Living a healthy life.
NOTOL
plant for the production of solid dosage forms
Krka is one of the world’s leading generic pharmaceutical companies, present in over 70 countries.

Our network of companies and representative offices abroad is strengthened by own production and distribution centres in Poland, the Russian Federation, Germany and Croatia.

Our basic activity is the manufacture and sale of prescription pharmaceuticals, non-prescription products, and animal health products, as well as Terme Krka health-resort and tourist services.

All our efforts are focused on the development of high-quality generic pharmaceuticals with added value, which we market under our own trademarks.

The major therapeutic groups in our range of products include pharmaceuticals for the treatment of cardiovascular diseases, gastrointestinal diseases and diseases of the central nervous system.

The vertically integrated business model allows us to manage the whole process from the phase of raw material development to the manufacture of finished products.
Technical data on the plant

Total surface area 32,000 m²
- Production area 13%
- Area for technical purposes and warehousing (5263 pallet places) 64%
- Non-production area (offices, corridors for visitors) 23%

Annual capacity
3.5 billion tablets and capsules

Value of investment
Over € 150 million

Designing and construction

The entire project was prepared by Krka’s project team in cooperation with internationally recognised domestic and foreign companies, experienced in pharmaceutical engineering and logistics, and in the system for managing and recording the production process. Leading Slovene and foreign equipment manufacturers and suppliers were engaged.
KRKA’s largest investment

The Notol plant for the production of solid dosage forms is Krka’s largest investment in the manufacture of finished pharmaceutical products. It represents the modern production philosophy through which we have achieved our objectives:

- to increase production capacities,
- to attain greater flexibility of the production which takes place in completely separated areas, both spatially and climatically,
- to ensure a high level of protection and safety of products and staff with production processes in closed systems, and to prevent cross-contamination,
- to optimise transport and to utilise warehousing capacities more effectively by introducing standard containers,
- to optimise the ratio between clean production areas and technical areas, thus reducing the costs of construction and maintenance,
- to automate production and transport processes.
The Notol plant comprises four interconnected buildings:
• production building,
• administrative and reception centre,
• packaging premises,
• small-batch production plant.

The concept of the vertical flow of material, the introduction of standard containers, and the automation of internal transport indicates the state-of-the-art approach to the organisation and management of production.

The production building, the central part of which is the production of bulk products, has five floors, two of which are production floors and three are technical floors.

In the centre of the construction, there is an automated high-bay warehouse which reaches up through all the floors. On the production floors, all phases of production from weighing to finished product packaging are carried out. The technical floors are designed for technological and technical installations and for internal transport.

The production is computer-controlled, with an efficient multi-level system which guides and controls the technology, production equipment cleaning, and transport of all materials by automatically guided vehicles (AGV).
Production process

The first phase of production is the receipt of raw materials, which are transferred to the temporary warehouse through the receipt and identification area. Raw materials needed for the manufacture of bulk products, packaging material and bulk products are kept in the temporary warehouse. Goods are transported to/from the warehouse by use of horizontal conveyors and lifting equipment.
Weighing through the connecting station is carried out directly into the container on the lower floor. After weighing, the container with weighed raw materials is dispatched by automated transport for homogenisation or mixing. When the procedure is completed, the mixture in the container is ready for the following production phase – granulation.

The granulation procedure prepares the mixture for compression into tablets. Powdery substances are processed in granulators with a solution of a binder. Dry granulate is sieved into a container and additives for tabletting are added. The tabletting mixture is now ready for tabletting.
Tabletting is performed on highly efficient, computer-controlled tabletting machines, equipped with automatic units for in-process control. The machines have the capacity to compress from 100,000 to 300,000 tablets per hour.

Some types of tablets are film coated. Coating can provide activity of the medicine at an exact place in the body, controlled release of the active substance and protection against humidity and light, and is also used to mask unpleasant taste.
Bulk product **packaging** is carried out on automated lines, fitted with special control systems which ensure the perfect quality of finished products.

The packaging premises are interconnected with other buildings and, via a special transport corridor, also with the central warehouse for finished products in the adjacent building.

The supply of the packaging materials and the transfer of finished products are ensured by use of automatically guided vehicles.
Small-batch production

The small-batch production is an interface between the development and the large-batch production. It follows the same production principles as applied in Notol.

The small-batch production is intended for:
- production of small batches,
- transfer of the technological procedure from the development to the production scale,
- optimisation of the existing technology.

Cleaning

Production equipment cleaning is automated and is conducted according to the prescribed recipes by use of fixed and mobile washing units.
The air-conditioning system is of exceptional importance in modern pharmaceutical factories. Controlled temperature, humidity, direction of flow and cleanliness of the air are essential for good manufacturing practice and provide basic conditions for the production. Adequate air-handling systems protect the products and ensure safe and healthy environment for the employees.

The distribution and supply of technological media (drinking water, purified water, compressed air, steam, etc.) are automated and under constant supervision by the central control system. Transport systems are also automated.
Quality and safety

The competitiveness of the company, and hence the associated business success, are increasingly dependent on the adherence to the world quality standards, and also on being equipped with modern and environment-friendly technology, as well as on adjusting quickly to market changes. In designing and constructing the plant, the Good Manufacturing Practice and the safety and ecological standards were strictly followed. The highest quality and most modern materials as well as state-of-the-art technologies were used.

Pharmaceutical production is extremely complex and must, therefore, constantly keep up with world standards. In Notol, these requirements can be met thanks to the new concept of the production which ensures quality, efficacy and safety of our medicines.
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