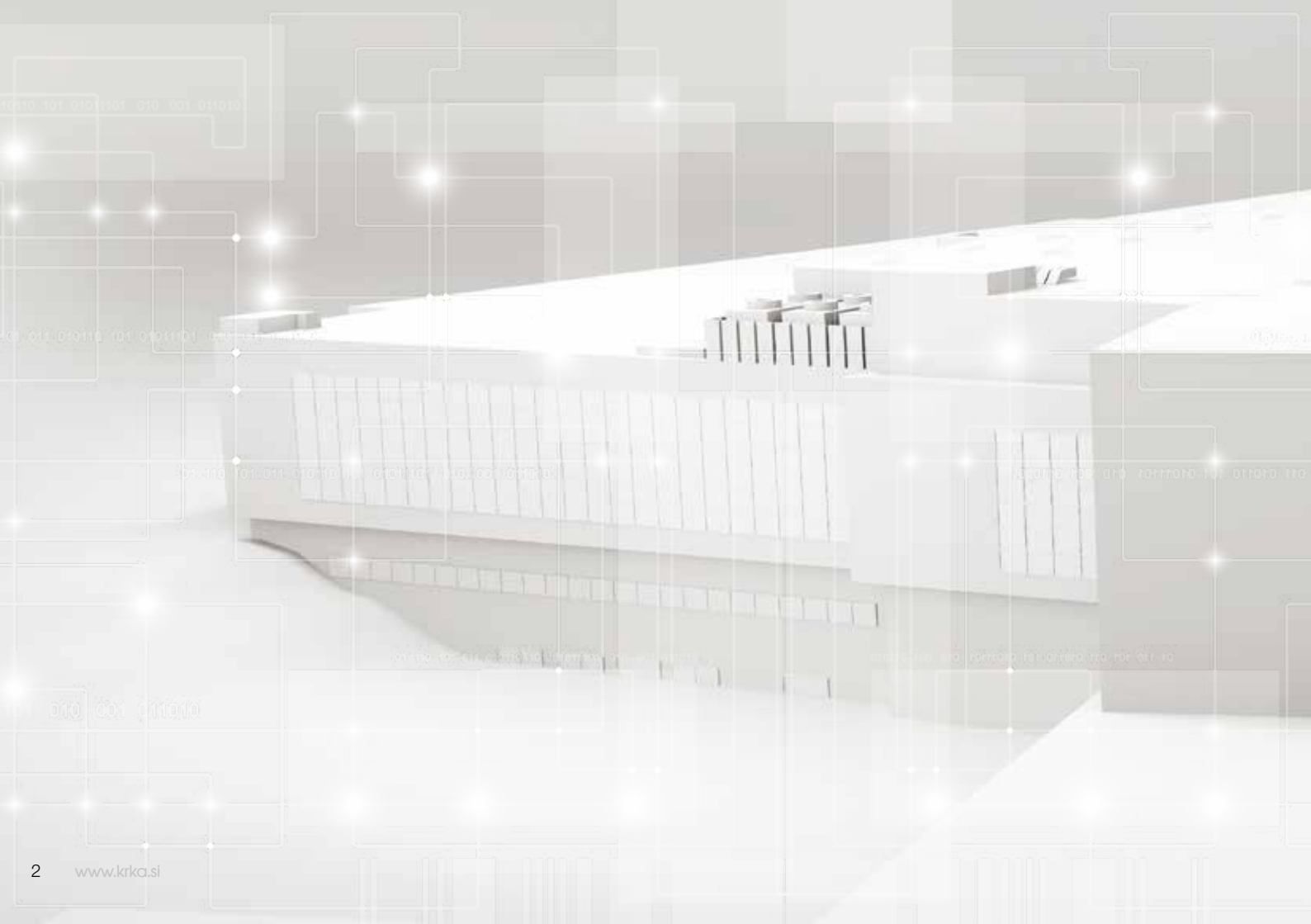


Notol 2

Solid dosage form production plant



Living a healthy life.





Krka produces generic medicines with added value in its **technologically highly sophisticated production plants.**

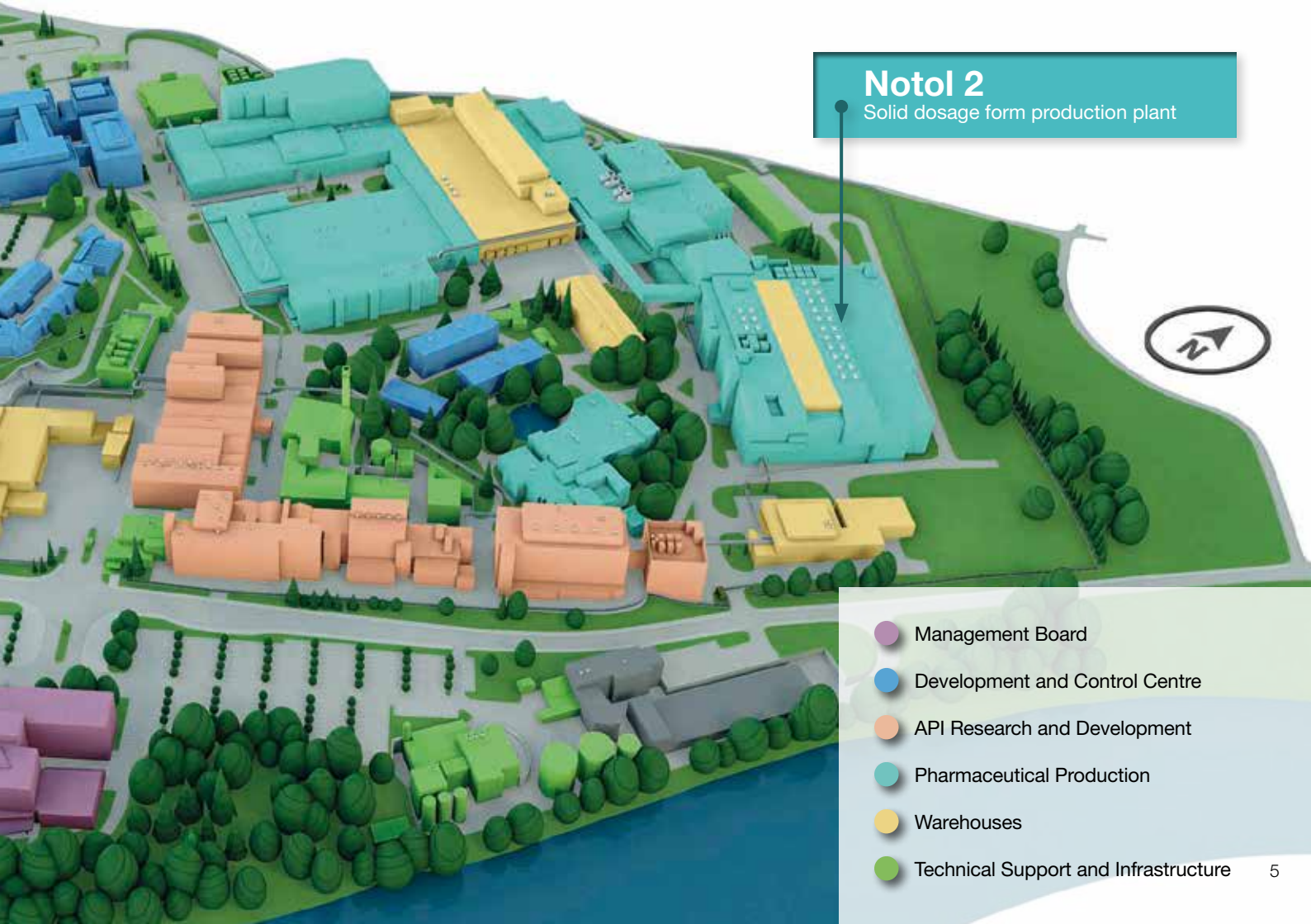
Active pharmaceutical ingredients (APIs) are made according to **our own synthesis procedures**. Krka's safe, effective and affordable generic medicines with added value are available to patients around the world.

Medicines are produced in technologically advanced production facilities. The largest and the most technologically advanced facility is **Notol 2**, the result of Krka's know-how and long-term experience in pharmaceutical manufacturing.



Notol 2

Solid dosage form production plant



- Management Board
- Development and Control Centre
- API Research and Development
- Pharmaceutical Production
- Warehouses
- Technical Support and Infrastructure

Notol 2
is the largest
investment
in Krka's history.

Size:
55,000 m²

Investment total:
€250 million

Production capacity:
5 billion tablets, film-coated tablets and capsules per year

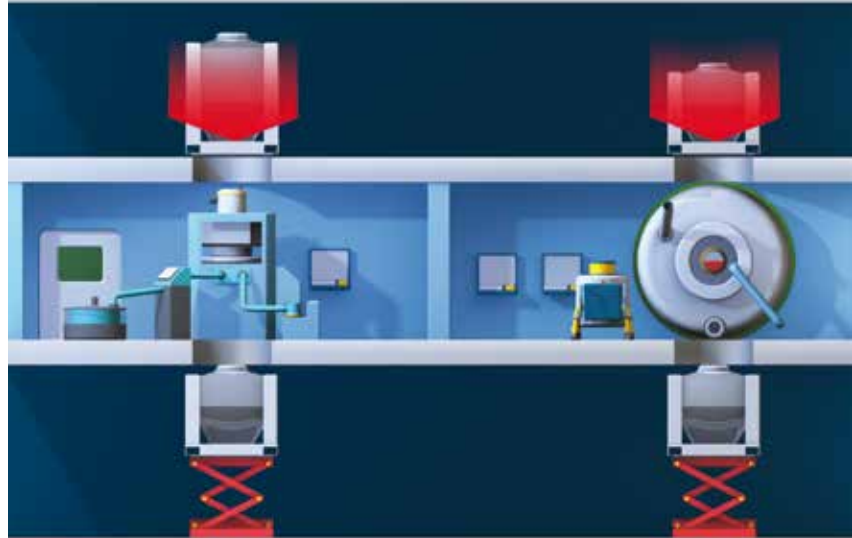




It was designed by **Krka's project team**. Domestic and foreign equipment suppliers from Germany, Italy, Switzerland and other western European countries were involved in setting up the plant.

Notol 2 combines the **vertical material flow, standard containers** and **automated internal transport** to pursue the sophisticated manufacturing philosophy.

Vertical material flow allows for greater flexibility in the manufacturing process.



Production machines are fed through docking stations from containers one floor above. The intermediate product is then transferred into a container on the floor below. It is then transported to the next docking station by the automated transport system.



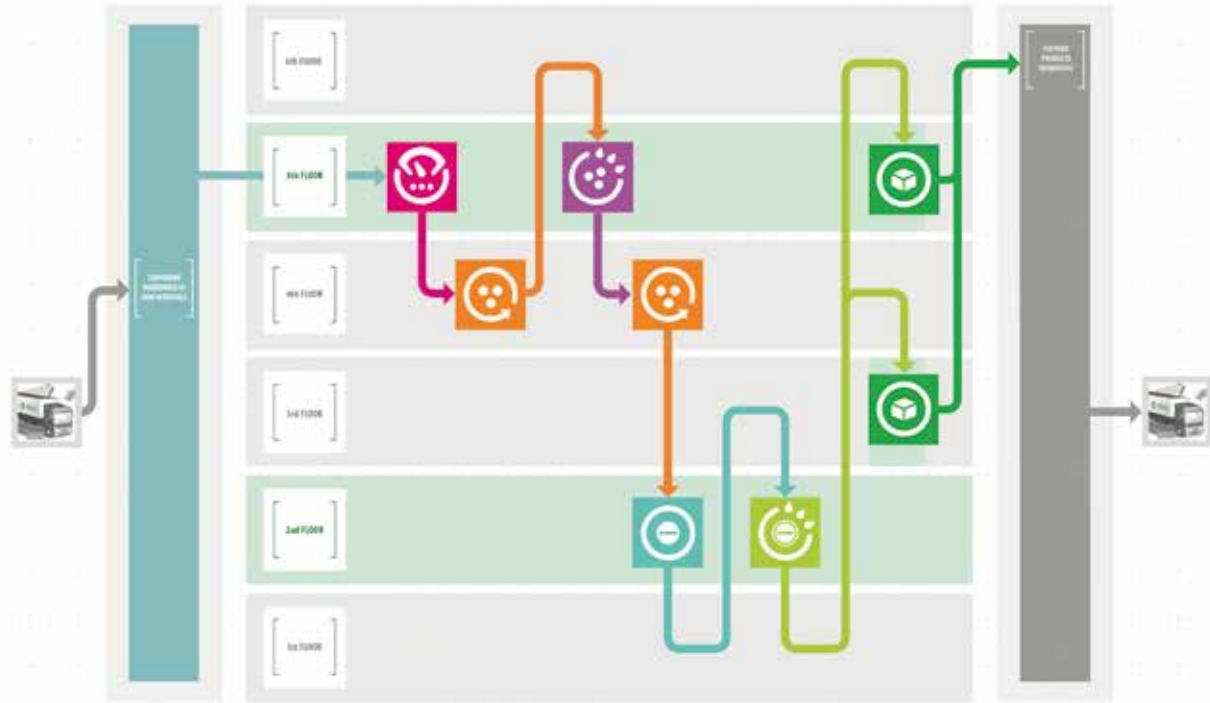
The heart of the factory is manufacture of bulk products.



Notol 2 consists of **three buildings**:

- 1 bulk product manufacturing plant
- 2 packaging plant
- 3 automated high-bay warehouse

Finished product manufacturing



The technological manufacturing procedure, which is prescribed in detail, is carried out in several phases.

It may take several days to manufacture a single medicinal product.



WEIGHING



HOMOGENISATION



GRANULATION



HOMOGENISATION



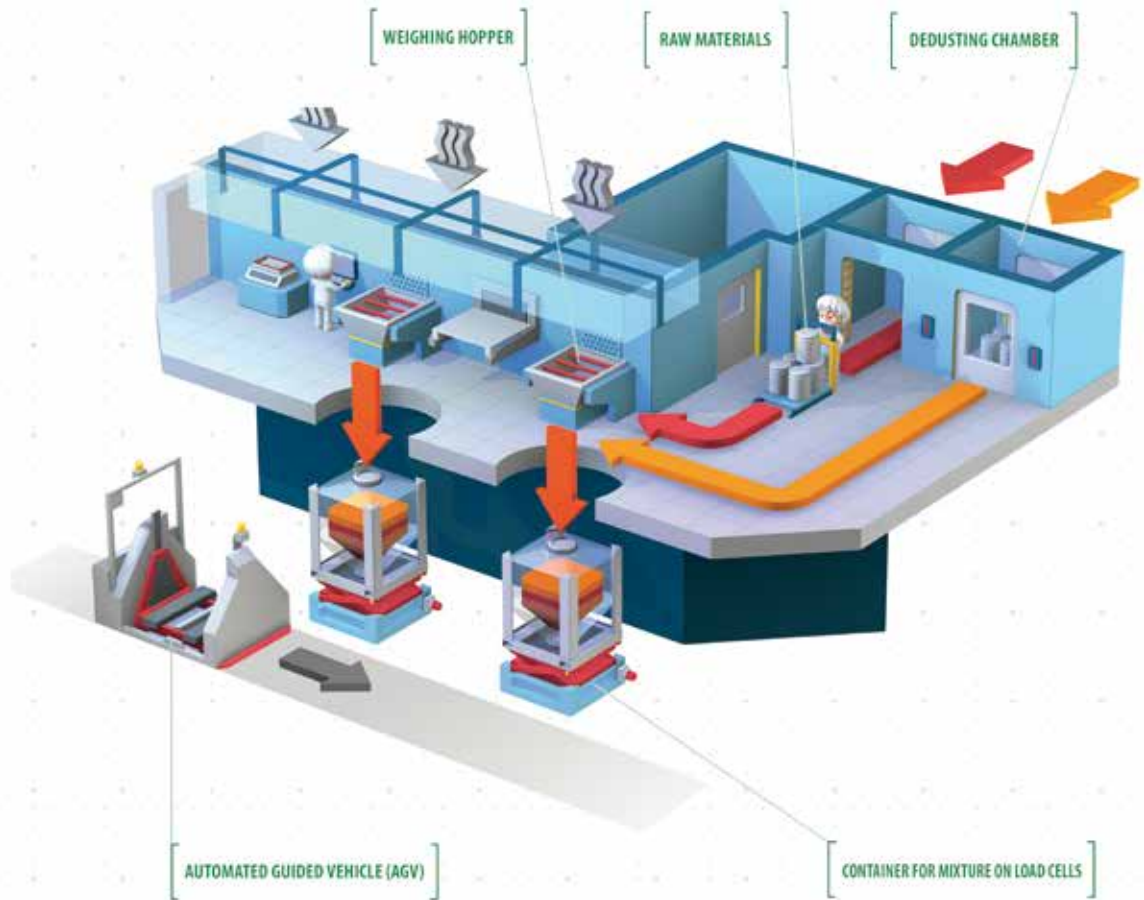
TABLET
COMPRESSION



COATING



PACKAGING

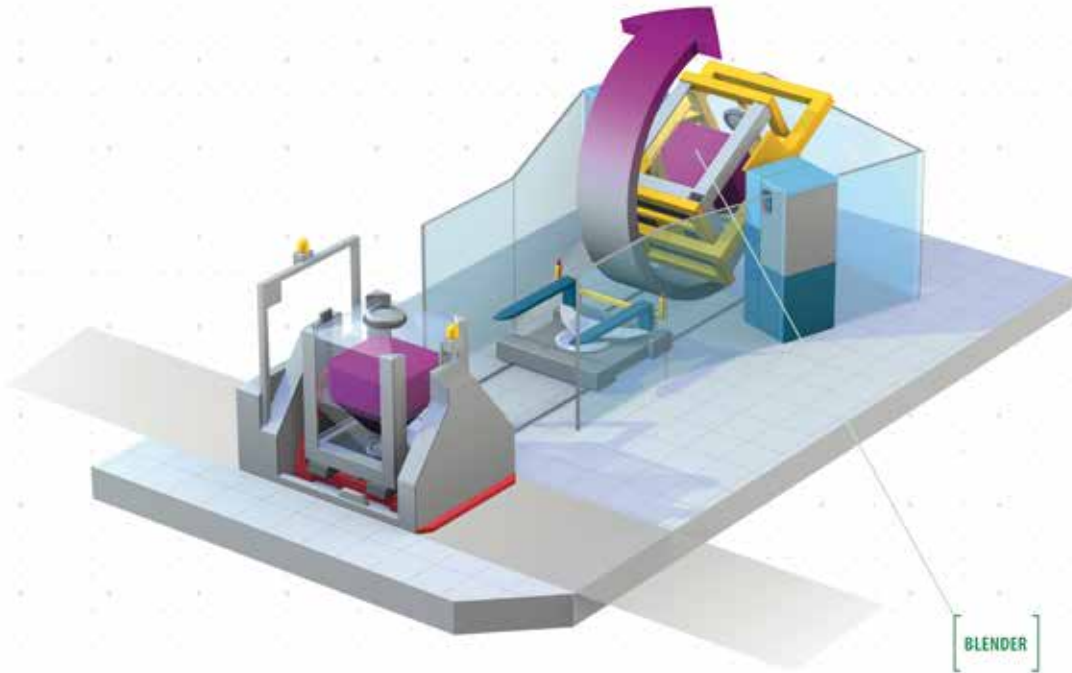


Weighing is a vital and extremely accurate procedure. The operator orders the ingredients for the manufacture of one batch of tablets or capsules through a production control system. An automated guided vehicle (AGV) brings a pallet with the required substances. Weighing is computer-controlled.



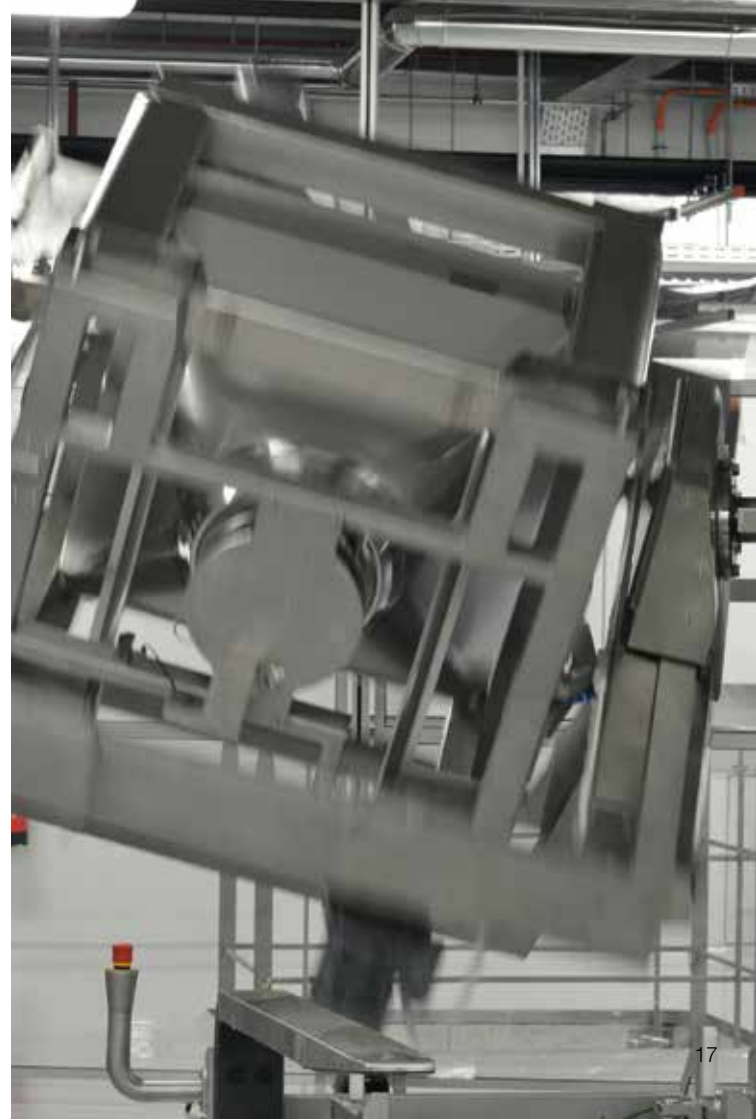


HOMOGENISATION

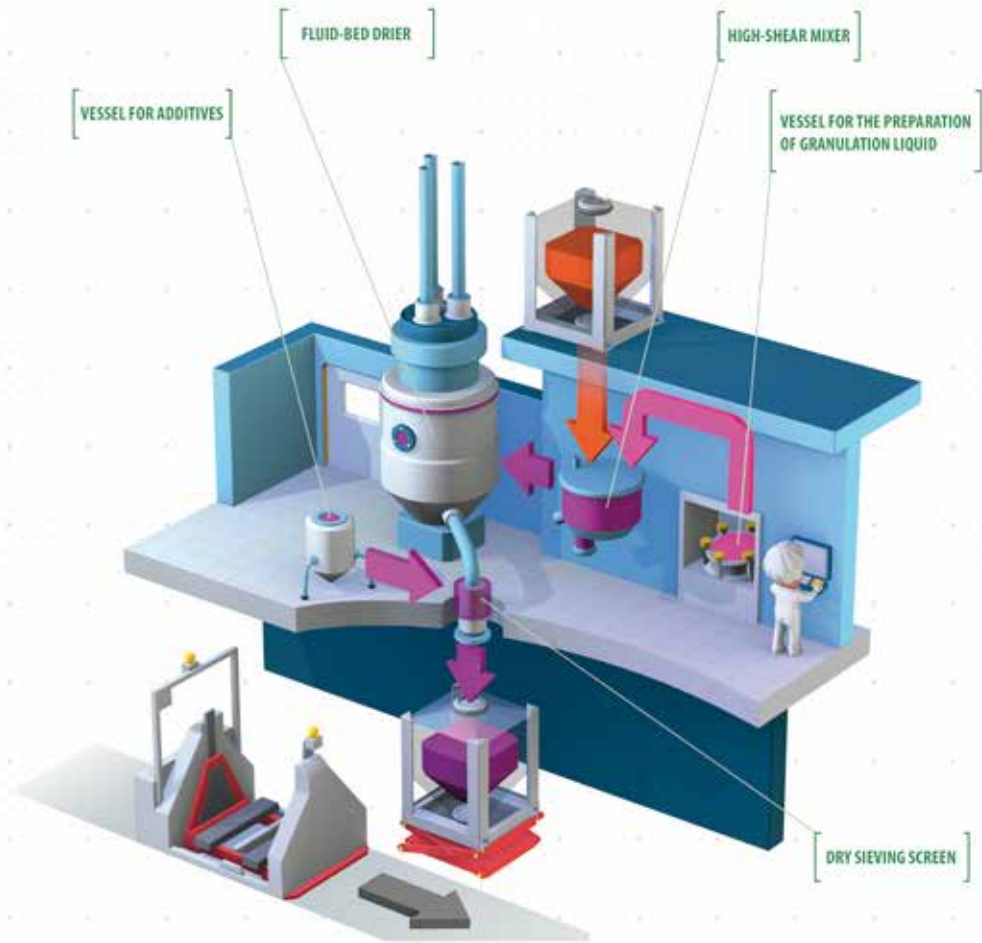


The weighed raw materials or the granulate are homogenised or mixed well into a homogenous mixture.

Before the blending process starts, the operator confirms the mixing time and speed of rotations of the container stated in the recipe.



GRANULATION



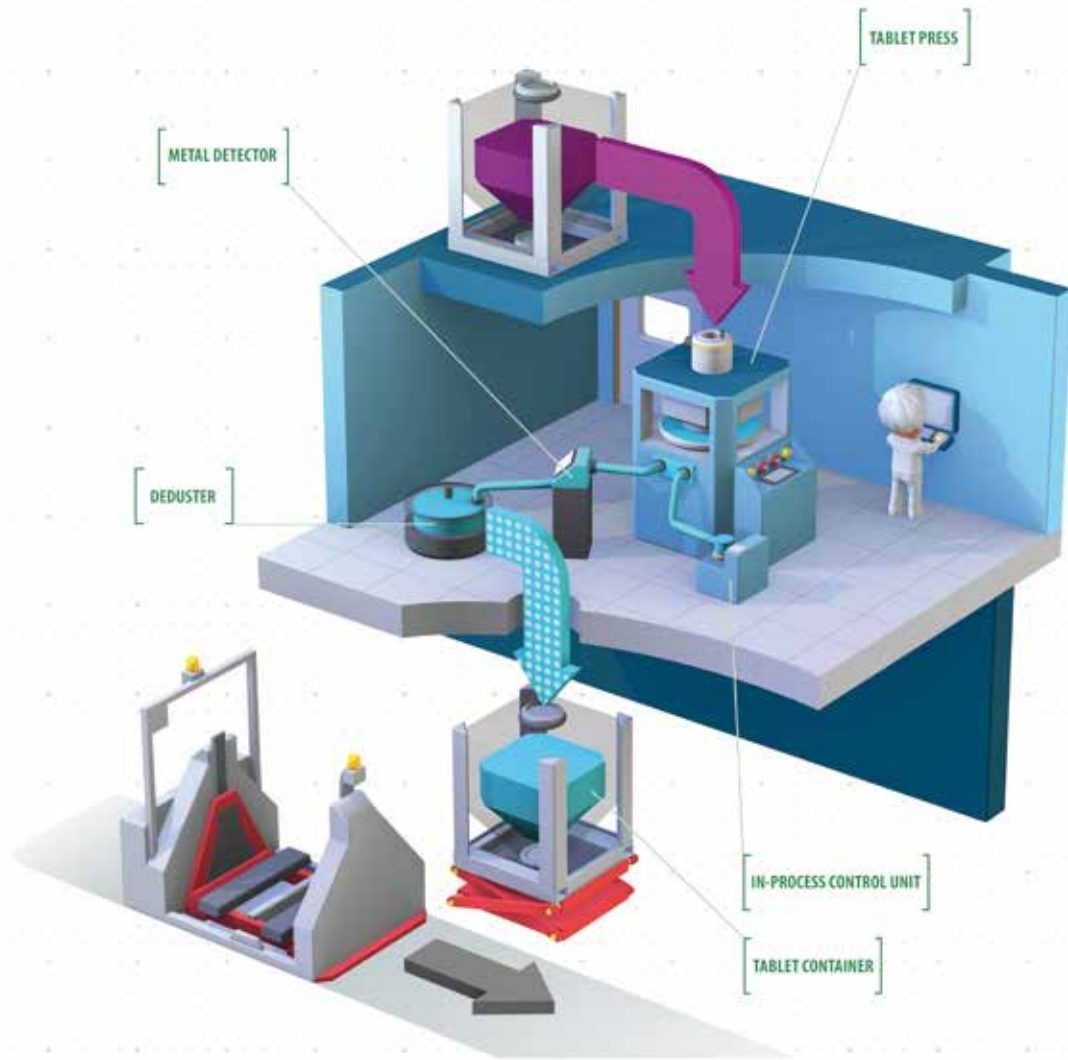
Granulation is a process of making agglomerates or granules from powder ingredients and excipients suitable for pressing into tablets.

Wet granulation, which is most frequently used, is carried out in a high-shear mixer, where during mixing powder ingredients are sprayed with granulation liquid. The wet granulate is then dried in a fluid-bed dryer. Another option is to spray the granulation liquid in a high-shear dryer, where granules are then also dried.





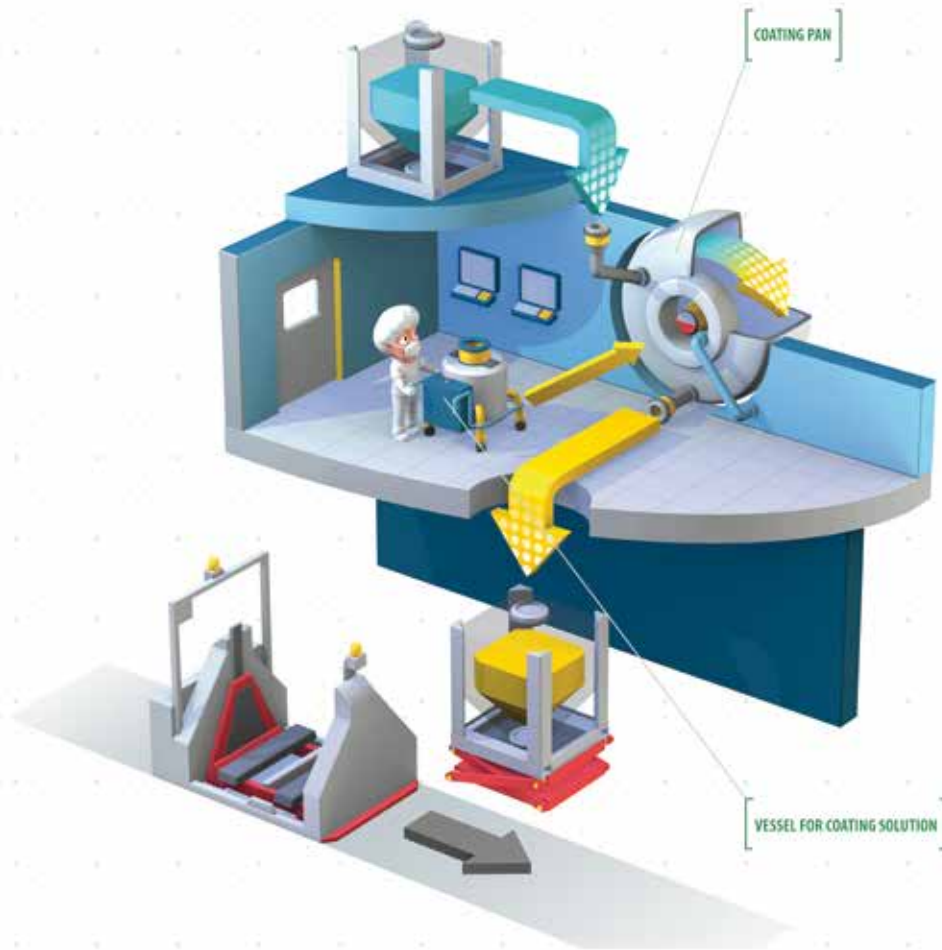
TABLET COMPRESSION



A compression mixture is compressed into tablets in high-capacity tablet presses.

A tablet press produces from 50,000 to 300,000 tablets per hour.





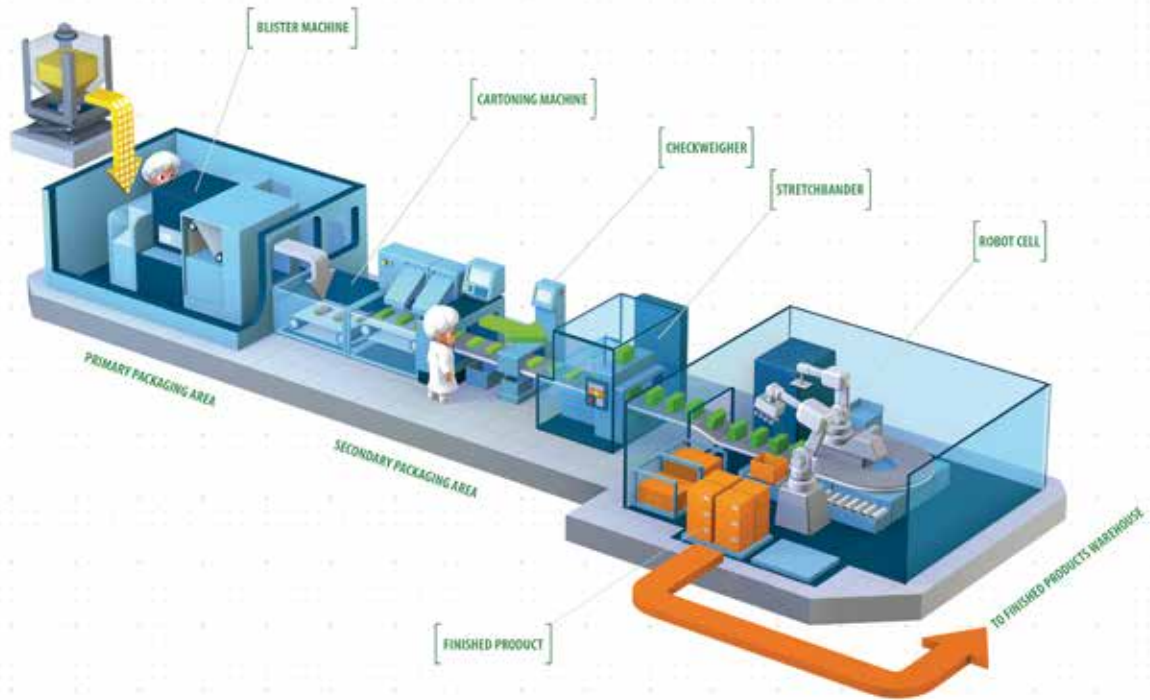
Certain types of tablets are coated with a thin film that protects them from moisture and light, masks the unpleasant taste of the active substance, or modifies its release rate or site.

Tablets are coated in coating pans. While the drum of a coating machine keeps rotating in order to mix tablets uninterrupted, the tablets are being sprayed with a coating liquid that turns into a smooth coating.





PACKAGING



On the packaging lines, tablets and capsules are first sealed into blisters. Together with patient information leaflets, they are inserted into folding boxes, and then sent to pharmacies, where they are available to patients.



At the end of the packaging line, two robot arms pick up the boxes, put them in large transport boxes, and load these onto pallets. An automated guided vehicle takes them over the bridge to the warehouse for finished products.



We ensure quality.

The production of medicines is carried out in line with exactly defined procedures and in controlled conditions.

In the manufacture of medicinal products, the principles of good manufacturing practice and other quality standards are pursued and the highest requirements of the current legislation in the pharmaceutical industry are fulfilled.

The quality of medicines is controlled and confirmed during the entire production and packaging process. Numerous analyses are performed on each product batch in Krka's control laboratories.

Because of this, Krka's high quality, effective and safe products are passed on to patients.



Certificates of good practice and quality standards

GMP

Good Manufacturing Practice

ISO 9001

Quality management system

GCP

Good Clinical Practice

BS OHSAS 18001

Occupational health and safety management systems

GQCLP

Good Control Laboratory Practice

ISO 14001

Environmental management systems

GDP

Good Distribution Practice

ISO/IEC 27001

Information security management systems

GPvP

Good Pharmacovigilance Practice

ISO 22301

Business continuity management systems

HACCP

Quality assurance system for foodstuffs at Krka

Cleaning is of utmost importance in the pharmaceutical industry.

After each manufacturing phase, the production equipment, containers and docking stations are washed and dried according to the stipulated procedure.





Adequate technical support is the first condition for the pharmaceutical production.

Advanced air-conditioning systems provide for suitable air cleanliness, temperature and humidity. The supply of potable and purified water, compressed air, steam and gasses required by working processes is supervised by the central control system. In this way we provide for health and safety of our employees and protect our products. **Centrally controlled air-conditioning systems supply one million cubic metres of air per hour.**

Automated transport system

All horizontal movements throughout the building (internal transport) are carried out by AGVs and the automated transport technology. AGVs are equipped with laser navigation.



Automated high-bay warehouse is in the heart of the logistics system.

It is designed for storing raw materials, semi-products, bulk products and packaging materials. It is the **highest Krka's warehouse**, which is 32 metres high and almost 100 metres long. It is designed to store 9,000 pallets. It is served by three fully automated high-bay lifting devices.

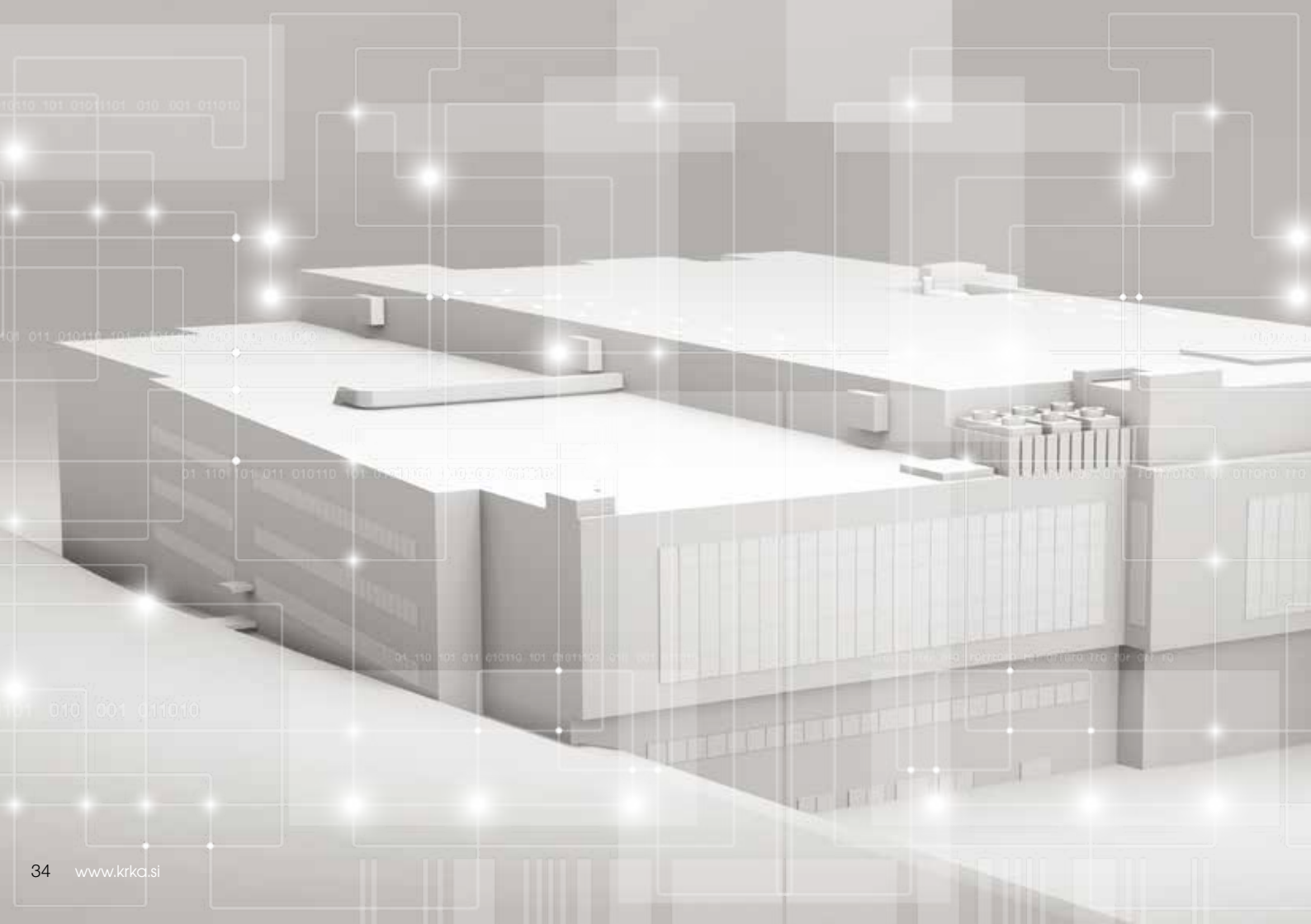


We are committed to health.

When it comes to health, only the best is good enough. Krka's high quality, effective and safe products are manufactured in state-of-the-art and top-notch facilities.









Issued and published by: Krka, d. d., Novo mesto
Design, production and photo archive: Krka, d. d., Novo mesto
Novo mesto, February 2017

Print: Gorenjski tisk storitve, d.o.o.

Krka, d. d., Novo mesto
Šmarješka cesta 6
8501 Novo mesto
Slovenia
+386 7 331 21 11
info@krka.biz
www.krka.biz

Gorenjski tisk, 3/2017, Slovenia, 1234B-2016, IF/MŽ.

