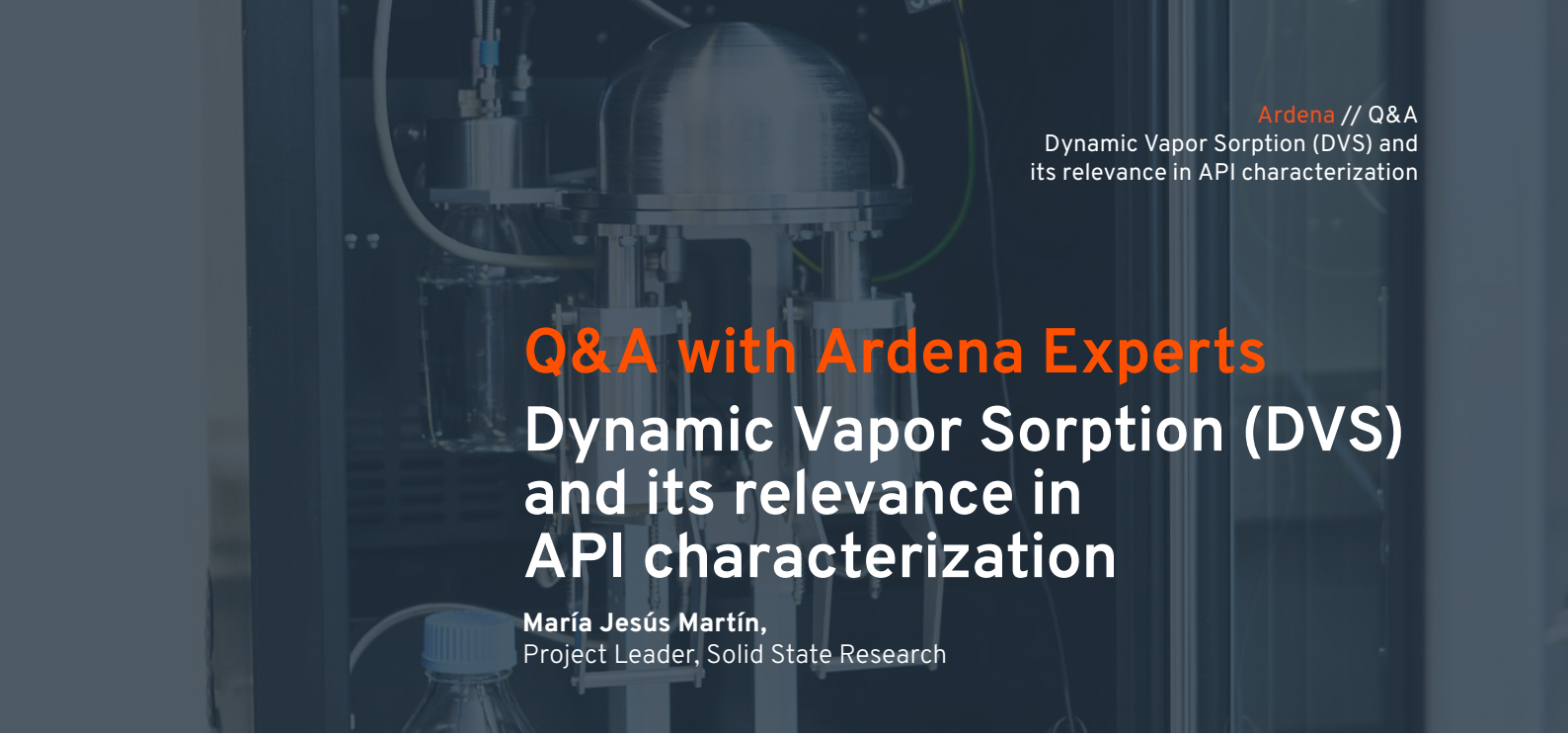

# Q&A with Ardena Experts

# Dynamic Vapor Sorption (DVS) and its relevance in API characterization

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*What is Dynamic Vapor Sorption (DVS)?*

DVS measurements involve exposing a solid sample to variable humidity conditions while continuously monitoring its weight change using a highly sensitive balance. The fundamental principles of DVS are based on the sorption and desorption isotherms, which provide information on the water-material interaction (adsorption or absorption), moisture sorption capacity and kinetics.

*Why is DVS important in pharmaceutical development?*

Information obtained from DVS measurements in the pre-formulation stage aids the selection of the optimal solid form of your API. DVS is a valuable tool for several reasons:

1. **Stability Studies**: API's can be sensitive to moisture and humidity, and their physical stability can be compromised in the presence of water. DVS is useful to investigate the water vapor uptake by the API over time. This helps in understanding and optimizing storage conditions to ensure the API's stability.
2. **Polymorphism and Hydrate Formation**: Crystalline hydrates usually have lower aqueous solubility compared to the anhydrous form. Conversion of an anhydrous form to a hydrate may impact the solubility and bioavailability of a drug substance. DVS measurements can highlight the relative humidity (RH) levels that induce the anhydrous-hydrate conversion. In addition, the isotherm sorption/desorption profile provides insight on the hydrate structure (channel hydrate or stoichiometric hydrate).
3. **Quality Control and Compliance**: DVS can be applied in quality control to ensure that API meet specific moisture content specifications.
4. **Drying Processes**: API synthesis often involves wet processes. DVS can be used to study the efficiency of drying processes and ensure that the API is free from residual moisture, which is essential for product quality and stability.

### *What equipment does Ardena utilize for DVS?*

DVS Adventure system from Surface Measurement Systems (London, UK).

Temperature range: 5-85°C.

RH range: 0-95%.

Camera: up to 60°C.

Possible to analyze highly potent API's

### *How does Ardena use DVS to study different solid forms of materials?*

DVS determination is part of our standard material characterization and can be used to investigate novel solid forms that are found in the investigations. We typically measure the material with XRPD analyses before and after a DVS measurement to determine if the solid form remained the same after the DVS measurement. Once we identified solid form changes due to different relative humidities, the material can be further analyzed with variable humidity XRPD. In addition, we can perform stand-alone DVS analyses with a specific aim, depending on the request of our customers.

### *What is the classification system for hygroscopicity?*

At Ardena we determine the hygroscopicity of polymorphs, salts, cocrystals and amorphous solids by DVS measurements.

The hygroscopic behavior is classified according to V. Murikipudi, P. Gupta, V. Sihorkar, Pharmaceutical Development and Technology, 2013; 18(2): 348-358 as follows:

| Hygroscopic class | Criteria* |
|---|---|
| Non-hygroscopic | <0.2% (w/w) |
| Slightly hygroscopic | 0.2-2% (w/w) |
| Moderately hygroscopic | 2-15% (w/w) |
| Very hygroscopic | >15% (w/w) |

** Percent water uptake at 25°C/80% RH in first adsorption cycle of sorption isotherm.*

The solid material subjected to DVS measurement is always analyzed by XRPD to verify any potential phase change.

### *What are the limitations of DVS?*

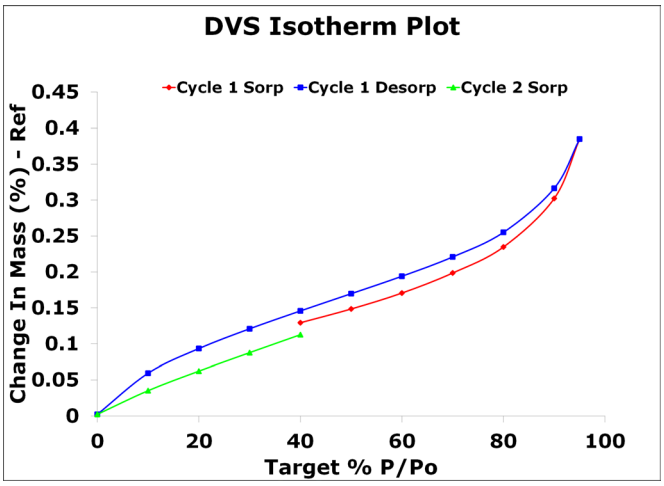
The DVS system has a temperature range between 5-85°C. Measuring at temperatures outside this range is not possible. Similarly, the technique is typically conducted at atmospheric pressure. If you need to study sorption behavior under different pressure conditions, DVS may not be suitable.

Finally, the size and shape of the sample can affect the results. Irregularly shaped or very small samples may not provide accurate data. DVS measures the material's sorption characteristics at its surface. It may not provide information about the bulk sorption properties of the material. Some materials may be sensitive to the dynamic sorption process, which can result in sample degradation or changes in the material's properties during the measurement.

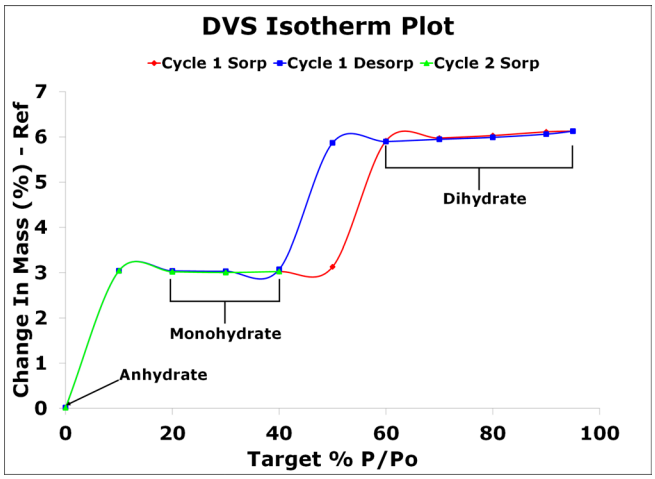
### *Can you provide examples of DVS profiles?*

Our default DVS method involves a RH profile 40-95-0-40% at a constant temperature of 25°C. The RH is changed in steps of 10%, after equilibrium is reached within dm/dt of 0.002% for 15 min or a maximum equilibration time of 6 h. Sorption and desorption cycles are shown as function of the RH %.

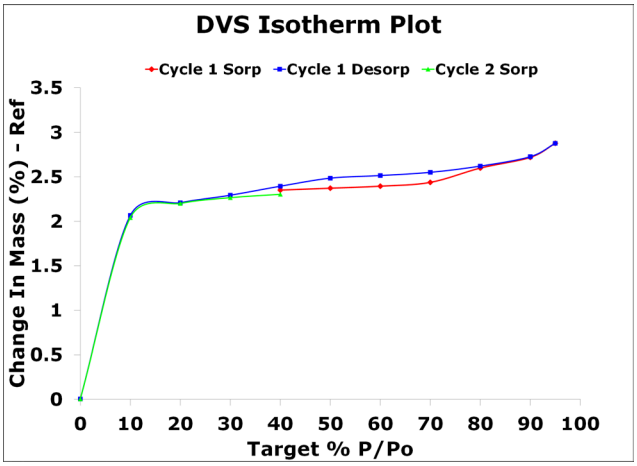
In the image below, the DVS sorption/desorption profile for a non-hygroscopic material is shown: the water vapor uptake at 25°C/80% RH was 0.1%:



In the image below, the recorded sorption/desorption profile shows hysteresis in the range 40-60% RH. Hysteresis usually suggests a phase change with formation of a hydrate by absorption of water molecules in the structure:




In the picture below, the typical sorption/desorption profile for a channel hydrate is observed: hydrated and dehydrated structures are isomorphic (i.e. no hysteresis during hydration/dehydration). Hence, the water sorption and desorption appear as overlapping reversible cycles.

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