

# Quantos Automated Dosing



## **Solution Preparation**

Precise concentrations

Process compliance

Minimize out-of-specs



## **Gravimetric Sample Preparation** The Alternative to Volumetric Flasks

**METTLER TOLEDO**

# 75 Years of the Volumetric Flask

## Remove the Errors in Sample Preparation

### History of the Volumetric Flask

Volumetric flasks have been produced with similar accuracies to what we have today for at least the last 75 years. Although instrumentation has dramatically improved, sample preparation methods have remained unchanged for nearly a century.

### Why Change from Volumetric to Gravimetric?

The two largest sources of laboratory errors come from sample processing and human operations. In addition to errors, the amount of laboratory time spent processing samples is estimated to be greater than 60%. Implementing a gravimetric sample preparation system reduces laboratory errors and Out-of-specification (OOS) incidents by up to 50 percent, while increasing laboratory efficiency.

### Make the Shift with Quantos

Quantos addresses the weak link in pharmaceutical analysis with gravimetric sample preparation. It is an innovative way to minimize the variability in sample processing and reduce the labor requirement.

No more

- Incorrect weighing
- Volumetric flask errors
- Transcription errors





Avoid manual volumetric sample preparation errors

# The Alternative to Volumetric Flasks

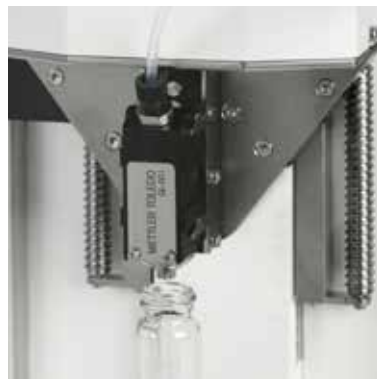
## Automated Gravimetric Sample Preparation

**Prepare powder, liquid, gel, and paste samples quickly, easily and error-free. Weigh your sample and Quantos will add the correct amount of solvent, by weight, to reach your target concentration – flawless accuracy in a fraction of the time.**

With gravimetric sample preparation, as defined in USP <1251>, the exact amount of substance dispensed, whether manually with a spatula or automatically using a dosing head, is recorded. This actual weight is used to precisely calculate the amount of solvent needed to reach the target concentration. The automated liquid dosing head delivers the correct amount of diluent to the container, based on the actual weight of sample. Save time manually trying to reach the precise sample weight, as the liquid dosing compensates for under or over-shoot to achieve the perfect concentration.

### Ideal for preparing:

- Analytical standards
- Stock solutions and final concentrations
- Multi-component standards



### Eliminate Variability & Errors

- Replace error-prone and subjective volumetric processes
- Avoid data transcription and labelling errors with traceable automated data management

### Boost Productivity

- Prepare more accurate concentrations in less time
- Don't waste time trying to weigh difficult samples precisely
- Gravimetric liquid dosing compensates

### Prepare Only As Much As You Need

- Not restricted to size of volumetric flask available
- Prepare smaller samples and save precious substance
- Use less solvent and create less waste for disposal



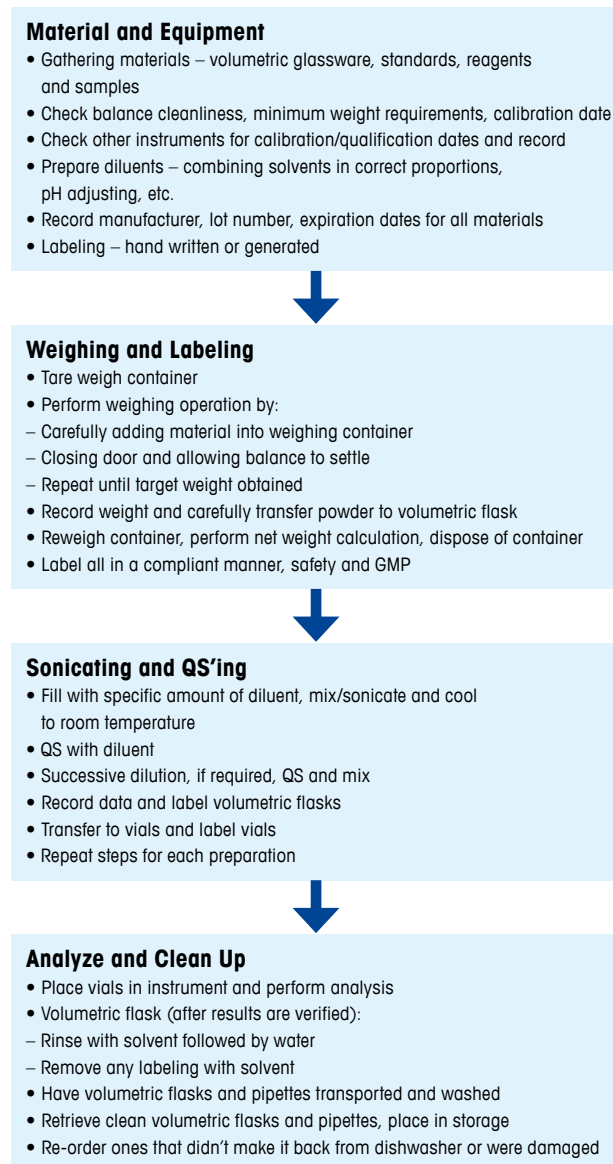
Prepare Concentrations With Confidence

# A New Era

## Leading Experts Are Paving the Way

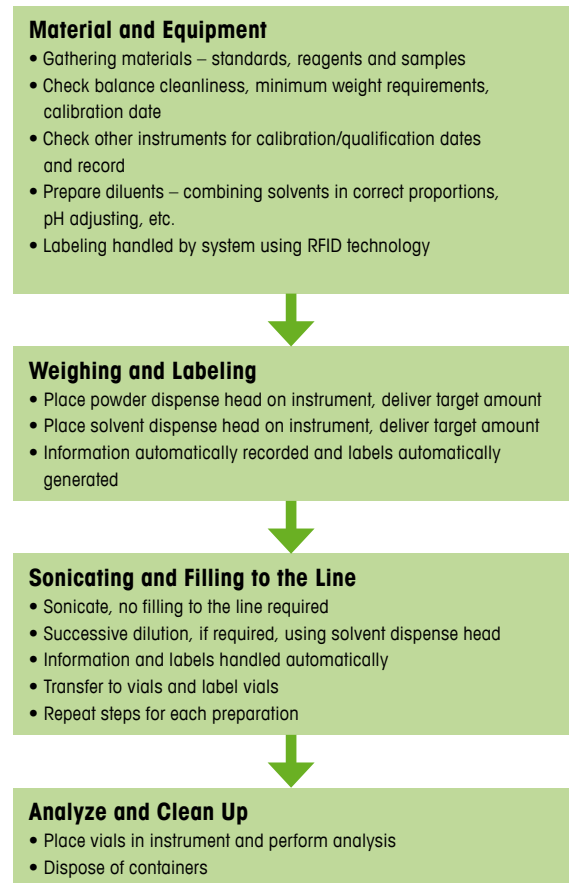
**Top pharmaceutical companies and experts alike have welcomed the technology that now provides a practical approach to gravimetric sample preparation.**

### Simple sample preparation process



**Total 22 steps**

### New gravimetric process



**Total 15 steps**



**Pfizer's Analytical Research and Development Group (AR&D) in Groton, USA has performed detailed studies that compare the differences between preparing samples and standards using manual volumetric processes and the new automated gravimetric methods.**

	<b>Manual Prep</b>	<b>Automated Prep</b>	<b>Difference</b>
<b>Amount of substance</b>	20 mg solid +50 mL diluent	5 mg solid +12.5 g diluent	<b>Save 75% substance</b>
<b>Time</b>	50 mins (total) 35 mins (FTE)	30 mins (total) 10 mins (FTE)	<b>Save 70% labour time</b>
<b>Precision</b>	%RSD = 1.67	%RSD = 0.49	<b>Improve precision x 3</b>

Reproducibility and precision:  
Comparison between manual and automated gravimetric sample preparation.

	<b>Manual Prep</b>	<b>Automated Prep</b>	<b>Difference</b>
<b>Sample size</b>	100 mL diluent	10 g diluent	<b>Save 90% substance</b>
<b>Time</b>	60 mins (total)	45 mins (total)	<b>Save 25% time</b>
<b>Correlation coefficient</b>	0.99473	0.99998	<b>Improved to near perfect</b>
<b>Unknowns (% intent)</b>	97 – 100 %	100 %	<b>Improved to near perfect</b>

Linearity:  
Comparison between manual and automated gravimetric sample preparation.



**“Sample preparation is an analytical workflow focus area. A targeted automated (gravimetric) sample preparation approach with Quantos has demonstrated improved precision, reduced sample and solvent consumption and less analyst time as compared to manual approaches.”**

Gang Xue  
Associate Research Fellow  
Pfizer ARD

# Make the Shift with Quantos

## Trust in Compliance

**Gravimetric sample preparation requires a switch from expressing concentration in mg/mL to mg/g. Although this may require a change for some laboratories due to existing SOPs, revalidation is not required and the benefits are considerable.**

### **Gravimetric Dosing Officially Recognized in USP <1251>**

Gravimetric dosing was introduced as an accepted method of weighing in the December 2013 revision of USP <1251> Weighing on an Analytical Balance. The definition states that "Gravimetric dosing typically is used for sample and standard preparations or capsule filling. For such weighing the analyst places the volumetric flask, vial, or capsule shell on the balance; tares the balance after the balance display stabilizes; adds the solid or liquid components into the receiver by means of dosing units; and records the respective weights."

### **Regulatory Basis for Revised or Alternative Procedures**

In the General Notices, USP indicates that "alternative methods and/or procedures may be used if they provide advantages in terms of accuracy, sensitivity, precision, selectivity", further stating that they should be validated as described in General Chapter <1225> Validation of Compendial Procedures. Since introduction of gravimetric procedures for preparation of analytical solutions is an improvement in terms of precision, the change is acceptable from the viewpoints of both the FDA and USP, and can be filed in an Annual Report as a minor change.

### **Implementing Changes to New or Existing Methods**

USP <841> Specific Gravity has been revised to allow the preparation of solutions gravimetrically: "Where the density is known, mass can be converted to volume, or volume converted to mass, by the formula:  $\text{volume} = \text{mass}/\text{density}$ ". In the case of an existing volumetric method, where the density of the analytical solution is known (or can be determined empirically), a straightforward conversion between volume and mass may be made. When new methods are being developed, the developer has the option of either incorporating specific gravity into the procedure, or simply using the GraviPrep approach and describing the sample preparation in terms of mass of solid and mass of solvent to be used.







► [www.mt.com/q-graviprep](http://www.mt.com/q-graviprep)





For white papers and webinars



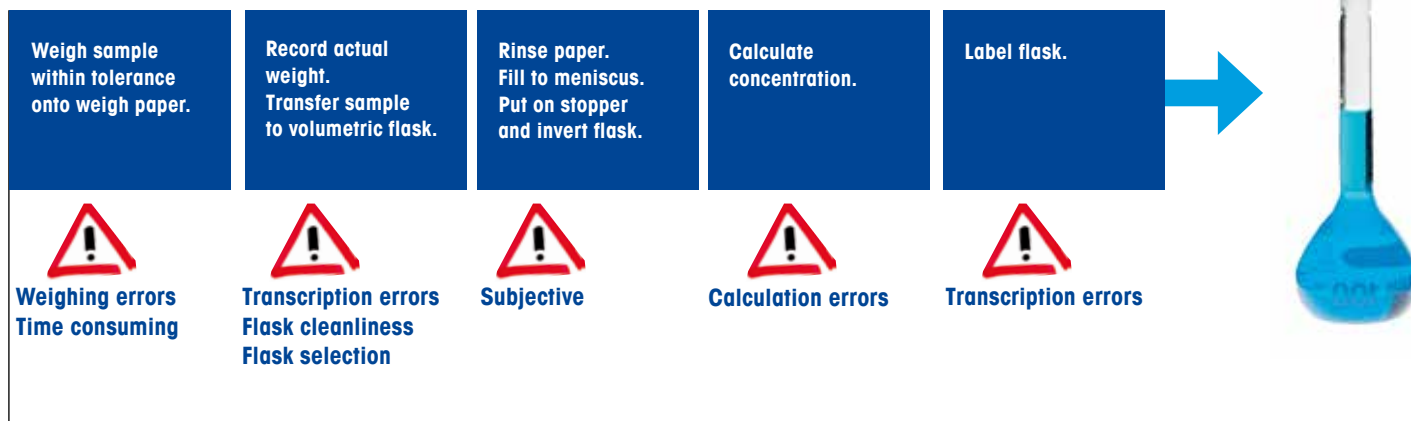
Manual process







Time consuming & source of up to 50% of errors in an analytical workflow

XPE Configuration	Step	Manual	Automated
<b>XPE balance + Volumetric flask</b> 	Sample weighed:	✓	✗
	Diluent calculated:	✓	✗
	Diluent added:	✓	✗
<b>XPE balance + Liquid dosing module</b> 	Sample weighed:	✓	✗
	Diluent calculated:	✗	✓
	Diluent added:	✗	✓
<b>XPE balance + Powder dosing module + Liquid dosing module</b> 	Sample weighed:	✓*	✓
	Diluent calculated:	✗	✓
	Diluent added:	✗	✓
<b>XPE balance + Powder dosing module + Liquid dosing module + LabX Software</b> 	Sample weighed:	✓*	✓
	Diluent calculated:	✗	✓
	Diluent added:	✗	✓

\* The system can also be used as a manual XPE balance, even when equipped with the Quantos powder dosing module. So, non-free flowing powders (i.e. sticky powders, pastes, gels, tablets or liquid samples) can be weighed manually. You still get all the benefits of gravimetric sample preparation, such as automated diluent dispensing to achieve a precise concentration based on the amount of sample weighed out.



Process Description	Output	Application Suitability
<p>Weigh sample precisely into volumetric flask with spatula (or onto weigh paper, then transfer into volumetric flask).</p> <p>Manually calculate sample weight and size of volumetric flask required based on concentration required.</p> <p>Fill to the line with pipette to prepare required concentration.</p>	 Volumetric = risk of errors	<ul style="list-style-type: none"> <li>• Sample preparation</li> <li>• Standard preparation</li> <li>• Stock solution preparation</li> </ul>
<p>Manually weigh sample approximately, directly into vial.</p> <p>Calculated automatically based on sample weight and target concentration.</p> <p>Precise gravimetric solvent dispense with liquid dosing head.</p>	 Required concentration prepared - error free	<p>As above. Ideal when:</p> <ul style="list-style-type: none"> <li>• Samples are difficult or slow to weigh precisely with a spatula or syringe</li> <li>• Very limited quantities of sample are available</li> <li>• Samples are not prepared repeatedly</li> </ul>
<p>Automated dispense of free-flowing powders. Manual for other samples. Approximate weight, directly into vial.</p> <p>Calculated automatically based on sample weight and target concentration.</p> <p>Precise gravimetric solvent dispense with liquid dosing head.</p>	 Required concentration prepared - error free	<p>As above. Ideal when:</p> <ul style="list-style-type: none"> <li>• Same powders are weighed repeatedly, e.g. standards</li> <li>• Powders are expensive or precious</li> <li>• Powders are toxic or highly potent</li> </ul>
<p>Automated dispense of free-flowing powders. Manual for other samples. Approximate weight, directly into vial.</p> <p>Calculated automatically based on sample weight and target concentration.</p> <p>Precise gravimetric solvent dispense with liquid dosing head.</p>	 Required concentration prepared - error free	<p>As above. LabX software enables:</p> <ul style="list-style-type: none"> <li>• Serial dilutions</li> <li>• Multi-component standards</li> <li>• Ability to convert between mg/mL and mg/g</li> <li>• Automated data management</li> <li>• Development and implementation of SOP-specific workflows</li> </ul>

# Application Specifications

Quantos gravimetric liquid and powder dispensing is available for a range of balances. The minimum sample weights for GLP/GMP and USP are listed below.

Sample Preparation	Volumetric	Gravimetric		
Configuration	<ul style="list-style-type: none"> <li>• XPE205</li> <li>• Volumetric flask</li> </ul>	<ul style="list-style-type: none"> <li>• XPE205</li> <li>• Liquid module</li> </ul>	<ul style="list-style-type: none"> <li>• XPE205</li> <li>• Powder module</li> <li>• Liquid module</li> </ul>	<ul style="list-style-type: none"> <li>• XPE206DR</li> <li>• Powder module</li> <li>• Liquid module</li> </ul>
Sample dispensed	Manual (with spatula)	Manual (with spatula)	Automated or manual*	Automated or manual*
Calculation of amount of diluent required	Manual	Automatic (based on actual sample weight)	Automatic (based on actual sample weight)	Automatic (based on actual sample weight)
Diluent dispensed	Manual (with pipette)	Automated	Automated	Automated
Diluent units	mL	g	g	g
Concentration units	mg/mL	mg/g	mg/g	mg/g
USP Minimum Weight** (0.10%, k = 2,5% load)	14 mg	14 mg	10 mg (automated) 14 mg (manual)	7 mg (automated) 10 mg (manual)
Minimum Weight*** (U=1.0%, k = 2,5% load)	1.4 mg	1.4 mg	1.0 mg (automated) 1.4 mg (manual)	0.7 mg (automated) 1.0 mg (manual)

\* = Automated powder dispensing for free-flowing powders. Manual dispensing for sticky powders, pastes, gels, liquid samples, etc.

\*\*\* = typical value

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

For more information

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