

Tessellations

News And Technical Updates From Tessella

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From wonder drug to packaged pills

With pressures to prevent and treat diseases coming from both governments and the general public, and with intense competition within the life sciences industry, pharmaceutical companies continue to race to bring the next wonder drug to market.

However, both drug discovery and drug development are expensive, and there are real financial pressures to improve the processes used at every stage. In this article we take a look at salt and polymorph screening – a vital step in the drug development process and an area in which technology is bringing significant rewards.

Salts and polymorphs

Once an active **drug substance** has been discovered, it is necessary to consider how it might be **administered** to the patient. Often a drug substance will have inappropriate physical properties, such as poor solubility in water, a lack of crystalline form, or poor stability.

To develop a viable product, pharmaceutical companies need to identify appropriate versions (**salts**) of the drug substance and different crystalline structures (**polymorphs**) that the drug can adopt.

The exact polymorphic form that a drug substance adopts in a given situation depends intimately on the crystallization conditions, and it is critical for a pharmaceutical company to research and understand these conditions for each drug substance it deals with.

If the manufacturing process suddenly started to produce a different polymorphic form than planned, then the drug may have to be **withdrawn from the market**. In particular, withdrawal would be essential if the physical properties of the new form meant that it could not be formulated for dispensing in the same way, or if equivalent bioavailability and efficacy could not be achieved. Another problem is that it is common to find meta-stable polymorphs that revert to a more stable form over the course of time. If such a polymorph was used to create a drug, this would have serious implications for the shelf life of the product.

The FDA, and other regulatory authorities, require pharmaceutical manufacturers to conduct extensive salt and polymorph screening until a form is found that is suitable for formulation, and to implement appropriate controls within their manufacturing processes to ensure the required form is produced.

However, salt and polymorph screening is a large consumer of time and resources, increasing the investment required in a new drug and slowing the return on investment. Furthermore, a significant quantity of the active pharmaceutical ingredient can be required, which may not be readily available during the early stages of drug development.

The salt and polymorph screening process can be highly labour intensive and rely on manual methods to store and track the experimental data and results. It can even become a bottleneck in the drug development pipeline.

Centralizing and improving

Across the pharmaceutical industry, salt and polymorph studies were traditionally carried out manually by individual chemists, each employing a slightly different approach. This lack of consistency meant it was difficult to understand and apply results elsewhere within the organization, or to make use of specialized know-how.

Hence, GlaxoSmithKline (GSK) initiated a project to centralize and improve their salt and polymorph screening process to make use of the latest technologies in automation and solid-state analysis. The aim was to enable the screening of a greater number of compounds earlier in the drug development process, and to increase significantly the range of experiments that were performed per compound.

Tessella worked with a core team of GSK users to analyze the new workflow and to develop a software system that would control the **automated equipment**, as well as providing workflow coordination, data storage, and sample tracking. A web-

based system was developed to allow system users better visibility of the results. A series of phased releases provided early opportunities for valuable feedback from users; Tessella then provided on-site support for the rollout of the system within the UK and US.

A screening success

A combination of **custom-built** software and hardware enables GSK to provide an efficient, high quality screening service that meets the needs of a changing drug portfolio. The centralization and automation provides a more rigorous and consistent scientific process, leading to higher quality information that can be shared and applied across the organization. There has also been a significant increase in the number of compounds screened per annum and in the complexity of experiments.

The increased use of automation has allowed GSK to realize many benefits. In particular, it is now possible to work with smaller amounts of material more accurately and reliably, resulting in significant cost savings.

For a fuller article on salt and polymorph screening, or for related back issues of Tessellations, please complete the enclosed order form or email info@tessella.com



There are real financial pressures to improve drug discovery and drug development processes

Over the last few issues of Tessellations we have discussed several other key areas of **drug discovery and development** – **in silico** techniques to speed up the drug discovery process (issue 53); **High Throughput Experimentation** to explore the chemical space (issue 51); new systems for **tablet design and manufacture** (issue 51); and **Process Analytical Testing** and the push for innovative development and manufacturing technologies (issue 54).

Cost-effective waste management in West Sussex

With an increasing world population, the problem of achieving sustainable waste management is one of the most critical social, environmental and economic issues facing our consumer-based societies. The European Union throws away over 1.3 billion tonnes of waste each year. The UK alone produces over 400 million tonnes of waste, with 28 million tonnes of this coming from households. Most UK waste currently ends up in landfill sites, with only 17% of household waste being recycled or composted. The picture is similar in the US, with the Environmental Protection Agency reporting that 'household trash' accounted for 236 million tons (equivalent to 214 million metric tonnes) of waste a year.

Internationally the problem is both huge and growing. However, increasing public awareness and concern for the environment is leading to more legislation and targets for waste reduction and recycling.

Reduce, Reuse, Recycle

The European Union requires waste to be closely tracked and monitored by responsible agencies, and has issued a significant number of directives related to waste management, including an upcoming target to reduce landfill of biodegradable waste to 50% by 2013.

'Reduce, reuse and recycle' are the cornerstones of an environmentally friendly waste management policy.

Any form of waste disposal or recycling has the potential to harm the environment or human health, so the first line of action is to **reduce** the amount of waste produced in the first place. **Reuse** is the next best option; using a product again, either for the same or some new purpose. **Recycling** and **composting** methods include the collection and separation of materials that can be sent to markets for reprocessing. The remaining wastes can then be subjected to **recovery** options, which include a variety of biological and thermal techniques. The final option is disposal by **landfill**. This has become recognized as the least desirable part of the waste hierarchy and the emphasis for local authorities is to reduce dependence on landfill to a minimum.

A groundbreaking contract

In the UK, **Waste Disposal Authorities** are responsible for the safe disposal of municipal waste collected by local councils, and for the development of plans to help the UK meet the tough European Union landfill reduction targets. West Sussex County Council is one such Waste Disposal Authority. Its Waste Management Services team is responsible for the safe disposal of municipal waste, collected by the seven District and Borough Councils in West Sussex plus the waste deposited at household waste recycling sites.

In early 2004 West Sussex County Council signed a multi-million pound **Private Finance Initiative** (PFI) deal with Viridor Waste Management Ltd for the provision of a new waste management service. The Recycling and Waste Handling Contract aims to deliver a recycling rate of 45% of household rubbish by 2015. This groundbreaking contract is the largest ever signed by the County Council, worth £540 million over the 25-year timescale.

As a result, Viridor now runs the county's eleven household waste recycling sites, waste transfer stations and composting facilities, and will also operate new facilities as they come online.

Cost-effective monitoring

Performance measurement, incentives and information sharing are key components of effective Public Private Partnerships. Innovative IT systems are also needed to drive down the management costs of such contracts. West Sussex County Council needed its IT system to:

- Catalogue the types of waste managed within the County
- Define waste management facilities used by the County Council and its contractors
- Define valid disposal routes for each type of waste
- Maintain a register of vehicles authorized to carry waste
- Record targets for each waste management contractor
- Define how the performance of contractors should be monitored
- Enable the Council to collate and reconcile data from all its waste service providers



Waste management is an international problem (photo © Viridor Waste Management Ltd)

Tessella was commissioned to develop and support an e-GIF compliant, web-based system to meet these needs and to enable **cost-effective monitoring** of both the PFI contract and the waste services within West Sussex. A roaming capability was implemented, using Pocket PC 2003 devices, to allow the Council to monitor and inspect waste management facilities.

The system produces statutory reports and Best Value Performance Indicators relating to the waste being collected and processed, and allows the **performance** of Viridor to be monitored through an issues and deduction framework specified in the performance-based contract.

Key to the success of the development was the early involvement of all relevant stakeholders within the Council, and the involvement of a representative of the Waste Collection Authorities.

The final system was delivered to West Sussex County Council in April 2005, on time and under budget. The Council now has an integrated and extensible system to efficiently manage their key waste management contract, and the system has been well received by the various waste service providers.

Extending the model to other contracts

For further information on how this system can be used to monitor other waste service provisions, or extended to monitor other types of contract, please email info@tessella.com



Phillip Russell; Head of Wastes Management West Sussex County Council



Simon Tessella Software Engineer

For further information and free Technical Supplements please complete the enclosed form or email info@tessella.com

Keeping critical assets operational

Industry is built upon critical assets: systems that are vital to the smooth operation of business. These assets might be production lines, servers, railway lines or water pipes, but they all share a common problem – how can they be kept operational for as long as possible, without sacrificing reliability?

The answer, of course, is appropriate **maintenance**. If this task is neglected, assets are likely to fail irreparably, leading to hours of downtime, halted production or, most seriously, potential fatalities. When schedules are tight, the effects of these asset failures can cascade well beyond any individual system. However, an overly-rigorous maintenance plan can be just as damaging to **profits**, with financial and temporal overheads of unnecessary maintenance and downtime quickly mounting up.

These problems can be mitigated by taking a systematic approach to the **active management** of assets. This can include designing systems to sense changes in assets and their behaviour automatically, and to update maintenance schedules dynamically in response. Such monitoring systems can drastically reduce the overheads that a business incurs through servicing assets, while still ensuring that production and services are reliable and efficient.

So what is asset monitoring?

Systems for monitoring of assets can range from simple instrumentation to highly integrated monitoring and scheduling systems, but the premise behind all of them is essentially the same. The system observes an asset for signs of failure, or degradation, and schedules maintenance intervention before critical failure occurs. This information is also used to maintain an up-to-date **asset register**, providing centralized and accurate information on the nature, location and condition of the full asset set across the business.

The core principles of most asset monitoring systems consist of:

1. **Data acquisition** – capturing information about the status of the asset being monitored
2. **Data analysis** – inferring the state of the asset from the acquired data
3. **Update the Asset Register** – capturing the results of monitoring into a central data source
4. **Decision support** – advising a course of action based upon the analyzed data
5. **Investment** – developing and implementing an appropriate strategy for maintenance and renewal

Each of these principles in isolation is mature and well-understood; asset monitoring simply combines these approaches in an intelligent and integrated way. There will still always be some monitoring that can only be achieved manually, but this can be evaluated in combination with more automated monitoring to provide a comprehensive picture of all related assets and consequences across the entire business.

But what do you do if constant, or even periodic, measurement is difficult or impossible; e.g. if assets are remote, inaccessible or in a hazardous environment?

In such cases we can turn to **modelling and simulation**, and use the data which is available to **forecast** the condition of those assets, backing this up with real measurement when possible.

Who benefits?

When discussing the advantages gained through such asset monitoring, the industry is rife with buzzwords such as 'proactive servicing' and 'reliability-centred maintenance', but the real benefits are concrete and measurable:

- **Reliability** – unforeseen disruptions to operations can be minimized, increasing confidence in the overall system
- **Availability** – the overall lifetime of individual assets is extended, and serious problems (which require time-intensive repair) are reduced
- **Maintainability** – better, more timely, information on the condition of assets, and their degradation characteristics, allows maintenance regimes to be streamlined to make optimum use of time and resources
- **Safety** – accurate and comprehensive data means that safety-critical problems can be predicted and prevented

Additional **business benefits** flow from these 'behind the scenes' changes.

Greater workloads can be taken on. Customers can rely on orders being fulfilled on time, since production delays are reduced. Maintenance costs are minimized as equipment lasts longer. It quickly becomes apparent that asset monitoring can reap positive gains for every facet of any industry that relies on critical infrastructure. Such systems have been deployed in industries as diverse as rail, power generation, mass-production, and petrochemical refinement and distribution.

The industries that often feel the greatest benefits are those with infrastructure spread over a wide geographical area; one of the strengths

of asset monitoring is its ability to reduce and manage the manual monitoring that these wide-area assets otherwise require. Nor is it just large-scale industries that stand to benefit. Thanks to their modular design and simple core technologies, asset monitoring systems can be scaled to almost any environment.

Find out more

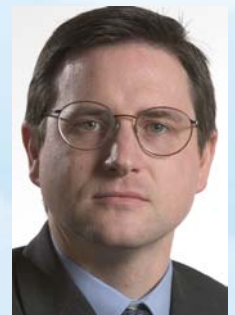
Asset monitoring systems are a **powerful tool** for protecting **critical assets** and maximizing their uptimes. Combined with other technologies, they can be used to produce an integrated system for business wide asset management and maintenance.

Tessella has a strong track record of delivering successful asset monitoring projects across a number of industries.

To request a free technical supplement providing a more detailed look at the relevant technologies, or to discuss how Tessella could help your business, please email info@tessella.com



Asset management is anything but child's play!



Nick
Tessella
Technical Manager

Developments in digital preservation

Efforts to manage the long-term maintenance of digital information are continuing around the world with a number of new initiatives.

In order to assess the nature and scale of the problem, the Digital Preservation Coalition has launched the UK Digital Preservation Needs Assessment survey; designed to reveal the extent of the risk of loss of, or degradation to, digital material held in public and commercial sectors. Tessella is carrying out the survey, which will look at current practice and future requirements in government bodies, archives, museums, libraries, education, scientific research organizations, and pharmaceutical, environmental, nuclear, engineering, publishing and financial institutions. The final report will identify priorities for action to accelerate and inform the development of a UK digital preservation agenda.

Pertinent information and practical tools will underpin any widespread responses to digital record problems. The UK National Archives is leading the way with PRONOM, a repository of file format information to support preservation and migration. Tessella has recently upgraded PRONOM to include a wider range of information, and to incorporate a downloadable tool for automatic file format identification using binary signatures (DROID). See www.nationalarchives.gov.uk/pronom for details of this new release.

Other European efforts are being rewarded, with the nomination of the Dutch Nationaal Archief's 'Testbed' project for the Pilgrim Trust Digital Preservation Award 2005. The award recognizes leadership and achievement in the field of digital preservation. 'Testbed' has researched a variety of strategies for long-term digital preservation, involving contributions from Tessella's digital preservation specialists over several years.

In the US, following a year-long preliminary design phase, the National Archives and Records Administration (NARA) selected the Lockheed Martin led team, which includes Tessella, to develop its Electronic Records Archives (ERA) system, to store, maintain and make available all federal electronic records. We are honoured to have this opportunity to continue working with NARA and Lockheed Martin to preserve the recorded history and heritage of the United States.

Tessellations is published by Tessella Support Services plc. Our aim is to provide you with interesting information on topical technology issues and to outline key projects which we hope you will find of use. We depend on the feedback from our readers to help us develop Tessellations and to maximize its usefulness. Your input is always appreciated; please send to The Editor (Alison Smith) at info@tessella.com

Tessella physics prizes

Each year Tessella sponsors prizes within the physics departments of several top universities. A prize is awarded, by each university, to the student who makes the most effective use of software in their final year physics project.

At Cambridge University, UK, Ainsley Mayhew-Seers of St John's College won the prize for his project on the comparison of two novel ways of simulating fluids; Stochastic Rotation Dynamics and the Lowe thermostat. Both of these methods are attractive in that they simultaneously reproduce both the Brownian fluctuations and the larger scale hydrodynamic interactions which are present in a real fluid but require far less computational power than traditional Molecular Dynamics approaches.

Although these methods are highly suitable for the modelling of more complex fluids, such as colloidal and polymer suspensions, Ainsley's work focused on obtaining comparative values for more basic parameters which define the fluid, such as the viscosities and the diffusion coefficients.



(photo © Dr Paul Linford)

From left to right, Ainsley Mayhew-Seers, Dr Werner Schulz of Tessella, and Professor Malcolm Longair Head of the Cambridge Department of Physics

Tessella Washington office opens

Tessella Inc has opened an office in Washington DC. This investment decision, Tessella's second office in the US, was a compelling one due to the convergence of high technology customers with complex R&D requirements, the potential of the US Federal Market, and the educated and enthusiastic local workforce.

These factors, plus our ongoing contribution to the Lockheed Martin led team building NARA's Electronic Records Archives system, made Washington DC the obvious location for our next office.

Tessella – Providing innovative software solutions to scientific, technical and engineering problems

Tessella adds value to its clients' businesses through the application of scientific methods and information technology. Our services cover software design and development, IT consultancy, infrastructure support, and project management. We are vendor independent and always offer the solution that is best for our clients.

We deliver creative and robust systems including: data acquisition and control, data analysis, database systems, digital preservation, GUIs, internet/intranet applications, modelling and simulation, visualization/graphics, workflow, and systems support.

Tessella's ability to understand and solve our clients' business and technical problems is based on the scientific and engineering excellence of our staff, our unique training program and our highly regarded quality system. We have a history of excellence spanning 25 years, and our offices in the UK, US and the Netherlands have built long-term relationships with organizations at the leading-edge of the scientific/engineering world.

For further information please visit www.tessella.com, return the enclosed order form, or email info@tessella.com

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