Moisture Control in Pharmaceutical Packaging:

Comparing Silica Gel, Molecular Sieve,and Equilibrium Technologies

Moisture is one of the most prevalent risks to pharmaceutical stability. From oral solid dosage (OSD) forms such as tablets and capsules to inhalation devices, fluctuations in humidity can compromise drug quality, alter dissolution profiles, and shorten shelf life. Excess moisture can catalyze hydrolytic degradation or polymorphic changes, while overly dry conditions may cause excipients and gelatin capsules to lose mechanical integrity.

Traditionally, packaging has relied on desiccants such as silica gel and molecular sieve to mitigate moisture ingress. These technologies remain widely used and effective in many applications. However, their inherent adsorption behaviours – either too gradual or too aggressive – do not always align with the specific needs of modern drug products. This has prompted interest in engineered equilibrium systems designed to maintain a target relative humidity (RH) rather than simply reducing it as far as possible.

This article reviews the strengths and limitations of silica gel and molecular sieve, and explores the role of equilibrium humidity stabilisers, such as EQIUS®, in balancing product stability with packaging efficiency.

Silica Gel:
Versatile and Economical Moisture Control
Silica gel, composed of amorphous silicon dioxide, has long been favoured in pharma-ceutical packaging. Its internal network of pores adsorbs water vapor through capillary condensation, allowing it to function across a broad RH range.

Advantages of Silica Gel

- **Cost-Effective and Scalable:** widely available, suitable for high-volume packaging with options to further moderate costs through bulk purchasing or optimised usage.
- **Versatile formats:** available as packets, canisters, capsules, or washers, adapt-able to different packaging designs.
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Limitations of Silica Gel

- **Limited efficiency at low RH:** struggles to achieve or maintain ultra-low humidity levels required by highly hygroscopic APIs or the amount of silicagel required to achieve low RH is very important.
- **Potential overdrying:** in certain cases, may reduce RH below optimal thresholds, causing gelatin capsule brittleness or tablet friability and can stress sensitive dosage form.

Silica gel remains a practical solution for many products where moderate moisture control suffices, but may fall short when precise or low-RH environments are essential.

Molecular Sieve:
Targeting Low RH with High Capacity
Molecular sieve, typically a crystalline aluminosilicate (zeolite), offers a sharper tool for moisture control. Its uniform pore sizes selectively adsorb water molecules, enabling aggressive uptake even at very low ambient humidity.

Advantages of Molecular Sieve

- **Strong low-RH performance:** effective in maintaining near-zero humidity, essential for APIs that degrade under even slight moisture exposure.

Limitations of Molecular Sieve

- **Risk of overdrying:** extreme adsorption can reduce humidity below the stability window for certain formulations, leading to capsule brittleness or altered drug release profiles.

Molecular sieve is therefore particularly useful for highly moisture-sensitive products, diagnostics, or biologics, but requires careful evaluation to avoid overdrying effects.

Beyond Traditional Desiccants:
The Role of Equilibrium Systems
While silica gel and molecular sieve provide broad moisture protection, their limitations underscore a key challenge: not all products benefit from an environment that is simply "as dry as possible." For many OSD forms and inhalation devices, stability depends on maintaining RH within a defined window rather than at extremes.

Equilibrium humidity stabilisers, such as EQIUS®, represent a different approach. Instead of adsorbing moisture indefinitely, these systems are engineered to buffer the internal package environment to a target RH – for example, 25–45% RH.

Working Principle of Equilibrium Systems
Equilibrium stabilisers are composed of materials conditioned to a specific RH. Once sealed within packaging, they act as a buffer – adsorbing or releasing moisture to maintain the defined equilibrium. This differs from conventional desiccants, which only adsorb.

Such stabilisation is valuable when product performance depends on avoiding overdrying. For instance, gelatin capsules may become brittle below ~30% RH, while tablets require strong moisture protection to prevent degradation or loss of efficacy.

Applications in OSD Packaging

- **Capsules:** Hard gelatin capsules are vulnerable to brittleness or cracking under excessively dry conditions. Equilibrium stabilisers help maintain capsule flexibility and integrity over time.
- **Tablets:** By controlling RH within the package, degradation pathways such as hydrolysis or polymorphic transitions can be minimised, supporting consistent dissolution and bioavailability.

Applications in Inhalation Devices

- **Dry powder inhalers (DPIs):** Powder flowability and aerosolisation efficiency depend strongly on moisture. Equilibrium stabilisers maintain consistent RH, safeguarding dose delivery.
- **Medical devices and biosurgery products:** Where device performance or sterility is influenced by environmental moisture, equilibrium solutions provide a controlled microclimate without extremes.

Regulatory and Industry Considerations

Moisture control strategies are increasingly guided by regulatory frameworks and quality standards. The USP <671> permeation test provides a benchmark for evaluating moisture barrier performance of pharmaceutical containers, while ICH Q1A stability testing underscores the need to simulate climatic conditions across global markets.

In this context, equilibrium technologies offer advantages in demonstrating compliance and predicting long-term stability. By maintaining a consistent internal RH, packaging systems can meet regulatory expectations for reproducibility and patient safety.

Strategic Implications for Packaging Science

From a broader industry perspective, equilibrium stabilisers illustrate the evolution of packaging from passive barriers to active environmental management systems. Rather than only protecting against moisture ingress, packaging can now actively regulate internal conditions to align with product needs – including avoiding excessively low humidity, which can be as detrimental as high humidity for certain sensitive products.

This shift supports a more holistic view of pharmaceutical stability, in which dosage form, excipients, packaging, and storage interact dynamically. For companies, it also provides a means of differentiating products by ensuring consistent performance across varied climates and distribution chains.

Conclusion

Silica gel and molecular sieve remain essential in pharmaceutical packaging, offering reliable moisture control for a wide range of products. However, both technologies have limitations silica gel may not provide sufficient low-RH protection, while molecular sieve risks overdrying and higher costs.

Feature	Silica Gel	Molecular Sieve	Equilibrium Stabiliser
RH range effectiveness	Low to medium	Very low RH	Targeted RH (e.g. 25–45%)
Risk of overdrying	Possible	High	None
Format flexibility	High	High	High
Suitability for capsules	Variable	Risk of brittleness	Maintains integrity
Customisation potential	Limited	Limited	High

Comparative Overview

Equilibrium humidity stabilisers, like EQIUS, go beyond traditional solutions by actively maintaining the precise RH level each product requires – unlike other desiccants that simply dehydrate. This tailored approach ensures optimal stability for oral solid dosage (OSD), capsule, and inhalation applications, protecting therapeutic integrity with unmatched precision.

As pharmaceutical formulations become more complex and global distribution grows, moisture control strategies will continue to evolve. Equilibrium systems mark a game-changing shift in packaging technology – from passive protection to adaptive, adaptive moisture management – ensuring medicines stay safe, effective, and reliable throughout their lifecycle.

Elisa Le Floch

Elisa Le Floch, Global Product Manager – Colorcon, has over 14 years of experience in active pharmaceutical packaging. At Colorcon, she is responsible for developing and deploying functional packaging solutions focused on improving drug stability and protection. Her expertise lies in controlling the drug microenvironment (moisture and oxygen), supporting pharmaceutical, nutraceutical and diagnostic applications. She leverages her background in pharmacy to maintain a practical, medicine-focused approach, always linked to real product use and patient safety.

Valère Logel

Valère Logel, Global Head of Innovation – Colorcon Functional Packaging, is a leading topic expert in the field of preservation packaging. With over 15 years of experience, he has led the development and market introduction of innovative packaging solutions for moisture control, oxygen adsorption and multi-layer polymer barriers.