Zach
Zambon Chemicals

ZACH CUSTOM SYNTHESIS:
SOPHISTICATED PRODUCTION
OF APIs AND ADVANCED INTERMEDIATES
FOR THE PHARMACEUTICAL INDUSTRY

CUSTOM SYNTHESIS
Services & Capabilities

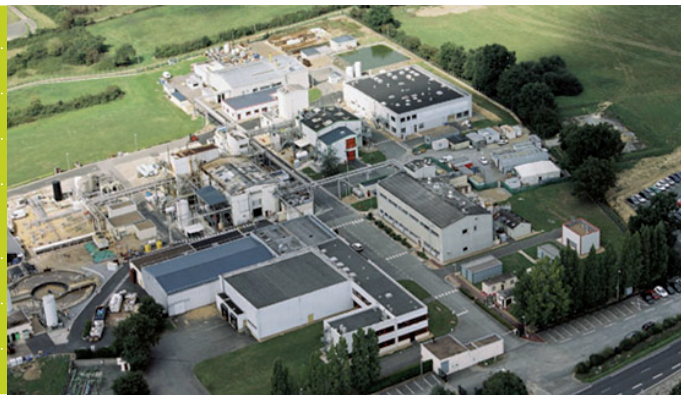
FACT SHEET

Zach Avrillé site has a long tradition in process development & API / pharmaceutical intermediates manufacturing.

> 170 people (18 in R&D)
> Strong track record with the Authorities (FDA, Local Authorities, PMDA, K-FDA)
> 215MT of API and GMP intermediates manufactured per year
> 70% of activity is in Custom Manufacturing
> 5-10 new projects/products developed per year
> Handling of HPAPI having an OEL> 1 µg/m^3 (OEB 4) at industrial scale
> Regular investments (new HPAPI laboratory, new Hastelloy filter dryer, Pin Mill)
> About 6000 samples analyzed per year in the QC lab
> Project management Team Organization
> Full Regulatory Support (DMF, IMPD)

CAPACITY / REACTORS

	AVRILLÉ/FRANCE
TOTAL REACTOR CAPACITY	100 m^3
PRODUCTION OUTPUT	215 MT/year
REACTION TRAINS	31
REACTORS: STAINLESS STEEL, GLASSLINED & HASTELLOY	34
REACTOR RANGE: KILOLAB	15 – 30 L
REACTOR RANGE: PILOT	50 – 1000 L
REACTOR RANGE: INDUSTRIAL	1000 – 10000 L



CORE CHEMISTRIES AND TECHNOLOGIES

CHEMISTRIES

> Asymmetric synthesis
> Lithiation (RLi, LDA, Schlosser's base, Li in liquid NH_3)
> Grignard (Mg/ether, AlkMgCl/ether) and low temperature Grignard (VinylMgCl/-80°C) chemistry
> Pd-catalyzed coupling (Heck, Suzuki, Sonogashira)
> Metal hydride reduction (powder and in solution LAH, DIBAL, $LiAl(O-tBu)_3H$, $NaBH_4$, etc...)
> Catalytic hydrogenation (Pd/C, Pt/C, PtO_2, Ir/C) up to 12 bar
> Asymmetric cat. hydrogen. (RhL*/RuL*; L*=chiral ligand)
> BH_3/THF reduction
> Carbonyl asymmetric reduction ((R)-DPP/BH_3)
> (Asymmetric) reductive amination
> TIBAL cleavage of ArO-Alk; TES cleavage of C-OH
> N,O-Methylation and demethylation
> Alkylation using DMS and DES
> Eschweiler-Clarke methylation
> Cyanation (alkali metal cyanides and substitutes)
> Amino acids protection and derivatization
> Ozonolysis + reductive/oxidative quench (in batch and continuous flow)
> Chiral epoxides chemistry (synthesis and processing)
> Periodate/permanganate oxidation
> High T/P amination/aminolysis with aq./gas. NH_3

TECHNOLOGIES AVAILABLE

> Cryogenic chemistry (-80°/-90°C)
> Autoclaves (max. 12 bar)
> Crystallization/Solid state engineering: large scale reactive crystallization, Spherical Agglomeration, handling of meta-stable polymorphs
> Particle downsizing: grinding, milling, micronization
> Spray-drying (PSD 1 and PSD 2)
> Bulk freeze-drying (50 m^2)
> Ultra-Filtration (cut off ≥ 1000 Da)
> Nano-Filtration (cut off ≥ 300 Da)
> Electrodialysis
> Wiped Film Evaporation down to 1mbar (pilot/indus. scale)
> PAT: RAMAN and FBRM ATEX probes

THE COMBINATION OF OUR PROFOUND CHEMICAL KNOW-HOW AND THE WIDE RANGE OF CAPACITIES MAKES US A STRONG PROVIDER FOR YOUR PRODUCTS

ANALYTICAL CAPABILITIES AND QUALITY CONTROL

In-house development of new analytical methods
Validation and transfer of analytical methods

CHEMICAL AND INSTRUMENTAL ANALYSIS

> HPLC, UPLC, GC, Headspace-GC
> IR, UV, NIR, Raman
> GC-HRMS, GC-MS
> HPLC-MS, HPLC-TOF-MS
> NMR (400 MHz)
> Ion chromatography
> DSC

PHYSICAL & POLYMORPHS ANALYSIS

> Wet and dry PSD analysis (laser)
> BET surface area analysis
> Polarimetry, Refractive index measurement
> Densimetry Powder colorimetry
> Turbidimetry

R&D

> Development of highly complex synthetic methodologies (up to 12-15 steps)
> Tech transfer and process optimization for large scale GMP manufacture (kg to MTs): NOR/PAR determination, critical parameters, QbD using DoE approach
> Process safety assessment (DSC, low/mid-high temp RC, ARC; TGA) - Risk analysis
> Analytical development (UV/CAD/RID-HPLC, GC, HS-GC), structural characterization (GC-MS, HPLC-MS, NMR, IR)
> Solid state/powder characterization (microscopy, XRPD, SEM, DSC, IR, RAMAN, PSD, flowability properties)
> Supply chain securing through new RM suppliers qualification
> Process troubleshooting through downscaling
> Solid state engineering (traditional or scale down approach using customized glassware reactors mimicking industrial equipments; lab-scale filter-dryer; lab-scale mill; lab-scale spray-dryer; FTIR/RAMAN/FBRM PAT; DoE approach)
> Continuous flow and microtechnologies (limited to Ozonolysis)
> Handling of High Potent APIs (OEB5, OEL>0.1mg/m^3)
> PAT: In-situ FTIR, Raman (ATEX), FBRM (ATEX), turbidimetry

API FINISHING CAPABILITIES

Our finishing equipments are located in clean rooms (ISO8) fed with purified / low pyrogen water.

ISOLATION & DRYING
> Filter Dryer
> Press filter
> Centrifuge
> Tumble dryers
> Pan dryers
> Tray dryer
> Freeze dryer
> Spray dryer (PSD1 & PSD2)

PARTICLE SIZE REDUCTION
> Pin mill under nitrogen
> Hammer mill under nitrogen
> Jet mill (200 & 300)

CLASS OF PRODUCTS:

> Classical APIs made in multipurpose equipments
> High potent APIs having an OEL> 1 µg/m^3 (OEB 4) including corticosteroids at industrial scale
> High Purity Low Endotoxins EXCIPIENTS

SERVICES

> Supply Chain Management
> Warehousing
> Logistics
> Reach Registrations
> Regulatory Filings (DMF, CTD, Ceps) Worldwide
> Intellectual Property Assessments
> Legal Support

REGULATORY & GLOBAL COMPLIANCE

	AVRILLÉ/FRANCE
FDA INSPECTIONS	From 1984
LAST FDA INSPECTION	October 2014 NO FORM 483
OTHER INSPECTIONS	ANSM - PMDA - KOREAN FDA
COMPLIANCE CERTIFICATES	ISO 14001

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