Medinsa

LABORATORIOS MEDICAMENTOS
INTERNACIONALES, S.A.

FROM OUTSOURCING TO RIGHTSOURCING

development and manufacturing of solid oral dosage forms

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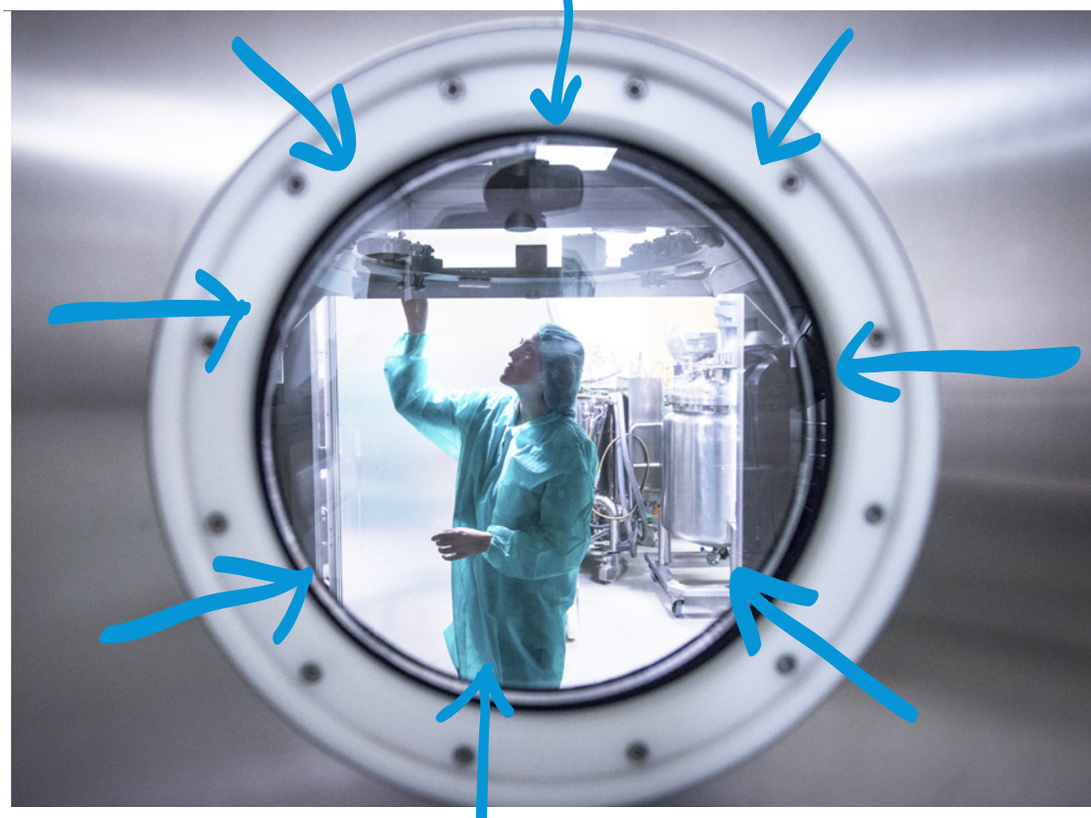

The company:

Continuously expanding technology and services

Laboratorios Medicamentos Internacionales, S.A. (Medinsa) started in the 40's as a small pharmaceutical production site becoming soon one of the major development and manufacturing companies of oral solid dosage forms in Spain and Europe.

Medinsa is authorized by the Spanish Health Authorities to manufacture medicines for human and animal use - including narcotics - and for manufacturing operations of investigational medicinal products for clinical trials.

Medinsa also holds the license to produce food supplements. A wide range of oral solid dosage forms are manufactured in Medinsa, among them film and sugar coated tablets, capsules, micro tablets, pellets and powders, all of them packed into blisters, bottles and sachets.

Although contract manufacturing is the main business, Medinsa also offers its customers formulations development, validation of analytical methods, stability studies, manufacture and packaging of clinical trial batches, and other documentation activities for dossier registration purposes.

JRS PHARMA Offers:

Excipientes

Family of High Functionality Excipients

The Next Generation of Modern Excipients:

All-in-One, Ready-to-Use Excipient Composite: Binder/Filler, Glidant, Superdisintegrant, Lubricant

PROSOLV® EASYtab SP
Microcrystalline Cellulose, Colloidal Silicon Dioxide, Sodium Starch Glycolate, Sodium Stearyl Fumarate

PROSOLV® EASYtab NUTRA
Microcrystalline Cellulose, Silicon Dioxide, Croscarmellose Sodium, Palm Kernel Oil saturated, DATEM

ODT Excipient Matrix - License and Royalty Free

PROSOLV® ODT G2
Microcrystalline Cellulose, Colloidal Silicon Dioxide, Mannitol, Fructose, Crospovidone

High Functionality Excipient Line

PROSOLV® SMCC
Silicified Microcrystalline Cellulose

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VIVAPUR®, EMCOCEL®
Microcrystalline Cellulose

EMCOMPRESS®
Calcium Hydrogen Phosphate Dihydrate and Anhydrous Dibasic Calcium Phosphate Dihydrate and Anhydrous

ANHYDROUS EMCOMPRESS®
Calcium Hydrogen Phosphate Dihydrate and Anhydrous Dibasic Calcium Phosphate Dihydrate and Anhydrous

EMDEX®
Dextrates

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Calcium Sulfate Dihydrate

Superdisintegrants

VIVASTAR®, EXPLOTAB®
Sodium Starch Glycolate, Sodium Carboxymethyl Starch

VIVASOL®
Croscarmellose Sodium

EMCOSOY®
Soy Polysaccharides

Lubricants + Modified Release

PRUV®
Sodium Stearyl Fumarate

LUBRITAB®
Hydrogenated Vegetable Oil, Hydrogenated Oil

Functional Fillers

ARBOCEL®
Powdered Cellulose

Thickener + Stabilizer

VIVAPUR® MCG
Microcrystalline Cellulose and Carboxymethylcellulose Sodium

Carriers

VIVAPUR® MCC SPHERES
Microcrystalline Cellulose Pellets

NON-PAREIL SEEDS
Sugar Spheres

Coatings

VIVACOAT®
Ready-to-Use Coating System

VIVAPHARM® HPMC
Hypromellose

Technology

PROSOLV TECHNOLOGY
Co-Processing of Actives

Members of the JRS Pharma Family

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ProJect Pharmaceutics

JRS PHARMA FAMILY

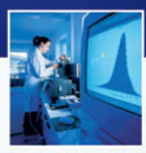
A Member of the JRS Group

• Excipients • Coatings • Biotech

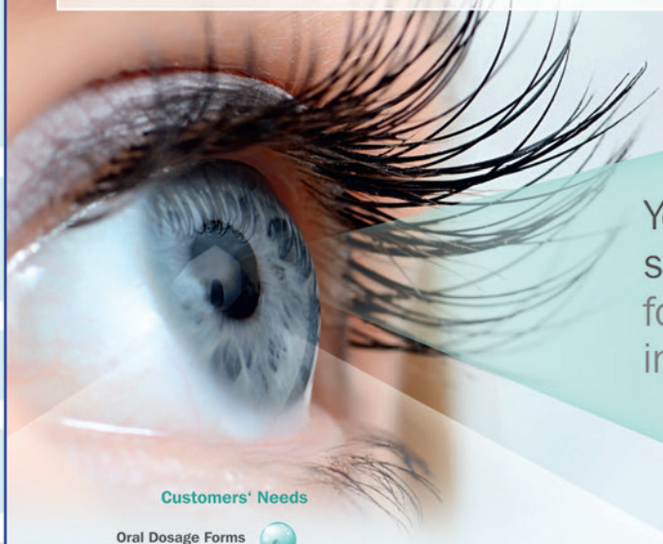
One Stop Shopping for

- Branded High-Quality Excipients
- Innovative, High-Functionality Specialities

And Added Value in Costs and Patient Compliance



3 Technical Competence Centers for R+D and Application Support



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The history:

From Grünenthal to Aristo Group

Medinsa started manufacturing pharmaceuticals for the local Spanish market as part of Laboratorios Andrómaco, expanding its operations into international markets during the ownership of Grünenthal (Germany). At the beginning of the current century - before the Aristo Group, headquartered in Berlin, acquired the plant in 2011 – the facilities were completely modernized. The technology investment strategy maintained over the past decades has been continued in recent years under new ownership.

1946
Establishment of the company Laboratorios Andrómaco, S.A. in Madrid.

1972
Laboratorios Andrómaco, S.A. installs its production facility at the current location in Torrejón de Ardoz.

1979
Grünenthal GmbH acquires 40% of Laboratorios Andrómaco, S.A.

1993
Grünenthal GmbH acquires 100% of Laboratorios Andrómaco, S.A.

1999
Foundation of Laboratorios Medicamentos Internacionales, S.A. (Medinsa) as a member of «Grupo Grünenthal España».

2003
Investment of 15 million Euros to expand and modernize the production plant.

2007
Refurbishment of Packaging area.

2008
Expansion of Quality and Development including new pilot plant.

2010
Construction of manufacturing area for effervescent products.

2011
Aristo Group (Berlin) acquires Medinsa.

2012
Investment in fluid bed technology with organic solvents.

Aristo Group:
"One of the fastest growing pharmaceutical companies in Europe"

Aristo Pharma GmbH was established in 2008 and vertically integrates several manufacturing companies in its production network:

- Steiner Arzneimittel
- Pharma Wernigerode
- Advance Pharma
- Lindopharm
- Esparma
- Medinsa

Within the corporate strategy Medinsa is the specialist for special solid dosages such as multi-particulate forms or effervescent tablets. While Aristo guarantees a solid baseline capacity loading, niche technologies are shared with external clients.

Capacity Overview

Entering new technologies

Within the segment of oral solids, Medinsa offers nearly all requested equipments. A strong investment has been done in recent years in order to cover niche applications, so the full range of technologies can be provided. Extrusion/spheronization, microtableting and organic solvent layering are worthwhile to be highlighted.

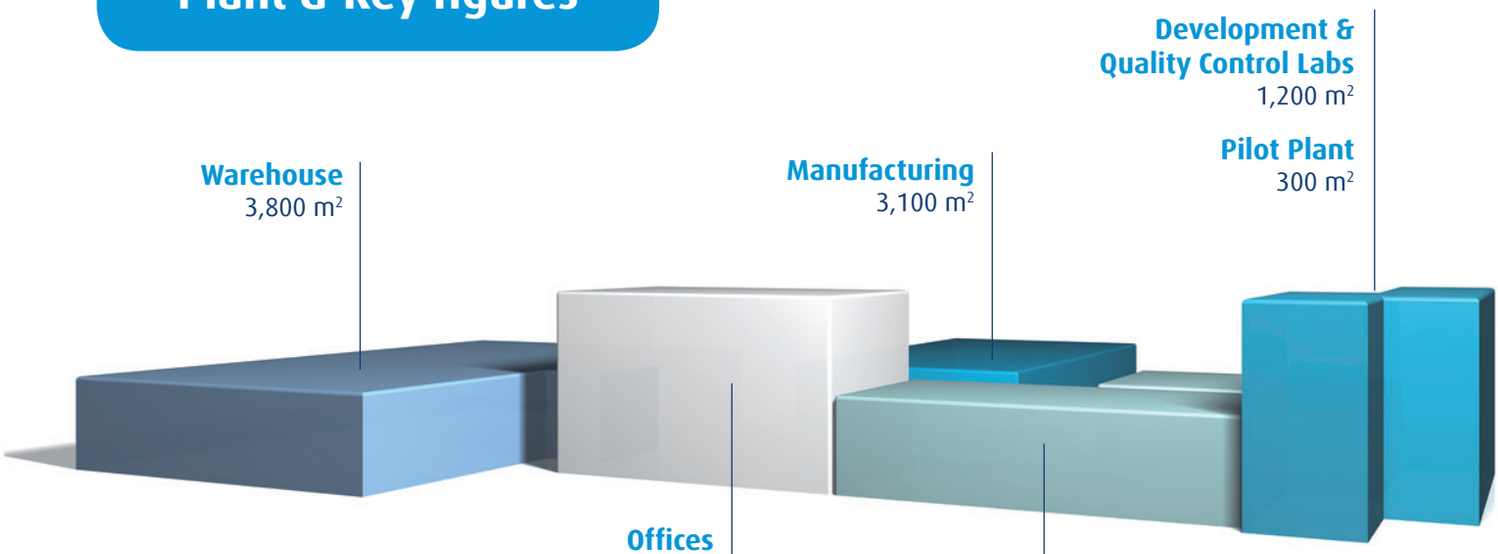
Manufacturing

Process	Capacity
Dispensing	600 tons
Granulation & Drying	530 tons
Mixing	1,000 tons
Pellet extrusion	130 tons
Pellet Coating	440 tons
Microtablets	2,500 mio. tablets
Tablets incl. Effervescent	620 mio. tablets
Capsules	640 mio. tablets
Coating	130 tons

Packaging

Process	Capacity
Finished Packages	60 mio. units
Tubes	11 mio. units
Strips	26 mio. units
Blister	100 mio. units
Bottles	5 mio. units

Plant & Key figures



Total Area
15,300 m²

Plant Footprint
12,700 m²

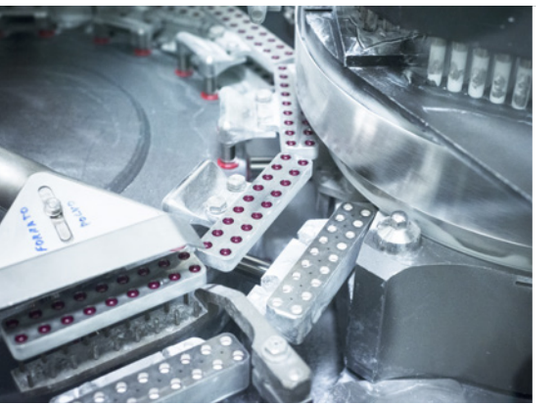
Premises

The growth experienced in recent years is majorly due to new products launched in production either through contract manufacturing or as a result of successfully staged development projects.

For the future years, a strong increase in operations – in particular in development – is expected.

Key figures

- **172** employees
- **13.5 mio.** packages
- **19.5 mio** Euro



Pharmaceutical
Dosage forms

Although our business is driven in the first place by standard formulations, customer demands have moved our focus to more sophisticated dosages or even combinations of them.

Tablet Formulation

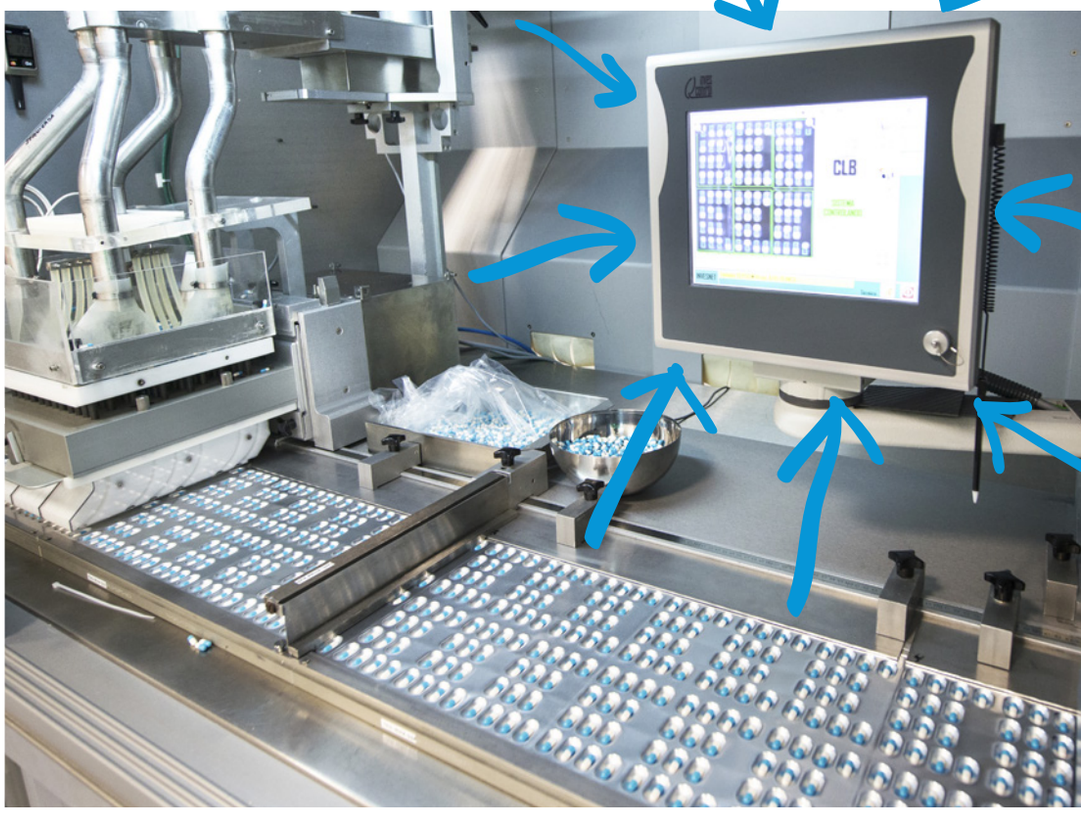
- ODT
- Effervescent
- Standard
- Sugar Coated
- Film Coated
- Micro-tablets
- MUPS

Capsule Formulation

- Powder
- Micro-tablets
- Powder + Tablets
- Pellets

Multi-Particulate

- Powder layered Pellets
- Liquid layered Pellets
- Extruded Pellets
- Micro-tablets



Tablets

The tablet is the most popular solid dosage form – a large variety of shapes and sizes is in our portfolio.

Apart from the standard tablet, in the past years we have introduced new variants such as chewable tablets, ODT, caplets, effervescent or multi-layer tablets to make patients life easier.

Delightful taste, the ease of in-taking, a gentle treatment of the stomach and a quick API absorption are among the advantages of most of the new applications. These properties are especially important for children or elder people or those with chronic disease.

Capsules

The hard-shell capsule is a very popular dosage form thanks to its convenient properties and widespread applications.

The filled material is not stressed as in the tableting process, the use of excipients can be minimized, capsules dissolve quickly and are easy to swallow. If particular low humidity is required, we employ HPMC (cellulose) capsule instead of gelatine.

We fill capsules with powders, granules, pellets, micro-tablets and combinations of the before mentioned. Our outstanding knowledge and expertise in the field of multi-particulate forms allow us to match even special customer requirements for encapsulation.

Multi-particulate forms

Multi-particulate drug delivery systems are mainly oral dosage forms typically consisting of spherical particles with diameter of 2.00 mm. The active substance is present as a number of small independent subunits which are either filled into capsules or compressed with excipients into tablets, so called MUPS (multi-unit-particular-system).

Multi-particulate forms provide many advantages over single-unit systems because of their small size. They are valuable for delivering both single APIs and combinations of multiple drugs, and can be formulated to provide customized release such as:

Pulsed release	→ Pulses of drug over several hours.
Sustained release	→ Steady levels of drug over several hours.
Modified release	→ Immediate release of some drug and delayed release of the remainder.
Delayed release	→ Dissolution in specific intestinal section through enteric coating.

We manufacture coated pellets applying a suspension on cellulose or sugar cores in a fluid bed sprayer. Alternatively, we produce matrix pellets by extrusion and spheronization. In the latter case the sphere containing the API is coated in order to achieve a customized release dosage.

Instead of pellets also micro- or mini-tablets can be chosen when technical advantages such as high flexibility of drug load and coating requirements shall be combined with clinical requirements like gastro-intestinal tolerance.

Packaging forms

As APIs and formulations become more demanding, also the requirements for packaging do. Nowadays only a minority of products is blistered in standard mono PVC blister. High barrier materials – whether based on glass, multi-layer films or aluminium – have gained importance and lead to a large variety of packaging solutions.

Blister → Thermofilms / Alu Coldform

Bottle → Plastic / Glass

Tubes → Plastic / Aluminium

Blister

Blister packs are useful for protecting products against external factors such as humidity and contamination for extended periods of time. Opaque blisters also protect light-sensitive products against UV rays.

We cover a wide range of primary packaging solutions - from medium barrier like simple thermoforming polymers such as PVC or PP to ultra-high barrier multi-layered foils or aluminium coldform for extreme protection requirements.

Multi-composite foils create an impermeable barrier to moisture, light, oxygen and other gases, being a protective enhancement to extend product shelf-life.

Our packaging machine pool provides maximum flexibility in order to meet volatile customer demands including all scales from high performance to small batch equipments. Machines are equipped with devices for processing unit dose and special lidding foils assuring child-resistance and senior citizen friendliness.

For effervescent tablets aluminium foil strips assure best protection for specific molecules.

Bottles

Specific geographic markets demand particular packaging solutions. Scandinavian countries for example traditionally ask for bottles. The same is true for UK or USA.

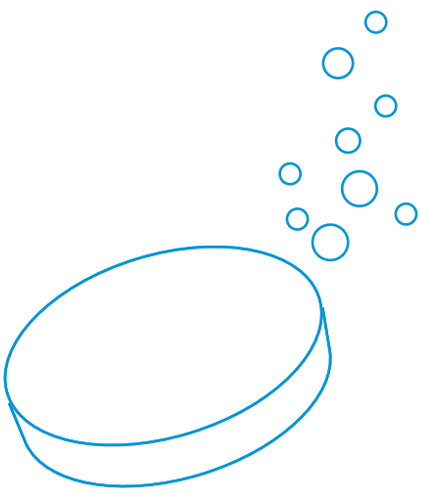
Food supplements are also often packed in glass or plastic bottles – in this segment we have experienced a strong demand increase.

Tubes & Strips

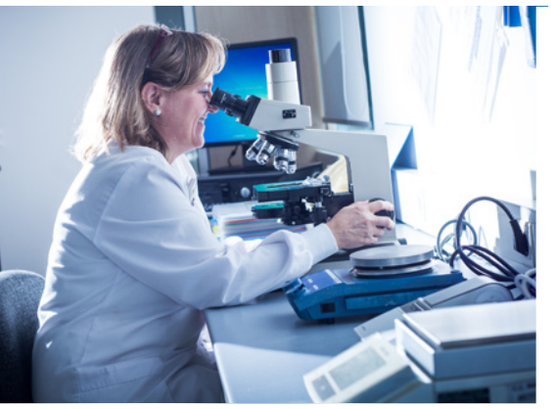
The fragility of effervescent tablets requires particular packaging. Either tubes or strips are most common in the market.

Tubes are either produced of polymers or aluminium. Apart from stability concerns the choice is majorly influenced by marketing considerations.

Aluminium strips allow single unit dose packaging. When dealing with narcotics, for example, higher requirements regarding child resistance can be satisfied with aluminium strips.



Pharmaceutical Development Services



From the product idea to commercialization

Our multi-disciplinary development team accompanies our clients from the first steps such as API source evaluation to scale-up and commercial launch. In our state-of-the-art and GMP approved pilot plant all our industrial scale machines are replicated in small scale so that any batch size required during the development process can be manufactured and packed economically. Within our project management we offer collaboration with selected global partners for complementary services, such as patent consultancy or bioequivalence study.

1 Project Start

2 Pre-formulation
- Selection / qualification of suppliers
- Compatibility studies
- Manufacture & Screening of pre-formulations
- Characterization of originator
- Product patent research

3 Formulation
- Manufacture of pilot batches
- ICH stability studies
- Validation of analytical methods
- In vitro / in vivo dissolution
- Pilot BE-Study
- Pivotal BE-Study

4 Scale Up
- Pre-discussion with authorities
- Decision how and where to register
- Compilation of technical documents
- Managing regulatory process

5 Regulatory
- ICH Stability Studies
- Manufacture of industrial batches
- Validation of production process

6 Manufacture
- Logistical preparation for launch
- Industrial scale manufacture
- Process improvement

Medinsa
LABORATORIOS MEDICAMENTOS INTERNACIONALES, S.A.

All pieces of the puzzle:
Special Capabilities and Innovations

Any contract manufacturing project can only be locked-in if all requirements can be met. We need to offer all pieces of the puzzle. This is why we continuously work on the innovation of our technology and service portfolio. New fluid bed technology and organic solvent layering technology is one of the recent major achievements.

In the field of method development we have introduced new software technologies for increasing productivity in the lab. Clinical trials supply is in our portfolio because customers have been asking for these complementary services within pharmaceutical development.

The packaging lines are equipped with devices that support anti-counterfeiting and serialization. Lidding foils will be printed on-demand on-site in order to increase flexibility and competitiveness.

Innovation also refers to entering new markets for which additional licenses are required.

Apart from the GMP Certificate for medicinal products for human and veterinary use, we have received the narcotics license issued by Spanish Health Authorities. They also inspected us regarding Clinical Trial Supply.

Due to the strong demand for food supplements, we also have applied successfully for the corresponding license.

All these continuous efforts allow us to offer "one stop shop" solutions making customer's life much easier.

Medinsa

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