Development	Phase I	Phase II	Phase III	Commercial Scale Up	Tech Transfer	Regulatory
R&D Labs – Building 70	Process Development/ Safety Studies	Organic synthesis R&D labs and AD	33 labs/170 ventilation hoods for organic synthesis and analytical development	•	•	•	•	•			
		Kilo lab	Up to 30 L glass reactors (-10°C – 160 °C), distillation column (20 plates), thin layer evaporator, filter dryer	•							
		Micro reactor / Flowreactor lab	Various flow reactors of different designs and construction materials (glass, metal, ceramics)	•							
		Process safety lab	RC1, DSC, Sedex, Friction sensitivity, Thermogravimetric analysis, adiabatic storage test, Flash point, Ignition temperature, dust explosion	•							
		Autoclave lab	50 mL to 2 L and up to 100 bar; stainless steel, Hastelloy	•							
	Quality Control (Also in Building 8)	Analytical equipment	HPLC (UV, VWD, DAD, RI, CAD, MS), UPLC, GC-MS, NMR (400 MHz), ion chromatography, FTIR (ATR, KBr, film, gas), ICP, DSC, TGA, microscopy, optical rotation, turbidity meter, refractive index, LOD, ROI, conductivity, titration (acid/base, chloride, KF), color analysis, particle size, GPC (RI, UV, light scattering), polarimetry, elemental analysis	•	•	•	•	•	•	•	•
	Crystallization Process Development	Optimax reactor	Focussed Beam Reflectance Measurement (FBRM) and Particle Vision and Measurement (PVM) probes	•							
		Crystal 16	Turbidimetric solubility and metastable zone width (MSZW) measurements	•							
		Digital optical microscope	Classification (particle size analysis). Bulk and tapped density measurement	•							
Pilot Plant – Building 30	Reactors	Glass-lined	1,000 L – 2,300 L, -80°C to 220°C			•	•	•	•	•	•
		Hastelloy	1,300 L, -80°C to 220°C			•	•	•	•	•	•
		Stainless Steel	1,000 L – 4,000 L, -80°C to 220°C			•	•	•	•	•	•
		Micro reactors for hazardous chemistry	BuLi reactions			•	•	•	•	•	•
			Carbene-type chemistry			•	•	•	•	•	•
			Nitrations			•	•	•	•	•	•
			Azide chemistry			•	•	•	•	•	•
			Ultralow temperature (-80°C)			•	•	•	•	•	•
		Hydrogenation	Stainless Steel Buss Loop reactor up to 90 bar (350 L)			•	•	•	•	•	•
			Glass-lined reactor up to 6 bar (600 L)			•	•	•	•	•	•
	Isolation/ Drying	Centrifuges	Stainless Steel and Hastelloy			•	•	•	•	•	•
		Filter dryers	Stainless Steel and Hastelloy			•	•	•	•	•	•
		Cone dryers	Stainless Steel (2,200L), Hastelloy (1,000 L)			•	•	•	•	•	•
		Flaker	Stainless Steel			•	•	•	•	•	•
		Sieving	Ultrasonic sieve			•	•	•	•	•	•
		Distillation	Columns, thin-film evaporators, short path distillation unit			•	•	•	•	•	•
		GMP isolation areas	Solid handling and packaging in cabins			•	•	•	•	•	•
Commercial Production – Building 52	R's	Glass-lined reactors	3,100 L – 8,200 L, -20°C to 160°C					•	•	•	•
		Stainless Steel reactors	2,000 L – 8,400 L, -20°C to 160°C					•	•	•	•
	Isolation / Drying	Centrifuge	Hastelloy					•	•	•	•
		Filter dryers	Stainless Steel and Hastelloy					•	•	•	•
		Belt filter	Stainless Steel					•	•	•	•
		Mixer Dryers	Stainless Steel (4,000 L)					•	•	•	•
		Fluidized Bed dryer	Stainless Steel					•	•	•	•
		Cone dryer	Hastelloy (4,000 L)					•	•	•	•
		Milling	Hammer mill, ball mill					•	•	•	•
		Sieving	Ultrasonic sieve			•	•	•	•	•	•
		Extraction	Continuous centrifugal extractors					•	•	•	•
		Distillation	Columns, thin-film evaporators					•	•	•	•
		GMP isolation areas	Solid handling and packaging in cabins					•	•	•	•
Commercial Production – Building 700	Reactors	Glass-lined	10,000 L – 16,000 L, -20°C to 160°C					•	•	•	•
		Stainless Steel	10,000 L – 16,000 L, -20°C to 160°C					•	•	•	•
		Micro reactors for hazardous chemistry	BuLi, Carbene-type chemistry, nitrations, azides, ultralow temperature reactions					•	•	•	•
		Hydrogenation	Stainless Steel Biazzi reactor up to 50 bar (12,500 L)					•	•	•	•
			Glass-lined reactor up to 12 bar (6,300 L)					•	•	•	•
	Isolation/ Drying	Centrifuge	Stainless Steel					•	•	•	•
		Filter dryers	Hastelloy					•	•	•	•
		Belt filters	Stainless Steel					•	•	•	•
		Cone dryers	Stainless Steel (2,500 – 6,000 L), Hastelloy (8,000 L)					•	•	•	•
		Extraction	Continuous centrifugal extractors, continuous extraction columns (pulsed sieve-plate, Glass-lined)					•	•	•	•
		Sieving	Ultrasonic sieve			•	•	•	•	•	•
		Distillation	Columns, thin-film evaporators					•	•	•	•
		GMP isolation areas	Solid handling and packaging in cabins					•	•	•	•
		Decanter	Stainless steel 12m³/h					•	•	•	•
		Fluidized bed dryer	Stainless steel					•	•	•	•

* For detailed equipment information please contact your Thermo Fisher Scientific representative.

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