Humidity Control in Pharma Processing

In conjunction with established cooling and heating systems, desiccant dehumidification technology can provide reliable and constant conditions all year round, resulting in better quality product and lower production costs.

By Simon Mills at HB Group

Simon Mills is Sales Director of HB Group Company, Sorption Wheel Services Limited. He has been working within the specialist area of desiccant dehumidification technology for 17 years, and has a wealth of experience in its application in all industry sectors including pharmaceutical, food and other specialist areas.

While traditional humidity control methods are still very effective, ongoing developments in desiccant rotor and dehumidification technologies provide unparalleled levels of relative humidity control and system efficiency. This article discusses the methods available, together with some of the benefits they can bring.

THE IMPORTANCE OF HUMIDITY

Even the simplest form of pharmaceutical manufacturing process can involve a range of steps before the finished product is packaged and finally reaches the consumer. These may include:

- Lab-scale development using glove boxes, small-scale process driers and coaters, and fluid bed driers
- Micronising
- Storage of powders or liquids
- Mixing
- Product drying
- Tablet compression
- Film coating
- Sugar coating
- Aseptic packaging
- Blister packaging
- Storage of the finished product

Throughout these processes, the effects of ambient humidity can have detrimental effects on product quality, yield, visual appearance and shelf-life – issues that can often effectively be avoided by the careful control of humidity in the production spaces.

Furthermore, R&D studies may have determined that a certain product either cannot successfully be manufactured, or may have significantly reduced yield at differing humidities. There can then follow a discussion about the balance of humidity control required at lab level, and the costs/benefits of these humidity controls once up-scale production is commenced.

It may also be true that some products cannot physically be produced without careful control of ambient humidities, as significant degradation of the product can occur above certain levels. Enzyme-based diagnostics, for example, are very susceptible to changes in humidities and to levels of relative humidity higher than 10%.

These control requirements are also affected by changes in the seasons, with summer conditions generally being worse than those in the winter (as far as airborne moisture is concerned). In a perfect world, summer conditions would be able to be controlled at winter levels, so that production rates remained constant throughout the year – leading to more reliable production.

HUMIDITY LEVELS

Generally speaking, a production suite can be maintained at or near to 45% relative humidity (RH) at a comfortable working temperature of 21°C using refrigeration-based air-handling systems, with either chilled water or direct expansion systems at their heart.

The issue of latent moisture load (from personnel, product or machinery) does, however, require careful plant selection to ensure that dewpoints within the air-handling plant do not approach 0°C with the attendant risk of freezing cooling coils.

At around 40% RH and 21°C, a potential issue arises with regard to the dewpoints necessary within the cooling plant, where conditions close to or at the freezing point of airborne moisture become necessary to achieve the required humidity control in the production area. This can lead to frozen coil surfaces, reduced air-flow through the plant, and a spiralling and rapid build-up of ice within the plant; defrost procedures are then
required, during which the conditions in the space may be lost. For onward validation and reliable production, this is obviously unacceptable.

It is also very important to realise that the delivery condition of air needed to meet the requirements of a room will always be less than the stated room requirements. Just as there has to be a difference in temperature between air entering a room or process to allow for heat gains within the room, where moisture has to be picked up, there has to be a similar difference in the moisture content of the delivered air.

LOWER HUMIDITIES

It is perfectly possible to achieve conditions of relative humidity well below 5% RH within a production space or packaging hall — or even within the enclosure of a tabletting machine, aseptic fill-line or coating pan, if this is what the particular product or process demands. These ‘micro-climates’ can represent a very cost-effective solution to production issues. These particular demands may have been introduced during the research phase, or may be due to other technical or product validation requirements.

A different type of technology is employed for these lower humidity conditions, and it is generally the case that for air conditions of less than 35 or 40% RH, the use of desiccant dehumidification technology needs to be considered. This technology is used extensively throughout the pharmaceutical industry and is a reliable method of producing controlled relative humidities in all areas of the process. It also provides for easily reproducible and constant production rates between winter and summer conditions, and between different locations — allowing production to be moved to another, more cost-effective base without having to worry about the effects of ambient humidity at the new location.

When very low RH conditions are required, care needs to be exercised in the choice of a working temperature. As the RH is lowered, the vapour pressure between the room and the operator is abnormally high, leading to increased evaporation from the skin and the impression of being cold due to the evaporative cooling effect. In these instances, it is usual to increase the dry bulb temperature in the room — typically to 23 or 24°C.

Particular benefits of the control of humidity levels as described include:

- Reproducibility of results
- Reduced friability during tablet compression
- Reduced drying time in fluid bed driers
- Improved appearance of coated tablets
- Reduced moisture retention in powders or liquid pharmaceuticals
- Reduced waste due to clogged machinery
- Reduced downtime due to cleaning requirements
- Improved packaging processes
- Improved shelf-life
- Reduction of micro-biological growth
- Reduction (or control) of static build-up

HOW DOES THE TECHNOLOGY WORK?

Desiccant dehumidification technologies work hand-in-hand with traditional refrigeration methods to create the required working conditions. Refrigeration is a very effective method of removing large quantities of moisture as a ‘first stage’ process; levels can then further be reduced using the desiccant dehumidifier.

The machines incorporate a rotor or wheel impregnated with a desiccant salt (usually silica gel) bonded to the surface of a corrugated structure. This typically offers a transfer surface to the air-stream of 2,500m² per m³ of media (on a macro scale), offering a highly efficient moisture-transfer medium. Construction of the rotors is such that a massive surface area is in contact with the air within a relatively small overall volume; quite often, therefore, the machines required to achieve a given humidity level can be very compact.

Within the machine, moisture is absorbed by the desiccant and air leaves at a much-reduced moisture content. This is delivered to the room and then further conditioned or mixed back into another air-stream to provide a lower ‘average’ condition for the space. Such is the efficiency of the desiccant dehumidifier that, usually, not all of the process air needs to be
conditioned and a mixing of air streams provides an adequate solution.

To remove the collected moisture from the dehumidifier, a second air-stream is heated using the available energy (typically steam, electricity, gas or hot water); this provides an environment for the moisture to be removed from the desiccant, leaving the building in a hot and (relatively) wet air-stream. At all times during this process, the moisture is adsorbed and desorbed in the vapour phase, meaning that no actual liquid is present at any time.

The absolute performance of this technology is determined by the method of application and, for processes where it is required, dewpoints as low as -60º can be achieved. This equates to a relative humidity of less than 1% RH at a sensible working temperature of 24ºC.

OTHER DESIGN CONSIDERATIONS

Generally speaking, RH levels as low as 20% do not need specialist room construction, as long as sensible housekeeping measures are employed. These include airlocks, the sealing of any wall and roof structures, and the minimisation of door openings and product transfer slots. Below this RH condition, the influence of ambient conditions surrounding the room will become increasingly relevant. In addition, the ambient air condition used in the design, and the quantity of air included for either personnel comfort or production requirements, becomes a major influence.

In the UK, for example, it is not unusual for the dehumidification requirements on a pharmaceutical production process to be designed to cope with an external ambient condition of 35ºC and up to 16g/kg. If the correct ambient design is not applied during the initial calculations, then there is a risk that the required RH in the space or process may not be met in the medium term due to general annual increases in the peak levels of ambient moisture as a result of overall climate change.

APPLICATIONS

As briefly discussed, there are many applications for this technology in a pharmaceutical setting. They include:

- Air onto fluid bed driers for product drying
- Air into micronising processes for powder stability and reduced static
- Air into tabletting machine enclosures for increased throughput and reduced tablet friability
- Air into coating machines for film- and sugar-coating
- Air for production suites in ‘whole process’ conditioning
- Air to packaging machinery for extended shelf-life
- Air at the same condition all year round to provide constant production rates
- Creation of a ‘micro-climate’ within the confines of a machine enclosure

PLANT REQUIREMENTS

Depending on the system requirements and the physical space available within any plant room, it may be preferable to incorporate the general air-handling components into a single machine, along with the dehumidification requirement. This will have a dramatic effect on the amount of space required.

Other features can be incorporated within such equipment, for example, cooling and heating requirements, high levels of filtration to HEPA, high system air pressures, control face and bypass arrangements, temperature and humidity control systems, and special finishes. Plant can be supplied in breakdown form for ease of installation and with electrical components to meet any existing site requirements or client preferences.

CONCLUSION

The technology available for the creation of these conditions has a proven reliability and performance track-record and, once installed, can provide the required conditions with minimal maintenance for upwards of ten years. Production rates can be set up either to meet previously established validation requirements or customer needs, and these can be maintained at all times of the year, or if the production process has to be removed to another location. In addition to the stable and reliable conditions achievable, there are added benefits in terms of reduced cleaning, improved product quality and lower drying times.

The author can be contacted at sales@dehum.com