

PILOT PLANT – UNIVERSITY OF ALICANTE

Summary

The Institute of Organic Synthesis of the University of Alicante has a wide-reaching expertise in organic chemistry, which allows to develop and scale up chemical processes from laboratory to industrial scale in a pilot plant working under ISO9001:2015, ISO14001:2015 and cGMP (current good manufacturing practice) with full traceability. Services offered include: process R&D, process scale-up, custom manufacturing of pharmaceutical active ingredients, intermediates and drug products under cGMP, as well as other chemical products (excipients, catalysts, impurities for method validation, etc.). These tasks can be carried out either at laboratory scale and in the general-purpose pilot plant, which is fully equipped allowing processes to be scaled up at pre-industrial and industrial level (batches ranging from milligrams to multi-kilogram).



Institute of Organic Synthesis - Pilot plant profile

The Pilot Plant has been designed to provide a complete service to pharmaceutical industry. It follows procedures that meet or better the requirements of ISO9001:2015. The Pilot Plant facilities and supporting warehouse, analytical and QC services ensure that potential clients receive products or processes with the necessary confidential and validated documentation, which are immediately transferable to their own production procedures and manufacturing facilities.

The day-to-day organisation and running of the Pilot Plant is controlled by qualified personnel (2 Chemistry PhDs) with a combined industrial R&D and production experience of more than forty years. This invaluable industrial experience allows the Institute of Organic Synthesis personnel to deal with potential clients on their “own terms” and allows for an adequate relationship between the client, his or her requirements, the possibilities of success with the resources available, the usual considerations of product/process economy and environmental impact, establishing reasonable specifications, product price and delivery time.

Technical description of services available

The resources of the Pilot Plant are divided into various physically separated but interrelated areas each of which has the necessary infrastructure to provide a complete service to potential clients.



(a) Production Equipment

The Pilot plant has the following general-purpose equipment:

(i) 250 L and 100 L glass-lined jacketed reactors, each of them equipped with: 50 L addition vessel, two distillate receivers of 25 L, glass header for reflux, distillation and Dean-Stark trap, bottom valve and baffle temperature probes. They have complete services of steam, compressed air, nitrogen, cooling water and glycol-water.

(ii) 250 L, 150 L and 100 L stainless steel reactors, each of them equipped with: 25-50 L addition vessels and stainless steel headers. The 150 L reactor has stainless steel condenser and the 250 L and 100 L reactors have glass-lined steel condensers. Reactors have complete services of steam, compressed air, nitrogen, cooling water and glycol-water, temperature probes incorporated in the reactor bodies and 50 L distillate receivers.

(iii) 25 L glass-lined jacketed reactor with borosilicate glass head. It also has 10 L addition vessel and 10 L distillate receiver, and complete services of steam, compressed air, nitrogen, cooling water and glycol-water.

(iv) 20 L, 10 L, 5 L, 3 L and 1 L borosilicate glass-jacketed reactors. The 10 L reactor has a double jacket for low temperature applications.

All reactors have a local extraction system for reagent/solvent load and are independently connected to the scrubber system. All electrical equipment is flameproof to EU standards.

(v) Two short-path high-vacuum distillation equipment for purification by distillation of high boiling or heat-sensitive materials.

(vi) Vertical-type centrifuges of 80 cm and 20 cm diameter, with 316 stainless steel basket. They are installed in clean rooms.

(vii) Rosenmund-type stainless steel nutsche filter with 0.375 m² filter area and 300 L of capacity. It is equipped for *in situ* drying of filtered products with solvent recovery. This unit is also installed in a clean room separated from the production area.

(viii) Büchner-type filter made of stainless steel and jacketed for inert gas purging.

(ix) Stainless steel and polypropylene cartridge filters for solvent polishing and in-line filtration.

(b) Drying Equipment

- (i) Vacuum tray dryer with eight 70×90 cm trays. The oven is thermostatted with capability for high-vacuum drying or inert atmosphere drying.
- (ii) Vacuum tray dryer with two 30×40 cm trays.
- (iii) 50 L stainless steel rotary vacuum dryer.



(c) Physical treatment:

- (i) Stainless steel rotary mill, model SR200, from 10 to 120 kg/h. Down to < 0.08 mm.
- (ii) Stainless steel pin mill, model PM-3A, from 25 to 100 kg/h for pharmaceutical materials (200µm-300µm).
- (iii) Vibratory stainless steel tumbler sieve.



(d) Stores/Warehouse:

The Pilot Plant has completely independent storage facilities for handling of raw materials, intermediates, final products, ancillary materials, etc., which have been divided into sections for the proper handling of materials under cGMP.



(e) Process Control and Analytical Laboratories:

The pilot plant has own independent process control and analytical laboratories that provide ample services of process and quality controls. The analytical laboratory has the following instrumentation:



FTIR, automatic titrator, automatic Karl Fischer titrator, GPC, HPLC with automatic injection and diode array, light scattering, and refractive index detectors, melting point apparatus, GLC, polarimetry apparatus, etc.

Other analytical services, such as GC-MS, NMR, ICP-MS, ICP-OES, elemental analysis, etc. are directly accessible through the Research Technical Services of the University of Alicante.

(f) Stability studies:

The pilot plant has its own climatic chambers to study regular and accelerated stabilities of any kind of products. Samples subjected to stability programmes are stored once analysed.

(g) Validation of analytical methods:

The pilot plant can develop and validate analytical methods for pharmaceutical products according to ICH standards. Some of these validated methods have been accepted in IMPDs and DMFs of different pharmaceutical products by the corresponding authorities.

Intellectual property rights

All technical exchanges between the Institute of Organic Synthesis and potential clients are totally confidential and protected through legally binding signed contracts and confidentiality/secretcy agreements. All Institute personnel involved in projects of a confidential nature are also required to sign non-disclosure agreements in order to fully protect both the University's and client's intellectual and commercial rights. It should be noted that contracts are constructed in such a way that the Clients' commercial interests are fully respected. All agreements are supervised and approved by the Service for Research Management & Technology Transfer of the University.

Cooperation sought and services offered

The Institute of Organic Synthesis of the University of Alicante has a wide experience and the facilities required to develop commercially viable industrial processes for the fine and pharmaceutical chemical industries. The Institute offers the following services to potential clients:

- Custom synthesis of intermediates and products to clients' specification
- Toll manufacture of products and intermediates
- Process R&D and process scale-up from laboratory to pilot plant
- Physical treatment of finished products
- Process and analytical method validations under GMP conditions

Market applications

The facilities offered by the Pilot Plant of the University of Alicante make them suitable for use by the following industrial sectors:

Fine chemical companies (fragrances, flavours, foodstuff, etc.)

Pharmaceutical companies

Veterinary companies

Agro-chemical manufacturers

Research and consulting companies