AUTOMATION OF SOLID/POWDER DISPENSING

much needed, but cautiously used!

This article investigates solid/powder dispensing in pharma and biotech, examines where it is most used, whether there exists a need to apply automation and what is motivating its wider use today. It reveals how concerns over problematic solids and the dispensing technology itself have hampered the perception that automation is a realistic proposition and led to the widely held industry view that automation cannot completely substitute for manual weigh outs. The article reviews the technologies and vendor offerings that are currently available to support the automation of solid/powder dispensing, and discusses their suitability for different dispense modes and as tools to open up new application areas. It concludes there are strong grounds for optimism regarding the wider deployment of automated solid/powder dispensing systems over the coming years.

By Dr John Comley

Many compound storage facilities are also referred to as compound dispensaries, highlighting the role that these labs have historically offered and still provide. On visiting such facilities in pharma and biotech it is not unusual to see rows of extraction hoods, each equipped with a micro-balance and a technician performing manual transfers. Given the variation in the types of solid encountered, many in the industry still think manual weighing is the best, if not the only, realistic approach to dispensing and transferring solids, although it is one of most tedious and time-consuming tasks expected of lab scientists. Over the past decade some companies have applied automation to solid dispensing, mainly based around the 'Archimedes Screw' mechanism (see **Figure 1**). However, the extent to which early Archimedes Screw devices were deployed was initially limited by the type of storage vessel the screw could be applied to, the significant starting mass requirement (ie to fill the device and the screw), the minimum dispensed mass and the flow properties of the solids themselves. Compound management groups are now responsible for the stewardship and distribution of solids. In early

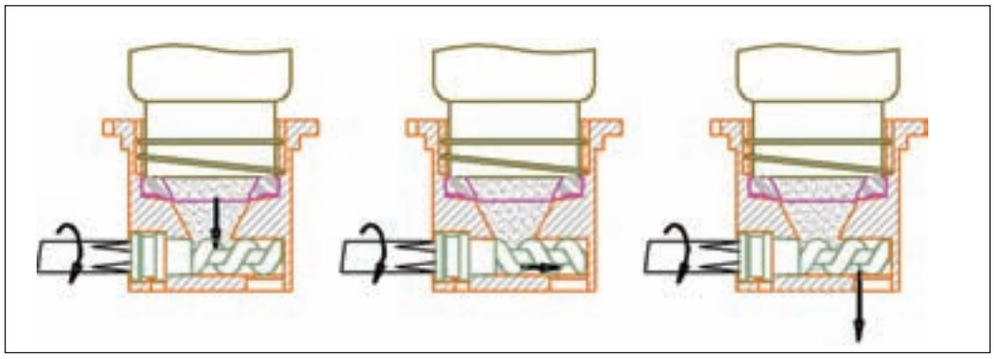


Figure 1
Schematic of the 'Archimedes Screw' dispensing mechanism offered in Mettler-Toledo's FlexCap2 device. As the screw is turned solid is moved from storage in the vial to the dispense outlet where it is displaced by tapping (left to right image)

Figure 2: Most used applications of solid/powder dispensing

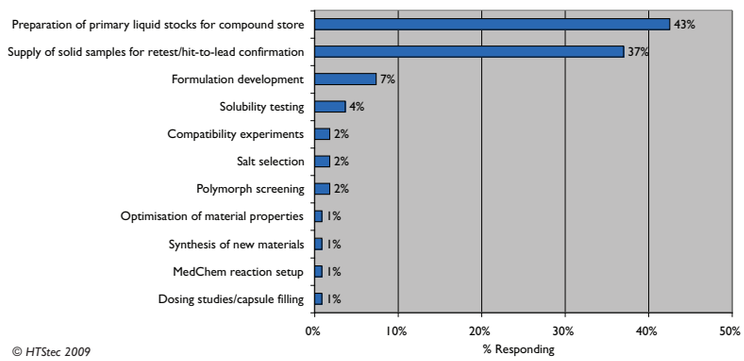
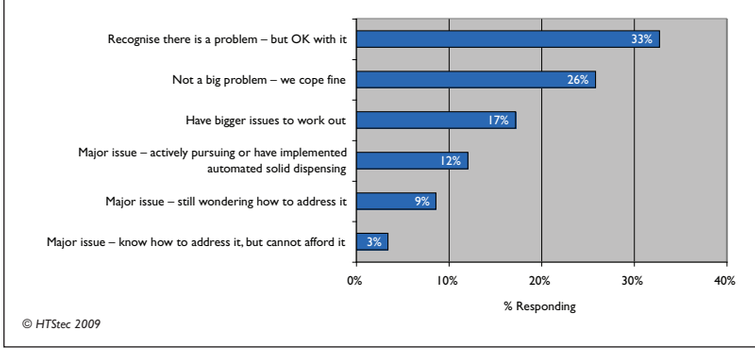


Figure 3: Size of solid/powder dispensing problem



discovery you typically have a large library (or deck) of compounds (in some cases several million accessible solids) and the need to regularly replenish your liquid library. This leads to large jobs of single dispenses from 1,000s of compound powder source vials into separate dissolution vials (ie if this process is fully automated it is usually referred to in the industry as many-to-many dispensing). To make this task more difficult, many compounds today are only available in limited (10-100mg) amounts and accurate dispensing (+/- 0.1mg) of minimal (less than a few mg) quantities is increasingly wanted. For downstream activities it is necessary to go back to solids to supply fresh compound for retesting, for some preclinical efficacy and ADMEtox studies, and even formulation testing which will trigger a few additional one-to-one or one-to-few dispenses, although some of these may have larger or more variable solid mass dispensing requirements. Finally, when clinical trials are initiated there may be the need to dispense a single solid into an array of destinations, eg to fill capsules (ie one-to-many dispensing). In addition, compound management groups are now facing the challenge of providing solid samples to chemistry groups involved in more novel activities (eg polymorph screening, salt selection, compatibility experiments etc) that were previously not considered routine. Such a diversity of requests is putting further pressure on a company's compound dispensing operation. To meet this challenge an increasing number of systems are being developed to facilitate automated solid dispensing. HTStec embarked upon its recent market survey[1] to try to understand the market of solid dispensing automation in pharma and biotech. In this article we report on some of the findings of that survey and review the latest vendor offerings in automated solid/powder dispensing.

Where is solid dispensing most used?

The main application focus of survey respondents' solid/powder dispensing activities in pharma and biotech was still the preparation of primary liquid stocks for compound storage (43% undertaking) and the supply of solid samples for retest/hit-to-lead confirmation (37% undertaking). The next

most investigated application foci were formulation development (7% undertaking) and solubility testing (4% undertaking). The survey also identified 7 other minor application foci, each with less than 2% of respondents undertaking (**Figure 2**).

Is solid dispensing a bottleneck?

The majority (33%) of survey respondents recognise there is a problem/bottleneck with solid/powder dispensing in their company today, but are okay with it. A further 26% thought it was not a big problem, they cope fine and 17% said they have bigger issues to work out. That left a total of 24% of survey respondents who thought solid/powder dispensing was a major issue in their company (**Figure 3**).

Is there a need for automation?

The majority (36%) of survey respondents' current opinion on the need for automated solid/powder dispensing was it was useful (I can see application niches that would benefit), with a further 16% thinking it was either essential (we cannot improve our logistics and productivity without it) and 10% thinking it was desirable (want to implement it widely, but limited by budget). That left a total of 38% of survey respondents who thought automation was either not feasible, not likely or not needed (**Figure 4**). To put these findings into context, the survey found 89% of all solid/powders transfers performed today are still undertaken manually, although by 2011 it was estimated this could decline to 70% with greater use of automation. Most importantly, survey respondents estimated that 39% of their solid compound library was in major need of automated sample transfer approaches (eg where compound supply was limited and material wastage was a major concern).

What is motivating automation?

Survey respondents rated their main motivation for automating solid/powder dispensing was to avoid tedious and time-consuming manual processing, this was followed by cut cycle time/significantly increase productivity, and then the need to conserve limited amount of solid available and reduce wastage. Real-time display and record storage (supports CFR Part 11 compliance) was least motivating for automating solid/powder dispensing (**Figure 5**).

Problematic solid dispensing

Survey respondents encountered problems during solid/powder dispensing with 63% of compounds (ie only 37% solids were considered non-problematic).

Figure 4: Current opinion on solid/powder dispensing automation

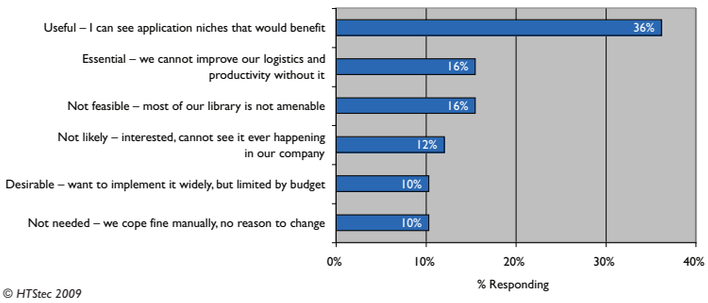


Figure 5: Main motivation for automating solid/powder dispensing

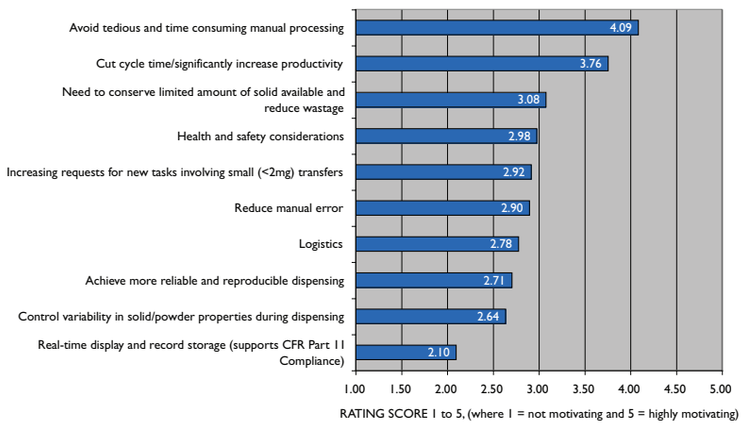


Figure 6: Frequency problematic compounds encountered during solid transfers

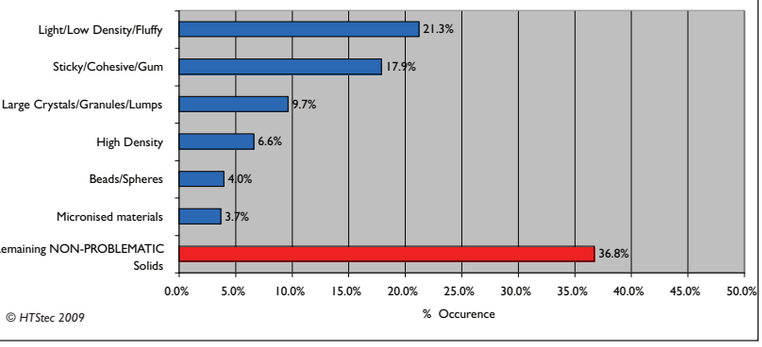


Figure 7: Biggest concerns about available solid/powder dispensing technologies

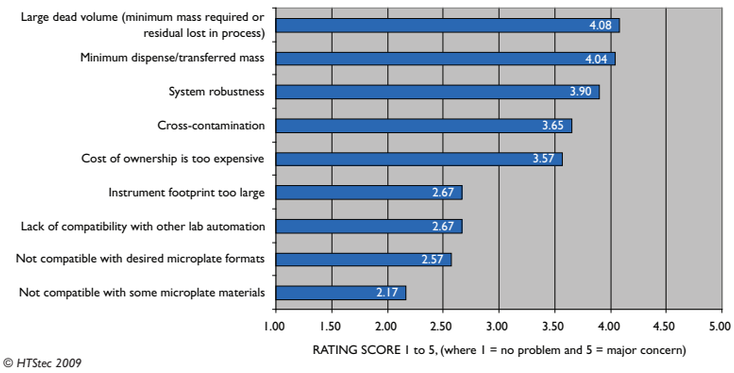
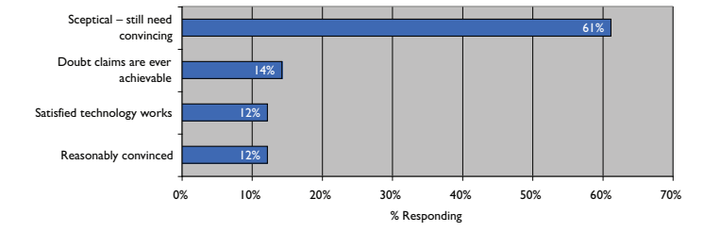


Figure 8: Opinion on vendor automated solid dispensing claims



The most frequently encountered problem was with transferring light/low density/fluffy solids (21% of time), sticky/cohesive/gum solids (18% of time) and large crystals/granules/lumps (10% of time). All respondents also placed greatest importance (ie considered it highly desirable) to be able to dispense problematic light/low density/fluffy solids using an automated solid transfer system (**Figure 6**).

Technology concerns

A large dead volume (ie a minimum starting mass required or the residual lost in the process itself) was rated as respondents' biggest concern about solid/powder dispensing technologies, this was closely followed by minimum dispense/transferred mass, then system robustness, cross-contamination and the cost of ownership. All other technology concerns were less of a problem (**Figure 7**). These findings need to be interpreted against the view that the majority (61%) of survey respondents are still sceptical about vendor automated solid/powder dispensing claims, with only 12% satisfied the automated technology works. So vendors still have something of an uphill struggle if they are to convince more end users to adopt automation (**Figure 8**).

Table 1 attempts to summarise the main vendor offerings that currently support automated solid/powder dispensing.

Latest vendor offerings

The following snapshots provide details some of the latest progress vendors have made in automation of solid/powder dispensing.

The ability to dispense dry powders and solids is a valuable tool for materials discovery, development and optimisation. There are few currently available options for manipulation of dry powders, particularly in the microgram mass range. The **BioDot** (www.biodot.com) DisPo™ Solid Transferring technology provides a means to deliver a wide variety of powders over the mass range of 100 micrograms to 100 milligrams (and greater) with CVs typically <=10%. With the DisPo technology, powders are dispensed via a volumetric delivery from a sample probe. The sampling of powders can occur from many different source vessels, including microwell plates, dram vials and tube-based storage systems. Sample delivery can occur to the same formats as well. The DisPo technology is available in both a Handheld format and in various automated platform configurations. The Handheld solid dispensers operate much like a conventional liquid pipettor and are available in fixed mass (M and MR Series) and adjustable mass formats (MA and MAR Series). The DisPo Handheld Dispensers can be used as standalone powder dispensers for semi-automated and manual applications and can also serve as companion products for optimising dispensing on our automated DisPo platforms. The automated platform versions of the DisPo technology allow for fully automated operation of powder transferring, including: programmable mass ranges, absolute mass record via an integrated 5 decimal place balance, plate shaking/vibration of powder samples, electrostatic control with chamber ionisation, on board wash station for sample probe cleaning (to minimise carryover) and multiple dispense heads. These automated platforms can also be integrated with plate stackers to allow for extended walk away time. The automated platforms allow for one-to-many, one-to-one, many-to-one and many-to-many modes of operation (**Figures 9 and 10**).

Table 1: Summary of solid dispensing products reviewed

SUPPLIER	PRODUCT	DISPENSING RANGE	DISPENSING PRECISION	MINIMUM MASS REQUIRED (DEAD VOLUME)	DISPENSE MECHANISM	PRIMARY DISPENSE MODE
BioDot	DisPo™ 1500 Powder Dispensing System	0.1 to 100mg	%CV <=5%	Typically 5mg	Volumetric delivery from a sample probe	One-to-many, many-to-many
BioDot	DisPo™ Handheld Powder Dispensing Pipettes	0.1 to 500mg	%CV <=5%	No dead volume – amount picked up is amount dispensed	Volumetric delivery from a sample probe	One-to-one, one-to-few
Chemspeed	Overhead Gravimetric Dispensing Unit	0.1mg to 100g	+/- 1mg	No minimum is required to dispense, but a variable amount of residual may remain in the container	Overhead gravimetric	One-to-one, one-to-many, many-to-one
Innovate Engineering & Design	Nova CCS™	0.2mg to 20mg	Tolerance +10% to 0%	N/A	Application of a controlled voltage to a collector pin	One-to-one, one-to-many
Innovate Engineering & Design	Electronic Spatula™ Handheld	0.2mg to 20mg	As needed	N/A	Application of a controlled voltage to a collector pin	One-to-one, one-to-few
Mettler-Toledo	FlexiWeigh	1mg to 5g	+/- 0.3mg	Varies, typically 15mg	Archimedes Screw	Many-to-many
Mettler-Toledo	Quantos	1 to 250mg	+/- 1mg	Varies, typically 15mg	Plunging pin with stirring mechanism	One-to-one, one-to-few
Symyx	Powdernium®	0.5mg to 10g +	+/- 0.1mg	100mg	Gravimetric, whisk-induced powder flow, metered by robotically controllable valve	Many-to-many
Symyx	Powdernium® SV	0.5mg to 200 mg	+/- 0.1mg	ca. 20mg	Gravimetric, vibration-induced flow, flow metered by disposable valve cap	Many-to-many
Zinsser Analytic	Calli®, Redi® Robotic Powder Handling Platforms	1mg to 2.5g	+/-5% at 1mg +/-2% at 5mg	No dead volume – amount picked up is amount dispensed	Volumetric delivery from a sample probe to a target weight gravimetrically	One-to-one, one-to-many
Zinsser Analytic	DryPette Handheld	5mg – 700mg	+/-5%	No dead volume – amount picked up is amount dispensed	Volumetric delivery from a sample probe	One-to-one, one-to-few
Zinsser Analytic	Redi Super	100mg – 100g	+/-2%	No dead volume – amount required is dispensed only	Continual vibration-induced dispense to a target weight gravimetrically	One-to-one as stand alone, one-to-many when integrated

Key to dispense modes: **One-to-one:** You have a single source and it can deliver to a single destination. In order to change sources or destinations, one needs to manually swap things out and reconfigure; **One-to-few:** You have a single source and it can deliver to multiple destinations (typically 10s). In order to change sources, one needs to manually change out the source; **One-to-many:** You have a single source that can deliver to an array of destinations (typically 100s). In order to change sources, one needs to manually change out the source; **Many-to-many:** The system has multiple sources that it can pick in a hands-free mode. Each source can be used to dispense to an array of destinations, which usually involves one but may involve multiple dispenses to each destination. While the dispenses are not simultaneous, they are automated and hands-free, so that an operator can start, walk away and achieve many-to-many dispenses; **Many-to-one:** The system has multiple sources that it can pick in a hands-free mode. Each source can dispense into the same destination. The dispenses are automated and hands-free, so that an operator can start, walk away and achieve many-to-one dispenses

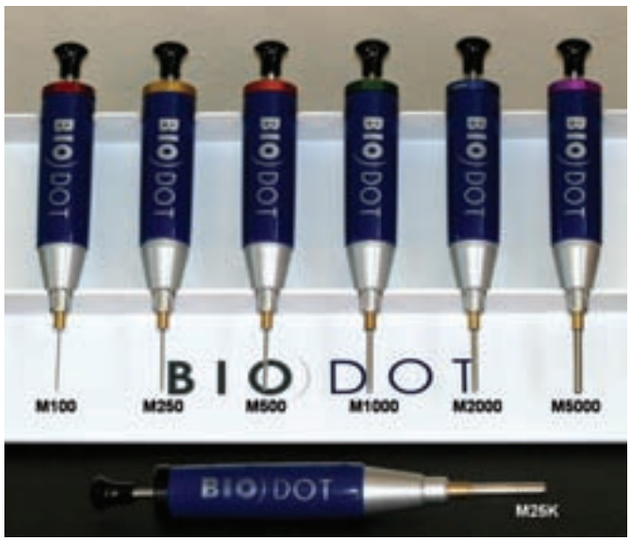


Figure 9: The BioDot DisPo™ Handheld Powder Dispensing Pipettes. The Handheld solid dispensers operate much like a conventional liquid pipettor and are available in fixed mass (M and MR Series) and adjustable mass formats (MA and MAR Series). The Handhelds can be used to dispense masses as low as 100 micrograms and as high as 500 milligrams

Figure 10: The BioDot DisPo™ 1500 Powder Dispensing System with Plate Stacker. The automated platform includes programmable mass ranges, absolute mass record via an integrated 5 decimal place balance, plate shaking/vibration of powder samples, electrostatic control with chamber ionisation, and on board wash station for sample probe cleaning (to minimise carryover)

Chemspeed Technologies (www.chemspeed.com) is a pioneer in the field of automated parallel chemistry with more than 10 years of experience worldwide. The company designs innovation driven solutions based on a strong portfolio of cutting-edge technologies, which cover chemical compound handling (liquids, solids, oils, etc), parallel synthesis and computer-controlled reactors and vessels. What makes Chemspeed unique is the overhead gravimetric dispensing unit (GDU) it has developed with a precision balance inside. The GDU robotic modules can dispense almost any type of compound directly into any kind of format, eg microtiter plates, high-output synthesis (discovery) reactors, disposable reactors, sample preparation and synthesis vials.

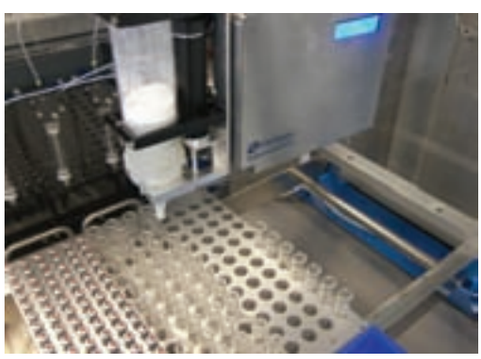


Figure 11: Chemspeed's overhead gravimetric dispensing unit mounted on its Formax robotic platform

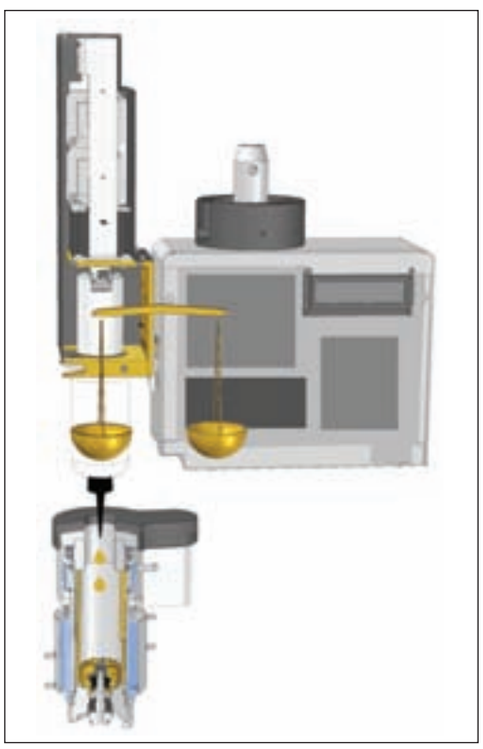


Figure 12: Schematic of Chemspeed's overhead gravimetric dispensing robotic tool with integrated overhead balance inside (shown in the diagram in gold). The schematic also shows dispensing of a high viscosity liquid into a high-performance formulation vessel capable of mixing, scraping, heating, refluxing and cooling

Figure 13
Mettler-Toledo's FlexiWeigh workstation for many-to many dispenses (left) with close-up of robotic gripper holding a FlexCap dispensing head fitted to a bar-coded source vial (right)

Figure 14
Mettler-Toledo's QB1 dosing system with auto sampler for one-to-few powder dosing applications

The GDU is mainly used in one-to-few and one-to-many dispense modes. Reactors or formulation vessels positioned beneath the GDU can also be mixing, heating or cooling while the solid is dispensed. Chemspeed started with tools for gravimetric dispensing of solids and liquids and currently this range of substances has been widened to high viscous liquids, powders, granulates, viscous liquids, gels etc. The other great improvement here is the universality of the overhead GDU and the fact that containers for solids can be closed when on storage or while moving towards the reactor or vessels, meaning dry storage and no powders are lost during the transfer. Before, you needed a different design for every type of compound. Now, with the current solid and powder dispensing unit, you can dispense a large range of powders from flowable to non-flowable, sticky or compacting character. The containers' size have been extended from 20 to 100mL; the weighing range from 20 to 100g, at a readability and precision of down to 0.1mg. Finally, Chemspeed teams are continuously improving the AutoTeaching algorithm to make it even more user-friendly and reliable (**Figures 11 and 12**).

Mettler-Toledo's (www.mt.com) FlexiWeigh automated powder dispensing technology was specifically developed for compound management applications, requiring many-to-many dispensing of 1-20mg targets, typically with 0.3mg precision and within 70 seconds. FlexiWeigh workstations have been used in pharmaceutical compound stores since 1999 for dispensing small quantities from the solid store for applications such as internal order supply and preparation of material for liquid stores. A patented FlexiWeigh dispensing head (FlexCap) is fitted to the source vial. The dispensing head has an Archimedes Screw mechanism with a triangular outlet. Dispensing is controlled by a self-adaptive algorithm with live balance feedback, which controls the speed of turning of the screw in combination with a tapping mechanism. The algorithm has been continually refined and optimised over the past 10 years to ensure that

Figure 15
The Symyx Powdernium® many-to-many powder dispenser is designed to flexibly dispense a wide variety of solids into wide variety of receptacles

Figure 16
Symyx Powdernium® SV uses conventional glass vials and a screw-on valve cap to dispense and to store solids. The robot head shown is able to grip the storage vial, actuate the valve cap with a drive motor and to impart a vibration using pneumatics, which enables dispensing

FlexiWeigh can successfully handle the widest range of materials possible, from free-flowing to sticky substances, as well as light, static and fluffy materials. User feedback indicates that FlexiWeigh can dispense in the region of 85% of a typical compound collection. More recently, the dispensing head technology has been extended to include a target range up to 5g. As a result, FlexiWeigh has recently found use in a variety of pharmaceutical discovery chemistry and process research applications where setting up and screening of parallel reactions is required. The latest product to enhance Mettler-Toledo's portfolio is the complementary Quantos dosing system with patented powder dispensing technology. The Quantos QB1 bridges the gap between manual and full automation and is ideally suited to one-to-one dispensing in applications such as sample preparation for QA/QC laboratories. The recent launch of the auto sampler (QS30) expands the offering for one-to-few applications where target vials are fed to the balance, enabling automatic dosing of up to 30 samples per batch. Quantos has a small footprint (320mm x 330 mm) and is ideal for dosing 1-250mg of free-flowing powders in 15-60 seconds, with a precision of 0.5mg. The Quantos dosing head relies on a pin that moves up and down to transport the substance, a stirring mechanism to homogenise the powder, and a tapper to ensure the powder collects at the base of the dosing head. The dosing head has the ability to optimise each dispense and learn, thereby increasing performance and precision. Heads are equipped with an RFID tag to store substance ID, quantity dosed, and date, etc for full process traceability. New accessories are continually being launched as Quantos expands into new application fields, eg stability testing and capsule filling (**Figures 13 and 14**).

The all-in-one Powdernium® workstation from **Symyx** (www.symyx.com/powder) is an automation solution of unmatched versatility and performance that dispenses powders and solids with precision and accuracy. It handles a wide range of powder types and receptacles, speeding development and improving overall R&D cost-savings. Symyx Powdernium® powder dispensing automation tools can be used effectively in the areas of reference standard distribution, clinical supply manufacture, preformulation, analytical and process development. Many of the top pharma and biotechs utilise Powdernium® advanced technology to handle a wide variety of clinical applications representing a wide range of material types and dispense weights. Powdernium® combines accurate balance weighing, an advanced software algorithm and GMP-compliant multi-use and disposable dispensing heads to precisely dispense and record the transferred weight of materials ranging from low density to free-flowing powders, from cohesive materials, to micronised powders, to polymer pellets and more. Powdernium® Technology offers turnkey systems for filling a range of receptacle including vials, tubes, capsule sizes 000-4, bottles, 96-well plates, and other containers; as well as a broad range of powder types including low density powders (lyophilised enzymes), fine powders (micronised lactose), sticky, inorganic salts, dense (metals), solid supports, polymeric beads, and non-spherical materials. Powdernium® delivers consistent and accurate filling, with between 1-5%CV depending on flow properties of powder; and

Figure 17: Zinsser Analytic Calli 2002® – a robotic platform featuring the new Redi Plus powder handling technology and fully integrated balance

Figure 18: Zinsser Analytic DryPette® – a range of manual powder pipettes with separate control unit plus pipetting handle, now with positive displacement dispensing

accuracy of up to +/- 0.05mg, depending on balance type. Easy-Dose Software provides data and information record about the dispensing cycle, including batch conditions and parameters. Symyx also recently introduced the new Powdernium® SV (Storage Vial) powder dispense technology to help organisations protect their investment in materials. Powdernium® SV uses conventional glass vials and a screw-on valve cap both to dispense and to store solids. The Powdernium® SV new shaker powder dispense technology is ideal for novel applications such as walk-up sample prep and reference standards preparation. Powdernium® SV's dual functionality vial hopper and storage vessel enables low-cost storage without the requirement to subdivide materials, helping to save and optimally manage precious resource materials. Powdernium® SV delivers enhanced ease-of-handling with no transfer of powder to the hopper required, just simple transfer of powder to the vial. Additionally, the new valve cap and vial hopper dispense technology is disposable, thus cleaning is not required and carry-over is not an issue (**Figures 15 and 16**).

Zinsser Analytic (www.zinsser-analytic.com) offers two robotic powder handling platforms: Redi® without liquid handing and Calli® with liquid handling. Both platforms have undergone recent changes and now include our new Redi Plus® powder handling technology. Housed within the robotic arm the Redi probe allows volumetric delivery to a defined target weight over the range 1mg to 2.5g directly on an integrated balance. Source powders can remain in their original containers. Contamination-free dispensing is achieved with the use of individual tips per powder, plus solvent washing and drying of the Redi® probe. Powders are levelled between dispensing with the use of shakers and/or stirrers. An anti-static module is now available for handling fine, flyaway powders. Areas of the deck can now be isolated for the economic use of gas to supply an inert atmosphere – essential for hygroscopic powders. For the dispensing of larger volumes of powder, Zinsser have developed Redi Super® which is available as both a standalone unit and fully integrated into a robotic system. Redi Super® is a vibration feeder for the gravimetric dispensing of powder to a target weight, in the range of 100mg to 100g, directly on a balance. Zinsser-Analytic's range of hand held manual powder pipettes, DryPette®, has also increased. Now available as a controller unit with separate, interchangeable pipette handles (including handles made to a custom design) and wider volumetric dispense range (25-770µL for DryPette Standard®, 90 – 1900µL for DryPette Plus®). In addition, Zinsser has introduced DryPette Varix® – an electronically controlled powder pipette with a twin dispense action – positive pressure and/or positive displacement – for the manual handling of difficult powders. Separate, interchangeable pipette handles allows the Varix to dispense a wide volumetric range of 5-795µL. Ongoing and future developments are focused on multi-scale systems for grinding, sieving and pelletising of dispensed powders for catalyst research (**Figures 17 and 18**).

Innovate Engineering and Design's (www.innovateengineering.com) NOVA Compound Collection System™ (Nova CCS™) and the Electronic Spatula™ are tools designed using the Nova Technology to speed the collection and transfer of compounds, especially particulate dry powders or crystallines. The basis of the Nova Technology is the application of a controlled and exact voltage to a collector pin creating an attractive force, a force that can be thought of as static cling. Through the unique control of electrical energy, the fully automated Nova CCS™ and the hand held Electronic Spatula™ can collect, isolate and dispense minute quantities of particulate substances. The Nova Technology is leading edge technology that harnesses a phenomenon only partially understood. Extensive testing has shown that the Nova Technology has no effect on the chemical structure of the compounds. One of the major issues addressed by the Nova Technology is the serious effect of static electricity encountered in almost all methods of manual, mechanical and automated compound storage and distribution. Compounds exposed to static electricity can be uncontrollably dispersed on to surrounding surfaces and equipment. Such uncontrolled dispersion can equate to a significant amount of product loss and cross contamination. What is significant with Innovate Engineering & Design's technology and in direct contrast with other manual and mechanical methods, is that with the Nova Technology performance improves in a static rich environment. Both the Nova CCS™ and the Electronic Spatula™ use disposable collection pins which eliminates the potential of cross-contamination. The fully automated system does not require any special source containers or lids and can collect from most common laboratory glassware. The Electronic Spatula™ offers an additional capability to the manual collection process, the ability to drive statically charged compounds from the walls of source containers. The Electronic Spatula™ is offered in two different power control options, a foot-controlled or a totally hand-controlled model (**Figures 19 and 20**).

Automated solid dispensing was selected as one of five best practice roundtable discussion topics at this year's IQPC Compound Management and Integrity Conference held in London on 20 May 2009. Donat Elsener, industry expert from **Innoco** (www.innoco.ch), chaired the discussion and kicked-off by presenting an overview of the dosing solutions which are currently being offered in the market. He briefly explained the basic working principles of the solutions before the group of 10

Figure 19: Innovate Engineering and Design's Nova CCS™ system

Figure 20: Innovate Engineering and Design's Electronic Spatula™

shared their experiences and expectations on automated solid dispensing solutions in compound management. In this arena the typical application is to weigh out 1 to 10mg of solid compounds to create normalised stock solutions for liquid libraries. Stock solutions then get aliquoted and sent out to the biology laboratories for screening, hit validation and lead optimisation. The typical powder dosing in drug research and early discovery is therefore a many-to-many process in contrast to a one-to-many procedure as required further downstream, eg for *in vivo* test preparation. Most experience represented by the group was of systems based on Archimedes Screw dosing caps attached to compound vials. Feedback on system reliability by users was very positive. On the other hand participants noted an increase in oily and sticky compounds being added to their collections, which can often not be used for automated weighing. Three participants stated that initially between 80 to 85% of their compounds had been suited for automated dosing. Those numbers are now down to 80%, 60% and even below 50% at one company. Participating compound vendors expressed much interest in automated dosing. They claimed to have mainly perfect crystalline powders but cannot ideally apply automation due to the enormous variation in their dispensing requirements. The round-table concluded that automated dosing does reduce manual work in the discussed applications but cannot completely substitute manual weigh outs.

Summary

Automated solid/powder dispense systems discussed in this article broadly fall into four technology types, all of which have a gravimetric (weighing) component: 1) metered/controlled flow of solid from the storage container into a destination vessel, which is positioned on an accurate balance, that gives real-time feedback of the amount transferred. This includes Archimedes Screw mechanism disposable caps, and other focused orifice/valve devices fitted with controlled feed, vibration, tapping or shaking (eg Smymx Powdernium, Mettler-Toledo FlexiWeigh and Quantos, and Zinsser Analytic Redi Super); 2) systems where the storage container itself has been designed to locate within (become part of) of an overhead balance. Solid is expelled, extruded or flows out from the storage hoppers tapered orifice into a destination vessel, which is positioned below, and the weight loss (amount dispensed) is automatically monitored in the head (eg Chemspeed Overhead Gravimetric); and 3) systems based on volumetric delivery from a sample

probe, operating much like a conventional liquid pipettor. The probe is inserted into the solid, pulls up an amount defined by the volume within the probe cylinder. Displacement of the plunger or piston within the probe ejects all or part of that amount into a destination vessel. Although the volume is a very good indication of the mass transferred it is usually necessary to confirm this by dispensing into a destination vessel located on an accurate balance. The probe may be disposable or reused after suitable cleaning (eg BioDot DisPo and Zinsser Analytic Redi Plus); and 4) a completely different approach that does not utilise vibration, vacuum, a mechanical valve or an Archimedes Screw but involves the application of a controlled and exact voltage to a collector pin creating an attractive force. It acts like static cling to attract (pick up) small amounts of solid until the voltage is shut off, when the solid disperses to the destination container (eg Innovate Engineering and Design's Nova Technology).

All dispense modes, ie one-to-one, one-to-few, one-to-many, many-to-many and many-to-one are catered for by the three technology types, although no single technology or system appears ideal for all modes. For example Chemspeed's Overhead Gravimetric type 2 appears most suited to many-to-one requirements of automated chemical synthesis (eg where 3-5 excipients may be combined into one vial) and less useful for the many-to-many dispensing requirements of most compound management groups (ie in the preparation of large numbers of primary liquid stocks). BioDot's DisPo, Zinsser Analytic's Redi Plus and Innovate Engineering and Design's Nova technologies can enable most dispense modes, but unlike other approaches are uniquely suited to handheld one-to-one operations, if you like a metered alternative to the conventional spatula. Collectively the available automated offerings have the capability to address most of the familiar existing solid/powder dispensing application requirements of pharma and biotech, yet their impact and penetration of this market still appears to be patchy today. There is, for example, no universal accepted deployment for certain key applications or widespread recognition as a platform technology and utilisation within organisations is sporadic. Although many claims are made about the suitability of these automated systems for the widest possible range of solid types and material properties, it is clear that end-users remain sceptical about applicability to their problematic solids, and are less inclined to take vendor's claims at face value. In addition, HTStec's survey revealed that end-user knowledge of available vendor offerings was relatively poor. As a consequence many organisations still rely almost entirely on manual transfers and weighings.

Yet there are positive signs on the horizon for the improved adoption of automated dispensing. Survey respondents expect their usage of automation to increase by 2011, and strong motivation was found to avoid tedious and time-consuming manual processing, to find ways to cut cycle time and to significantly increase productivity. More encouragingly, automated solid dispensing tools have opened up new application areas, eg in solid state chemistry. However, improved awareness by end-users of what is available, how it works and what might realistically be achieved using it is pivotal to greater use. Vendors must share some responsibility here, not least for over-hyping their products and for their failure to clearly promote and adequately position their offerings. In conclusion, there are strong grounds for optimism regarding the wider uptake of automated solid/powder dispensing systems within pharma and biotech and prospects for the successful deployment in new application areas look favourable.

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Reference

1 Automated Solid Dispensing Trends 2009 Report, published by HTStec Limited, Cambridge, UK, May 2009.