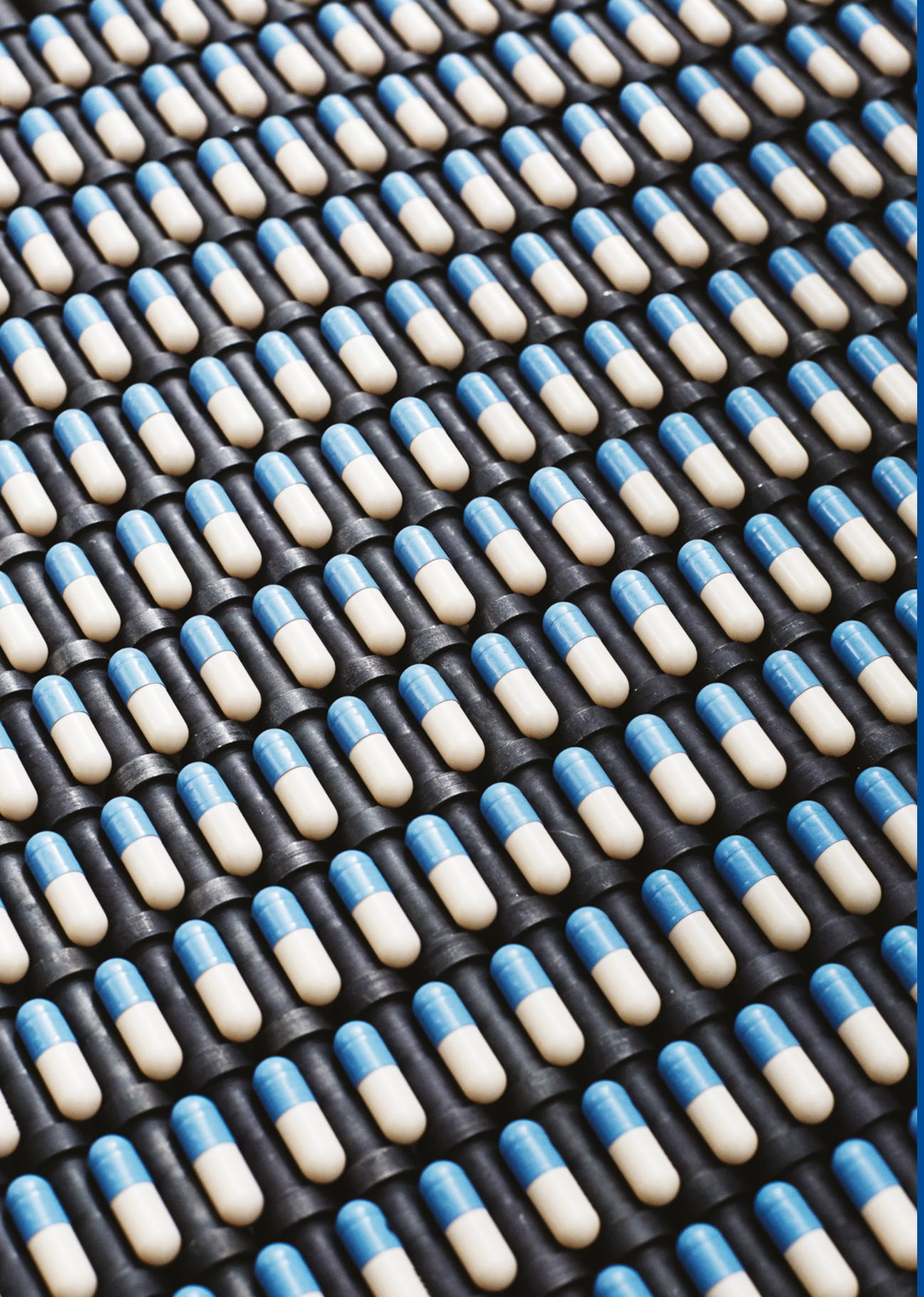
Quali-V®-I
Inhalation

HARD TWO-PIECE
HPMC CAPSULES FOR
PHARMACEUTICAL
APPLICATIONS
IN INHALATION

Qualicaps Engineered to perform



QUALICAPS®

HISTORY

Over one hundred years of experience in the manufacturing and filling of hard two-piece capsules

Qualicaps® originated within Eli Lilly & Co., as a capsule manufacturing plant in Indianapolis opened in 1897. This **century-long heritage** dictates a profound understanding of the needs of our pharmaceutical customers, for whom we have focused on delivering at **high-quality standards** since the very beginning.

Along with our innate **customer-centric perspective** that accompanies a lifetime of dedicated service to our customers, Qualicaps® also has a **proven record of innovation**. We were the first to develop a preservative-free gelatin capsule, the first to produce a pharmaceutical-grade capsule of vegetal origin with a dissolution profile similar to that of gelatin, and the first to design and offer a capsule for use in inhalation.

And beyond the capsules themselves, the Qualicaps® group offers a wide range of equipment to support the needs of solid oral dosage production, including capsule filling and sealing, visual and weight inspection, imprinting, and softgel manufacturing.

PARTNERSHIP

More than just a supplier, Qualicaps® is an implicated partner to our stakeholders

Qualicaps® is a **long-term capsule partner** for most of the leading global pharmaceutical companies, as well as for many relevant local and regional ones. We know that these customers value us in terms of quality, anticipation of market requirements, and flexibility to fulfill special customer needs.

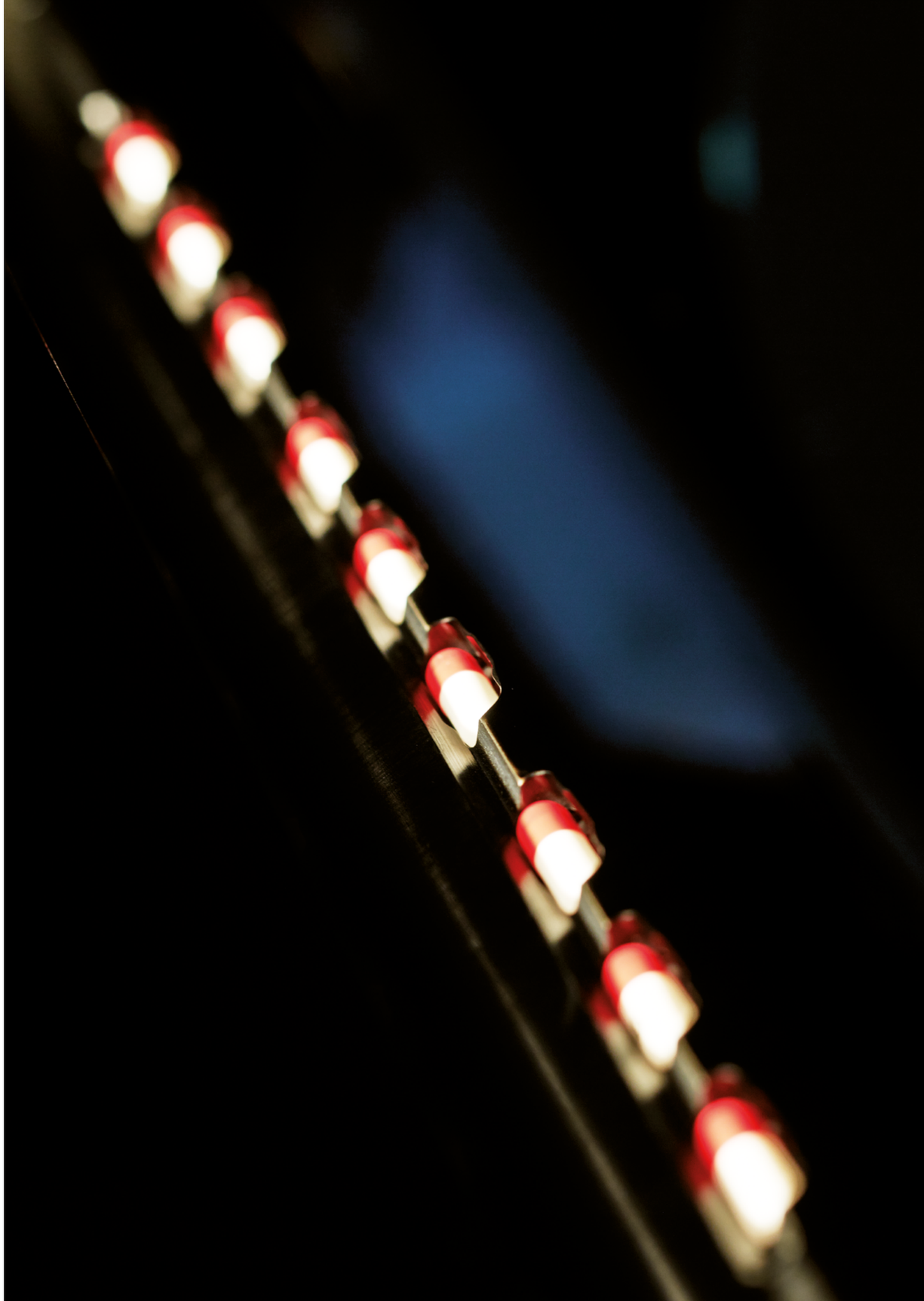
Our **global presence** in all major pharmaceutical markets and the stability and solidity we offer as part of **Mitsubishi Chemical Holdings Corporation** (MCHC) guarantee the assurance of supply necessary for successful product launches and ongoing market requirements.

The Qualicaps® team is comprised of not only expert commercial representatives, but also **highly knowledgeable and experienced personnel** that collaborate with both R&D and academia in more scientific endeavors, as well as technical engineers that support our customers' production centers in runnability and yields.

ENGINEERED TO PERFORM

QUALICAPS® CAPSULES ARE DESIGNED AND MANUFACTURED WITH FUNCTIONALITY AND PRECISION IN MIND AND DEED

- We take pride in engineering and producing each individual capsule with the objective of delivering superior performance
- We analyze performance from many perspectives: pharmaceutical-grade quality, productivity in filling machines, stability through shelf life, protection of the active ingredient contained within, and patient adherence and ease-of-use
- We not only offer high standards of performance from our capsules, but also from our team, made up of subject matter experts who collaborate with our customers on meeting their business goals



THE KAITEKI COMPANY

QUALICAPS® INTEGRATES THE “KAITEKI” PHILOSOPHY INTO THE BUSINESS

- Commitment to sustainable development for the benefit of individuals, society, and the Earth
- Value philosophy based on the management of three strategic pillars within the company: economy, technology, sustainability
- Contribution to the resolution of social and environmental issues through our products and services, and as a driver of innovation
- Collective consciousness and joint efforts among the 55,000+ employees of the Mitsubishi Chemical Holdings Corporation (MCHC) Group, of which Qualicaps® is a wholly-owned subsidiary

QUALI-V®-I CAPSULES FOR INHALED DRUG DELIVERY

CONTRIBUTING TO BRIDGE THE GAP BETWEEN MEDICINE AND TREATMENT

Inhalation delivery offers significant and unique benefits in the treatment of a variety of illnesses. The lungs serve as a portal of entry to the body that enables a drug to infiltrate the bloodstream from the airways in a time-effective manner, thus presenting inhaled formulations as **an interesting alternative to oral dosage forms, especially when a rapid response is required.**

INHALATION DRUG DELIVERY SYSTEM

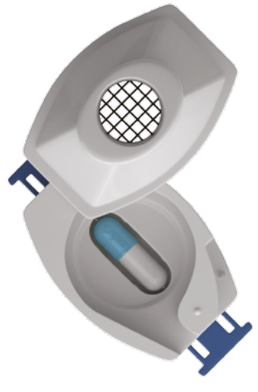
The main inhaled drug delivery systems are:

1. Nebulizers
The active ingredient is dissolved or suspended in water and can be delivered continuously over an extended period of time. Their size limits portability, thus limiting use to home or hospital.

2. Metered Dose Inhalers (MDIs)
The active ingredient solution within an MDI is dispensed from a pressurized aerosol container, which is small, portable, and simple to use. In the past, MDIs lacked dose counters and were not breath-activated, but today's MDIs possess both important features. Nevertheless, they still have an issue with emitting high doses, and therefore suspension formulations are generally limited to maximum doses of about 1 to 5 mg/actuation.

Originally developed for respiratory diseases, **DPIs have seen their use expanded recently to a growing field of therapies**, including antibiotics, insulin, opioids, oxytocin, vaccines, and drugs for neurological disorders.

3. Dry powder inhalers (DPIs)
DPIs are either single-dose devices filled with a capsule or a blister, or multi-dose devices that consist of a powder reservoir and dispensing system. DPIs are easy to use, as they are breath-actuated and do not contain propellants. Their particular characteristics make them the ideal delivery system for chronic diseases, for which patients must take doses at regular intervals.

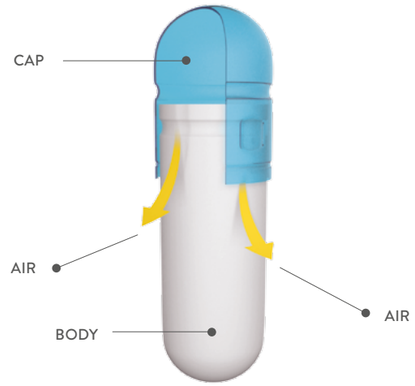


QUALI-V®-I CAPSULES

QUALI-V®-I CAPSULES ARE DESIGNED WITH SUPERIOR FUNCTIONAL PROPERTIES SPECIFIC TO INHALATION, FOR USE IN DRY POWDER INHALERS

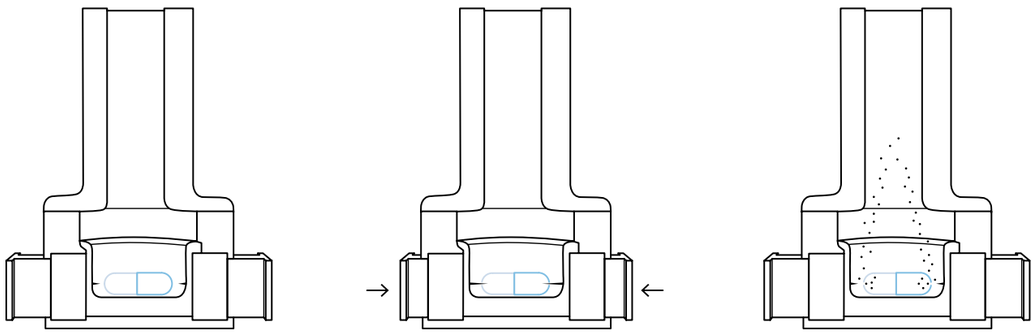
Strict Microbiological Control · *Better Aerosolization* · *Inner Surface Control* · *Reduced Powder Adhesion* · *Superior Puncturing Properties*

- **Pharmaceutical-grade quality**. The manufacturing process is carried out following strict pharmaceutical criteria and certified according to ISO 9001 and ISO 14001. Drug MasterFiles for the US and Canada have been registered.
- **Unique composition**. Quali-V®-I capsules have a special composition for use in dry powder inhalers. Based on Quali-V® hypromellose capsules, Quali-V®-I is also 100% plant-based, and is therefore free of animal ingredients. Also like Quali-V® and Quali-G™ gelatin capsules, Quali-V®-I does not use preservatives in its formulation.
- Quali-V®-I capsules are **continuously monitored by Quality Control experts** in the production process to ensure compliance with the most demanding of pharmaceutical requirements.
- All Quali-V®-I capsules are **inspected using an automatic camera system** to detect and remove defective units.
- Qualicaps® manufactures axial, radial and laser printing machines that provide a **superior print quality**. Laser technology is effective as an anti-counterfeit measure, as very fine details of logos are visually ascertained.
- Most DPI capsules are transparent, enabling the patient to verify that the dose has been correctly released upon inhaling (powder emptying). Quali-V®-I capsules are **available in a wide range of translucent colors**, developed in-house and made using market-accepted colorants.
- Quali-V®-I capsules are **available in size 3** (the most common size in inhalation) **and sizes 2 and 0** (for use with active ingredients that require higher doses).
- Qualicaps® offers weight-sorting to **customize capsule weight** and guarantee a maximum level of mass uniformity.
- Our scientists and subject matter experts can provide **R&D support** in capsule-form dosage delivery. Qualicaps® also has the luxury of tapping into resources available in the Mitsubishi Chemical Holding Corporation (MCHC) research laboratories.
- Quali-V®-I capsules have the required dimensions and strength that enable them to be filled and packaged on **automatic high-speed machines**.
- The **unique POSILOK® design** makes Quali-V®-I capsules suitable for high speed filling machines.
- Our technical service engineers can **assist in achieving productivity yields in capsule filling**, applying their vast knowledge and experience with leading equipment suppliers.



Quali-V®-I Inhalation

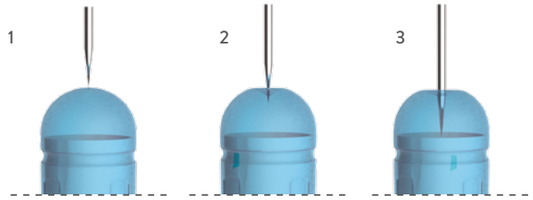
QUALI-V®-I CAPSULES ARE SPECIFICALLY DESIGNED FOR INHALATION WITH OUTSTANDING PROPERTIES IN TERMS OF PUNCTURING, MOISTURE CONTENT, POWDER AEROSOLIZATION, AND MICROBIOLOGICAL CONTROL



PUNCTURING

The grades of hypromellose capsules used in the manufacture of Quali-V®-I have been optimized for puncturing, and as a result these capsules have a moisture content slightly higher than that of Quali-V® capsules for oral dosage delivery (4.5% - 6.5% versus 4.0% - 6.0% respectively). Capsule punctures are more reproducible than for gelatin capsules, and less particles of the shell wall and resulting flap are shed in the process.

STAGES IN CAPSULE PUNCTURING



1. Pin comes in contact with capsule, cap or body.
2. Depression forms in dome of capsule.
3. Pin penetrates shell.

MOISTURE CONTENT

As the active ingredient in inhalation formulations is moisture sensitive, then the use of a capsule with low moisture content is optimal. Quali-V®-I has a moisture content of 4.5% to 6.5%, significantly less than the 13% to 16% in gelatin capsules used for this application. In addition, Quali-V®-I does not become brittle upon moisture reduction, capable of being dried to 1.0% RH without losing its physical properties.

AEROSOLIZATION

Aerosolization is a key parameter for powders to effectively penetrate deep into the lungs. Not only does capsule moisture content play an important role in aerosolization, but also the quantity of lubricant internal to the capsule shell. Since the use of lubrication is essential to the capsule manufacturing process, the amount applied to the stainless steel pins on which the capsule shells are formed is carefully controlled during production for the optimum level in aerosolization. In addition, Quali-V®-I capsules are made with an internal lubricant specially formulated for this application.

MICROBIOLOGICAL CONTROL

As active ingredients are inhaled directly into the lung, capsules for this delivery route require lower microbial levels than those used in oral administration. Qualicaps® complies with the microbiological requirements of Quali-V®-I capsules by the use of controlled manufacturing procedures that enable offering two specifications: the standard <100 cfr/g and the more stringent <10 cfr/g upon request. Strict process controls allow for these results without the use of preservatives.

Qualicaps® innovation: 1st in developing a hypromellose capsule with superior functional properties specific to inhalation

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