

# Case Study

Pharma Automated Powder Dosing Solutions



## Enhancing Safety in the Laboratory – using Quantos and the QSE1

**There is a high level of awareness within the pharmaceutical industry of the hazards involved in handling drug compounds. One specific hazard is that of airborne contamination which is present during dispensing and handling procedures. Weighing out powdery, often hazardous substances on an analytical balance is an everyday task in the laboratory.**

The trend in pharmaceutical development is towards smaller particle sizes that are easily soluble, have a greater overall surface area per mg and reach deep into the lungs for faster effect. Whilst this makes drug delivery more effective, the trend towards micronized drugs consequently puts analysts at a greater risk.

### Pharma & Contract Research and Manufacturing Companies

Class II to V regulated compounds

Analytical Laboratories



Quantos QB1

METTLER TOLEDO

■ Obviously smaller particle sizes are also lighter and so will become airborne much more readily. The generation of smaller particle sizes using processes such as milling will generate more static effects and can mean substances react very energetically when sample containers are opened. From an analyst risk perspective these small particles can be inadvertently inhaled and of course will be able to react very effectively.

The weighing process has been identified as the most obvious risk of exposure to airborne contaminants due the way in which the analyst works with a balance. Open bench weighing (weighing without the use of an enclosure system) is not recommended for active drug compounds and it is standard industry practice to enclose the weighing process if an active or potent drug is to be handled.



### Exposure risks

■ Exposure to potent compounds can occur through four main routes:

**Inhalation** is the most effective route for absorption of drugs into the blood stream. Inhalation drugs ideally need to be below 10 microns. 1-5 micron particle sizes can reach deep into the lungs where they can be transferred into the blood stream fast. Particle sizes from 5-10 microns can easily be inhaled but will typically be trapped in the nasal passages and branching airways where they will be trapped or dis-

solved. Even particle sizes in the 50-100 micron range can be inhaled easily. At this size, however, they will also be visible which will make the inhalation hazard more apparent to the analyst.

**Digestion** is an obvious exposure route and although it may be painfully obvious to the analyst not to swallow the drugs they are developing, poor hygiene control when leaving the laboratory may mean drug transfer from hands to food can occur.

**Dermal absorption** of drugs can also occur very easily. When cleaning surfaces with solvents, drugs can easily be transferred through the skin if gloves are not worn or are damaged.

**Touch contamination** can occur easily if the analyst transfers contamination from a glove to mucus membranes either in their eyes or nose simply by not being aware and making adjustments to glasses or face masks.

The development of more effective, higher potency drugs has great advantages for patients, as lower dosage forms have greater effectiveness over longer periods. However, there will be greater risk for the analyst, as smaller physical quantities of the drug will have greater pharmacological effects to the analysts exposed to these compounds. There will be an increased risk of over-exposure and active drugs will have effects at nanogram levels. Another danger is that at these levels, the airborne exposure simply cannot be seen!

### Automation - a safer alternative

■ Mettler Toledo has addressed the everyday challenge of manually weighing hazardous substances with Quantos, an automated powder dosing system complete with process-specific safety enclosure. Implementing automation instantly reduces the risk of repeated exposure to a hazardous substance.

The Quantos dosing head is initially loaded with the active compound and then repeated sample dispensing can begin. An

RFID chip embedded in the dosing head stores relevant information such as substance ID, amount dosed and the date. Once the dosing head is charged, the vial or bottle is stored with the head attached, avoiding the need to re-open during the lifetime of the dosing head. After a maximum of 500 doses the dosing head can be safely disposed of, avoiding unnecessary and time-consuming cleaning procedures and further risk of exposure.



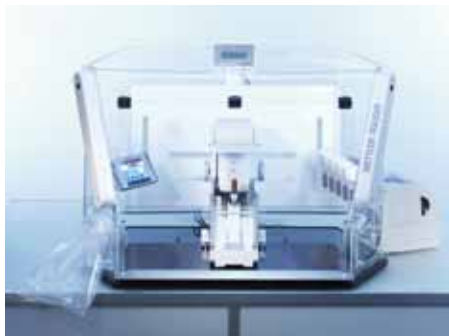
An added benefit of automation is the controlled and reproducible manner of processing. Quantos dispenses accurately and reproducibly down to 1mg (10 mg USP) into vials with an opening as small as 6 mm diameter. Eliminating spillage immediately increases process safety and results in cost savings due to less substance waste.

An analyst manually weighing 100 mg inside a safety enclosure typically takes 2-3 minutes per weighing. Quantos speeds up the weighing process itself to increase overall throughput, and perhaps more importantly, the drug is handled quickly and efficiently to reduce the time for airborne contamination and exposure to occur. 1mg - 250 mg is dosed in 30 – 60 seconds and the system can be operated from outside a glove box. Up to 30 doses of a single substance can be achieved automatically, without user intervention using an optional autosampler (Quantos QS30).

### Safety features of Quantos and QSE1

■ It is worth identifying that the weighing procedure is probably the most common procedure carried out within a laboratory

and also the fact the analyst will be in close proximity to the drug if manual weighing is employed - typically within 300 mm - which is recognised as the breathing zone.



Employers have a responsibility to minimise this risk and a first line of defence is the use of personal protective equipment, which can range from gloves and safety glasses to masks and even whole body suits. Additionally, regulation requires that hazardous substances must be weighed in a containment system. Whilst these measures increase personnel safety, they are often uncomfortable and restrictive, resulting in longer process times and increased risk of substance spillage. Hygienists and safety managers aim to engineer out the use of personal protective equipment by introducing containment technologies or improved sample handling techniques. Quantos and the QSE1 offer an efficient combination of both strategies.

Exposure risk can be significantly reduced by the correct selection of containment system for the process being carried out.

**al Safetech**, a leading supplier of containment technologies, has worked closely with Mettler-Toledo to develop the QSE1, a purpose-built safety enclosure for the Quantos powder dosing system. It is ideally suited to the process of weighing powders and specially designed for ergonomic operation that is ideal for relieving the inconvenience of manually working inside an enclosure, especially with restrictive personal protective equipment. Together they offer the ideal solution to address safety risks.

A Quantos and QSE1 system combination

provides an ECL of  $< 10 \text{ ng/m}^3$  which is at the limit of current detection levels, due to the following safety features:

1. The QSE 1 is specially designed to be an ergonomic working environment. It has easy access features for more comfortable daily operation, such as:
  - Keypad/terminal holder
  - Sample and dosing head storage rack
  - Label printer dispenser
  - Easy to clean
2. Integral instrument and work surface LED lighting allow good visibility within the workstation
3. It has a turbulence free airflow, in order to allow the Quantos instrument to operate efficiently
4. There are in-built waste disposal chutes on either side of the enclosure which helps the operator to maintain a well-organised and safe work area.
5. The QSE1 has a safe change HEPA filtration system tested to EN1822.
6. A FlowTech Dual Sensor alarm system measures the airflow across the face of the enclosure at two locations and warns the user in the event of an airflow failure.
7. The system has a polished black granite base, for added chemical resistance and durability, allowing easy visibility of contaminants.
8. The QSE1 has superior safety and containment performance, proven by independent safety testing, which is described in more detail later in this document.

In addition, the QSE1 is also a low energy use portable system.

Quantos is not a standard balance. It is a weighing station. It has an organised work area, with power and data cabling hidden. QSE1 encourages the analyst to work in a controlled and safe manner. Quantos takes far more control of the weighing procedure

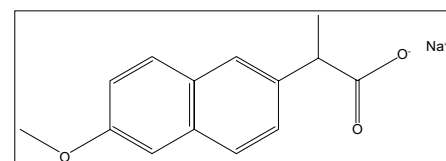
than a standard balance system because the way in which a Quantos system is used minimises the risk of exposure. Dispensing the drug from a sealed container reduces the risk of airborne contamination. Dispensing the drug compound automatically eliminates the handling of a drug with a spatula. Dispensing the drug compound from directly over the sample vial eliminates the risk of spillage.

### Safety performance evaluation

■ Containment system performance testing is a critical step and the Quantos Safety Enclosure QSE1 has been independently tested using surrogate sampling techniques to ISPE guidelines in accordance with EN689 sampling techniques.

European Standard EN689 provides a methodology based upon statistical principles to assess whether an occupational exposure limit of an airborne substance will be exceeded. The principles can be applied to establish control performance, area airborne concentrations and personal exposure.

Naproxen Sodium, a non-steroidal anti-inflammatory drug (NSAID), was chosen as the surrogate material, instead of the more commonly used alternative of lactose, because it represents a more rigorous challenge than lactose when evaluating the performance of a control device. It has the same physical properties as many active drug compounds such as small particle size and due to the crystalline structure and electrostatic nature of the powder. It becomes airborne easily and tends to be attracted to surfaces in the close vicinity. It is of low toxicity (OEL  $5 \text{ mg/m}^3$ ) and a highly sensitive analytical method is available which allows detection of  $5 \text{ ng/m}^3$  in air over a 25 minute period.



Samples were collected during operation of the Quantos QB1 weighing system both within the QSE1 Safety Enclosure and on the open bench. Both area sample and personal samples (in the operator breathing zone) were collected during each evaluation. To assess variability in control performance the automated weighing operations were conducted three times. The procedure consisted of weighing three different quantities (50 mg, 100 mg, 250 mg), repeated five times.

The results obtained from this evaluation showed that Quantos in the QSE1 provided airborne ECL (exposure control limit) of

< 10 ng/m<sup>3</sup> compared to Quantos directly on an open bench which produced airborne concentrations not normally exceeding 67 ng/m<sup>3</sup>.

### Conclusion

■ A range of safety measures can be implemented to improve the process of handling and dispensing of hazardous substances. These include automation of the dispensing process, namely with the Quantos systems, and implementation of appropriate containment technology, such as the QSE1 - a safety enclosure specifically designed for Quantos by a1 Safetech.

The use of Quantos in a safety enclosure compared to manual weighing in a safety enclosure offers significant benefits in speed and savings, due to higher throughput and reduced wastage and cleaning time, as well as important safety aspects such as reduced exposure of analysts to the substances.

Quantos offers a solution to reduce the overall exposure risk, combining accurate automated powder dosing with a process-specific containment system.

► [www.mt.com/quantos](http://www.mt.com/quantos)

## Specifications

### Quantos Technical Data

Balance	In standard range	In fine range
Maximum load	220 g	81 g
Readability	0.01 mg	0.005 mg
Repeatability (1 - 250 mg) with < 20 g preload		0.003 mg
Repeatability (1 - 250 mg) with < 80 g preload		0.004 mg
Typical minimum weight (USP 0.1%)		10 mg
Typical minimum weight (1%, 2sd)		1 mg
<b>Typical Dosing</b>		
Dosable substances	80 - 90% of free-flowing powders	
Dosing repeatability (typical sample sizes 50 mg)	< 0.5mg	
Dosing speed (50 mg)	20 - 30 sec	
Minimum dosing quantity	1 mg	
Maximum dosing quantity	250 mg	

### QSE1 Safety Enclosure

Dimensions (width x depth x height)	770 x 790 x 1200 mm
Bench space required	1600 x 800 mm
Height of working opening	225 mm
Base material	Black polished granite
Filtration efficiency (HEPA H14)	99.995% by particle size of 0.3 µm
Extracted / supplied air volume flow	306 m <sup>3</sup> /hr
Face velocity (Lo to Hi)	0.3 - 0.45 m/s (approx.)
Exposure Control Limit (ECL)	< 10 ng/m <sup>3</sup>
Electrical connection	100 - 240 V, 50/60 Hz
Power consumption	3300 W

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