

# Manufacturing of semisolid pharmaceuticals: equipment ready to meet ever-changing market demands

## THE SOLUTION



 Qualiphar



For liquid processes

**AZO.**  
LIQUIDS

»The requirement for increased capacity is fully met. With this equipment, Qualiphar can now produce four times the amount of Algipan in one shift. Compared to the former equipment: one week's work is now completed in two days, cleaning included.«

Johan Janssens, Validation Engineer, Qualiphar



batch vacuum processing plant with separate melt vessel

## Ultimate flexibility for the production of creams, ointments and gels

### Our customer Qualiphar

Qualiphar-Gifrer. The company employs 430 persons spread over two production sites: Qualiphar in Bornem (Belgium) and Gifrer in Lyon (France). All products manufactured are sold exclusively in pharmacies and hospitals. Qualiphar was founded in 1937 and since 1970 has been owned and managed by the Verlinden family. From the outset, the company has focussed exclusively on the production of self-care medication. The goal of

its original founders was to make the job of pharmacists easier and to reduce their workload: From the pharmacist, for the pharmacist. An extensive programme of portfolio diversification commenced upon the takeover by the Verlinden family. Qualiphar experienced an explosive growth in contract manufacturing. Substantial investments in the logistics department allowed for rapid delivery within the Benelux countries. Development of own

products, driven by the R&D department, makes it possible to launch several new products a year. In 1999 this growth enabled an international breakthrough which resulted in setting up an European Export department. Recently, export has expanded with an office in Dubai for Outside Europe Export. Qualiphar is cofounder of BACHI (Belgian Association of the Consumer Healthcare Industry).

BACHI represents the interests of industry partners specialised in the manufacturing and sales of OTC and healthcare products in pharmacies. Its subsidiary Gifrer is specialised in two branches. The manufacturing of sterile unit-doses for hospitals and for self-care, and furthermore the processing of over 250 different herbs for the pharmaceutical, cosmetic and food industries. Creating different herbal extracts that are exported to over 30 countries.

### Qualiphar's product portfolio

#### Non-prescription medicines:

pain-relieving drugs, antiseptic agents, cough medicines, haemorrhoid treatments and laxatives, mouth and throat wash solutions, tablets, sprays and drops for nose, throat and ears, tranquilisers, skin care and vitamins

#### Cosmetics and

#### food supplements:

Digestion aids, vitamins and other food supplements (biocure range), hair care, insect repellent, treatment for head lice, mouth and throat care, nose and ear care, skin care

### Goals of the investment

- High-quality systems which deliver multiple advantages
- Increase in capacity
- Increase in production speed
- Increase in flexibility to respond quickly to changing market demands
- Simple and powerful Cleaning In Place
- Documentation for all production and cleaning processes
- Improved quality as a result of automation of workflows

»The pharmaceutical industry is governed by stringent laws and directives, such as GMPs. As a manufacturer we need to abide by these laws. As such, any equipment acquired must be able to support these laws and comply with a set of user requirements. Therefore a close collaboration between supplier and client is vital during design and development of process equipment. AZO LIQUIDS has always kept Qualiphar's interest at heart. This is why the system meets all specified criteria for production, cleaning, handling and maintenance.«

Johan Janssens, Validation Engineer,  
Qualiphar

Flexible emulsion and suspension production in batches from 400 to 2,000 litres

### Company strategy

- Increase the range of OTC products and para-pharmaceuticals, distributed through pharmaceutical distribution-channels.
- Expand export business
- Enhance quality and cost-efficiency in contract manufacturing
- Provide the best customer relationship and services

### Advantages of the new system

- The vacuum processing plant type zoatec® BG2000 makes it possible to manufacture emulsions (water/oil mixture) and water-based suspensions
- Batch sizes from 400 up to 2,000 litres
- Manufacture of a complete batch within a single shift
- Simple, rapid cleaning of the plant thanks to the integrated, high-performance CIP system
- Protection for the machine operator and the product with an airtight and dustproof process
- Less manual intervention within the production process

Optimal discharge of product for economical reasons, especially when products are frequently changed

Insulated double jacket: rapid heating and cooling

Homogeniser: good accessibility and low wear through good design



Spray nozzles for a powerful CIP without manual intervention

Agitator combinations: optimal customisation to product requirements

Homogeniser: excellent dispersal of droplets and particles in emulsions and suspensions



Good access to process vessel and melt vessel

# Batch vacuum processing plant type zoatec® BG2000

## Versatile, fast and high quality

### The solution in detail

#### Plant layout

The AZO LIQUIDS system is essentially composed of the following components:

- Process module with process vessel and homogeniser
- One hopper for adding powders and one for liquids
- Pump for CIP
- Supply unit with vacuum generator and heating/cooling system
- Preparation vessel to melt fat compounds or heat oils

#### Process module

The process vessel, with a working volume of 2,000 litres, is supported on load cells and has an insulated double jacket for indirect heating and cooling. In the vessel is found an agitator with PTFE scrapers. The scrapers are keyed on the agitator without additional fastening elements and will prevent local overheating or undercooling, thus no crystallisation can occur on the vessel wall. Also installed in the

vessel is a vortex breaker to ensure a more thorough mixing. The agitator and vortex breaker are each powered by a gear motor with a frequency converter, making it possible to select the optimum mixing speed according to the product properties. The manhole in the lid has a built-in sight glass and can be used to manually insert raw materials.

#### Homogeniser

The homogeniser has a critical impact on the production of ointments and crèmes. Excellent dispersal of droplets and particles is required to manufacture stable emulsions and suspensions. With the powerful homogeniser, times for homogenisation are considerably shorter. The sophisticated design reduces wear on the parts, mechanical seal included, thus increasing their lifetime.



Feeding hopper for powdered raw materials



Feeding hopper for liquid raw materials



»The system can cover a wide range of batch sizes: from 400 up to 2,000 litres. It allows us to successfully transfer other products to the new system. Thanks to the powerful homogeniser, we are able to produce larger quantities in a single shift.«

Johan Janssens, Validation Engineer, Qualiphar

Good accessibility to the homogeniser

Furthermore the homogeniser does not require any cleaning. During CIP, the homogeniser can be used at any speed and thus will clean itself. Another advantage is the easy accessibility for handling and maintenance, thus reducing down time.

**Feeding hoppers**

A mobile feeding hopper with a usable volume of 100 litres is

provided for adding raw materials in powdered form. The hopper with a cover is located in front of the process module at ground level. Powders are sucked into the process vessel under vacuum using the homogeniser. Liquids, like perfumes, can be added via a smaller hopper mounted on the process vessel's lid. The perfume hopper has a usable volume of 10 litres.

**Melt Vessel**

The melt vessel has a usable volume of 1,000 litres and is fitted with an insulated double jacket similar to the process vessel. Since melting requires a lot of energy, steam is used on the melt vessel. An agitator with PTFE scrapers is also fitted to prevent burning and local overheating of the fat compounds. The melt vessel is connected to the process vessel via an insulated supply line;

heated fats can be transferred automatically using the homogeniser. Process steps in the melt vessel and in the process vessel can be controlled independently. This enables considerable time savings in the complete production process.



Agitator with scrapers in the melt vessel



Melt vessel for melting and heating of fats and oils

»The built-in, high-performance CIP system makes it possible to clean the plant automatically in a short time. Individual cleaning programs can be created and saved. The CIP functions are optimised in close collaboration with AZO LIQUIDS. This testifies to the excellent customer focus at AZO LIQUIDS.«

Johan Janssens, Validation Engineer,  
Qualiphar



Spray nozzles for a powerful Cleaning In Place

## The most stringent standards of hygiene with CIP and separate supply module

### Cleaning In Place (CIP)

CIP is conducted automatically without any alterations to the plant. Both the process vessel and the melt vessel are cleaned and freed of any residues using the spray nozzles mounted in the vessels. The spray nozzles are fed by a CIP pump at a pressure of 2-3 bar and a flow rate of over 2 m/s. Modular workflows for cleaning can be created using the recipe builder. Thus it is possible to specify a pre-cleaning that removes all pharmaceutical residue and have it collected in an

external waste vessel. Afterwards cleaning, rinsing and drying of the plant continue automatically. As Qualiphar is a pharmaceutical manufacturer, cleaning of the plant is subject to validation. Due to the SCADA controls, every cleaning can be traced in minute detail.

### Technical modules

Together with the vacuum pump for generating a partial vacuum, the energy module for heating and cooling the process vessel is installed in a technical area close

to the separated production area. In this area the main and electrical control cabinets, and the valve terminal are also installed. The benefits: no obstructions when carrying out maintenance work and less build-up of noise and dirt in the production area.

### Process control

The zoamatic professional controls are based on a SCADA system and can be upgraded at any time. A touch panel provides clear visualisation and intuitive operation.

### Control functions:

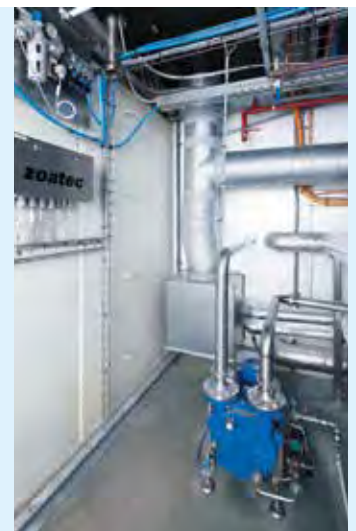
- Batch-oriented documentation complying with 21 CFR Part 11
- Comprehensive audit trail
- Recipe operation in accordance with S88.01
- Batch log with all events and graphs for key parameters
- Storage of an almost unlimited number of recipes
- Manual and automatic operation



Insulated transfer line from the melt vessel to the process vessel



Supply module for heating and cooling the process vessel and melt vessel



Vacuum pump for generating the partial vacuum in the process vessel



»The zoamatic controls are convenient and easy to use. They allow production processes to be perfectly adjusted. The process visualisation gives a clear, practical and intuitive overview of the system. Operators are informed and guided through recipes by means of prompts. The recipe editor provides an intuitive way to create recipes and to manage them using version history and control.«

Johan Janssens, Validation Engineer, Qualiphar

Entire process monitored by the zoamatic controls

## Convenient operation of the system when manufacturing an ointment

### Manufacture of Lamiderm®:

Lamiderm® is a water/oil emulsion for treating burns, sunburn and reddened skin. A batch of 2,000 litres, with the BG 2000 vacuum processing plant, is produced in only approx. 6.5 hours. Once the recipe has started, the process vessel is automatically filled with the necessary amount of demineralised water. At the same time, the operator fills the melt vessel with pre-weighed amounts of paraffin pellets, liquid oils and

other fats. The water in the process vessel is heated while the fats and oils are heated and melted in the melt vessel. After approximately one hour, the powdered gelling agent is fed into the process vessel from the powder feeding hopper. Once the swell time has passed and the correct temperatures have been reached in the melt vessel and the process vessel, the contents of the melt vessel are transferred

into the process vessel. Only then does the cooling cycle start. When the entire mass has cooled to 50°C the active substances, extremely sensitive to temperature, are added directly into the process vessel. When the mass has cooled down further to 40°C, the liquid perfume is added. The cooling endpoint is set below 30°C. The agitator with scrapers runs throughout the entire process. The homogeniser is actuated

when products are added and at certain points to stimulate recirculation and mixing of the mass. Before the cream can be discharged into drums, a QC sample is taken and analysed in the laboratory.



Booster pump for Cleaning In Place



Discharge of products into drums



Process vessel with zoamatic control



## Conclusion:

»Investing in a vacuum processing plant of AZO LIQUIDS has been highly beneficial. The resulting increase in total production capacity, reduced batch times and plant versatility has left us room for future expansion, allowing us to react quickly to changes in market demands while complying with all the necessary directives. We are now able to significantly improve our market position both as a manufacturer of our own products and as a contract manufacturer.«

Johan Janssens, Validation Engineer,  
Qualiphar (on left in photo)