

## Focus on Pharmaceuticals

Hello to all you Engineers involved in the Pharmaceutical industry. This is the first edition of a regular newsletter aimed specifically at mechanical engineers like you. It is designed to keep you updated on current issues and events and give you a chance to communicate with colleagues who have similar interest to yourself. In this edition we will introduce you the Chair of the Pharmaceutical Group at IMechE and his team of committee members who are working on your behalf. Provide an update on IMechE events that may be of interest, updates on Industry and regulatory activities relevant to Mechanical Engineers and a section for members' correspondence. We hope you enjoy the Newsletter and we welcome any feedback on the Newsletter or IMechE and look forward to receiving your contributions to future editions.

All correspondence should be addressed to Angela Theobald at [a\\_theobald@imeche.org](mailto:a_theobald@imeche.org)

### Welcome from Paul Merrick, Chair of the Pharmaceuticals Technical Activity Committee



My name is Paul Merrick and I am Chair of the Pharmaceuticals Technical Activity Committee, part of the Process Industries Division within the IMechE. I am a Chartered Mechanical Engineer and a Fellow of the IMechE, starting my career in 1972 as an apprentice with ICI and since working in numerous Engineering roles. I have a 1st Class Hons degree in Mechanical Eng and an MSc in Pharmaceutical Eng from Manchester University, I am also a visiting lecturer at Manchester University on the Pharmaceuticals Engineering MSc. I work with the Derbyshire Education Business Partnership as a Science and Engineering Ambassador (SEA) promoting Engineering in schools. Until recently I was Packaging Engineering Manager responsible for all aspects of packaging equipment at AstraZeneca's Macclesfield Works, including specification,

design, commissioning, validation, exploitation, new pack design, new technologies with some Global interaction, and latterly working on aspects of LEAN implementation.

The Pharmaceutical TAC is part of the Process Industries Division and meets three times a year.

We have the following objectives :-

- Raise awareness of this field within the professional engineering community.
- Provide knowledge sharing.
- Provide seminars and training opportunities.
- Link with other related bodies such as IChemE and ISPE.
- Encourage suppliers to meet cGMP solutions in a cost effective way.

Committee members are typically involved in the pharmaceutical industry either in research, manufacturing, service suppliers, consultants or academics. Part of our role is to share knowledge and raise awareness of our industry sector and we organise seminars which we hope may be of interest to others in the industry.

We would appreciate any feedback on possible seminar topics if you have suggestions that you believe will be of sufficient interest to the members of the mechanical engineering community. It would be a good opportunity for any of you who would like to share knowledge with others in the industry and I would therefore encourage you to send in technical articles or articles of interest for inclusion in a future newsletter.

## Future IMechE Activities

These are many IMechE events planned for the future that may be of interest to you. For more information go to [www.imeche.org/events/](http://www.imeche.org/events/)

## Industry News

### **AstraZeneca**

AstraZeneca is to invest \$120 million in a new Process Research and Development (PR&D) Laboratory at its Macclesfield site, Cheshire, adding to the company's significant investment in the UK over recent years.

### **Ortho Clinical Diagnostics**

Ortho Clinical Diagnostics is a subsidiary of Johnson and Johnson is building a new pilot plant for Diagnostic kits and materials at its Whitchurch facility near Cardiff. The cost of this project is believed to be around £16M Target date for completion is Q1 2008.

### **Cancer Research UK**

Cancer Research UK is building a new Biotechnology pilot plant at its site in South Mimms north of London. The project is estimated to be worth £10M and is expected to be completed at the end of 2009.

## Regulatory News For Mechanical Engineers

### **A New Approach to Validation - Is this the end to the validation 'V' model?**

A summary of ISPE Boston/NE joint chapter meeting on Standard ASTM E2500

In June this year many representatives from pharmaceutical companies in North America joined to discuss the future of validation. The main subject of interest was ASTM E2500 which is titled "Standards for Specification, Design & Verification of Pharmaceutical & Biopharmaceutical Manufacturing Systems & Equipment". This standard has been developed with input from industry and with the support of the FDA, EMEA and GAMP and was approved in May 2007 and published in July 2007.

*(continued on page 5)*

### **EMA to Update GMP Guide With Starting Materials Section**

The European Medicines Agency (EMA) plans to update Chapter 5 of its GMP Guide to reflect the agency's requirements that active substances and certain excipients, also known as "starting materials" used as components for pharmaceutical products, be manufactured according to good manufacturing practices (GMPs).

Under the EMA Ad Hoc GMP Inspection Services Group's (GISG) proposed timetable for publication, the consultation will be released in late September with a deadline for comments in March 2008.

“Although [Chapter 5] does provide some guidance on the qualification of suppliers, it does not emphasize the obligation to ensure that active substances are produced in accordance with GMP,” the EMEA said.

Special attention will likely be given to the traceability and confirmation of the origin of active substances, the EMEA said. In addition, testing of starting materials will be detailed in a new section of the GMP Guide.

“Some member states require the manufacturer to test starting materials itself while others permit the use of certificates of analysis provided by the supplier. A harmonized approach, taking into account principles of quality risk management, is desirable [for] striking a balance between assurance of quality ... and the efficient use of resources,” the EMEA said.

Testing harmonization of starting materials is not expected to have a negative effect in industry. In fact, the GISG said, the update “should help some manufacturers use existing resources in a more effective way.” The EMEA added that the revision should bring clarity and transparency into this area of GMP to the benefit of both industry and inspectors

## Your IMechE Pharmaceutical Group Support Committee

This is the team of individuals who have volunteered to support the IMechE members with a specific interest in the Pharmaceutical industry. Please contact one of us if you have any suggestions or want to get more involved in the group:

Paul Merrick	PRiMe Technical Services Ltd	<i>Chairman</i>
Karen Stevenson	Cardinal Health	<i>Vice Chairman</i>
Robert J Hayes	SeerPharma (UK) Ltd	<i>Vice Chairman</i>
Angela Theobald	IMechE staff	
Stuart Aitkenhead	Aptuit (Edinburgh) Ltd	
Nigel Beard	Acetate Products Ltd	
Andrew Davies	STI Pharmaceuticals Ltd	
Andrew Derry	Schering Plough	
Norman Harris	20CC Ltd	
Chris Hurst	GSK	
Ian Johnson	AstraZeneca	
Federico Loterijman	Anders Associates	
David Palmer	Lonza Biologics Plc	
Keith Wickert	3M Cuno	
Maurice Worthington	Stopford Projects Limited	

## Member Correspondence

Take this opportunity to ask questions or for help, offer opinions or advice or simply get something off your chest.

All correspondence should be addressed to Angela Theobald at [a\\_theobald@imeche.org](mailto:a_theobald@imeche.org)

## And Finally...

It was the time of the French Revolution and three people were arrested as enemies of the people. One was a priest, another a lawyer and the last an engineer.

They led the three men out to the guillotine and first placed the priest in the stock and pulled the lever. The blade thundered down the rack and stuck just before it severed the priest's head. The crowd roared in unison *"It's God's will – let him go free!"* And so he was released.

Next the Lawyer was placed in the rank and again the blade stuck on the way down.

Finally, the engineer was placed in the stock. He looks up and says "Wait! I think I see what the problem is..."

This newsletter has been kindly produced on behalf of IMechE by 3M Cuno Filtration Group.  
**Visit our new website at [www.3M.eu/filtration](http://www.3M.eu/filtration)**



### A New Approach to Validation - Is this the end of the validation 'V' model?

(Continued from page 2)

#### A summary of ISPE Boston/NE joint chapter meeting on Standard ASTM E2500

In June this year many representatives from pharmaceutical companies in North America joined to discuss the future for validation. The main subject of interest was ASTM E2500 which is titled "*Standards for Specification, Design & Verification of Pharmaceutical & Biopharmaceutical Manufacturing Systems & Equipment*". This standard has been developed with input from industry and with the support of the FDA, EMEA and GAMP and was approved in May 2007 and published in July 2007.

So what is ASTM E2500? Basically it's a consensus standard with legal relevance and global impact. Based on sound scientific, engineering and quality principles it is intended to separate business risk from patient safety risk. So basically it is a risk based approach to verify patient protection.

This standard proposes the almost complete destruction of the validation "V" model. Out goes the Design Qualification (DQ) with a Design Review (DR). Also for those that do them, Impact Assessments are out. Commissioning and Qualification are replaced by "Verification", so the qualification phases (IQ, OQ, PQ) are obsolete.

So what does ASTM E2500 propose? Upfront things look similar to the process most Pharmaceutical engineers are used to. Product and process designs are to be well defined and detailed through URS, FRS and DDS type documents. The aim is to have the critical quality attributes satisfied by the design with the risk to product quality and patient safety appropriately considered. Any unacceptable risks are mitigated by the design (preferred) or defined by practice. This design is then reviewed and approved by the relevant subject matter expert. The big change comes in the verification stage of this approach. ASTM E2500 states that verification is "*A systematic approach to prove that Critical Elements, acting singly or in combination, are fit for intended use, have been properly installed, and operating correctly*". This verification would normally be documented in IQ, OQ, and PQ documents however the new approach just states that the verification approach must be documented. The extent of verification and the level of detail of documentation should be based on risk to product quality and patient safety. This approach also allows more flexibility if the design changes before the final acceptance with GEP change managed by and approved by Subject Matter Experts (generally engineers). After acceptance GMP change is managed and approved by quality. So another key factor of this approach is that things change and as long as they are managed and documented correctly this is acceptable.

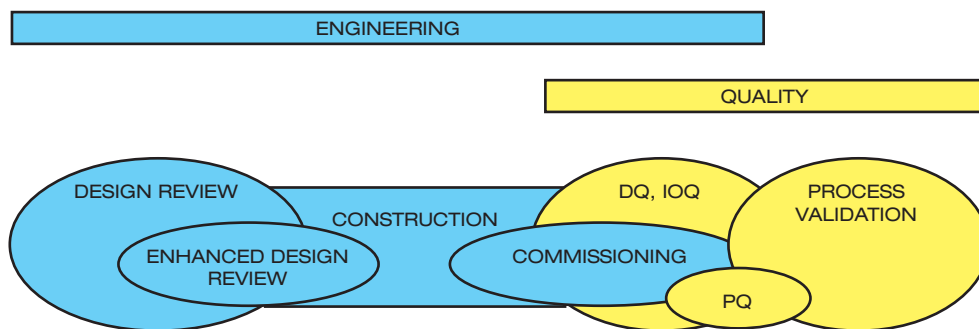
What are the drivers? The main driver for this new standard is to try and simplify the verification process and hence reduce the associated time and cost. As it is estimated that this cost currently can add up to 25% of the total installation cost for new facilities and project there are potentially some large saving here. There is also a saving to be made in not repeating the same testing between commissioning and qualification. The hope is that this new process will improve the time it takes to get drug products to the market.

So when will this happen? The answer to this is not clear. This standard has the support of the FDA, EMEA and GAMP so technically many sites could implement this process. However, although many Pharmaceutical engineers and companies have been talking about a different approach to validation, it will take someone to take the first step in using this standard. This new process will also have a large impact on company practices which are defined by policies, plans and procedures which will need to be updated. So we will all have to wait and see who and how this standard will be interpreted and implemented by. In the meantime the validation "V" model will continue to be the standard approach.

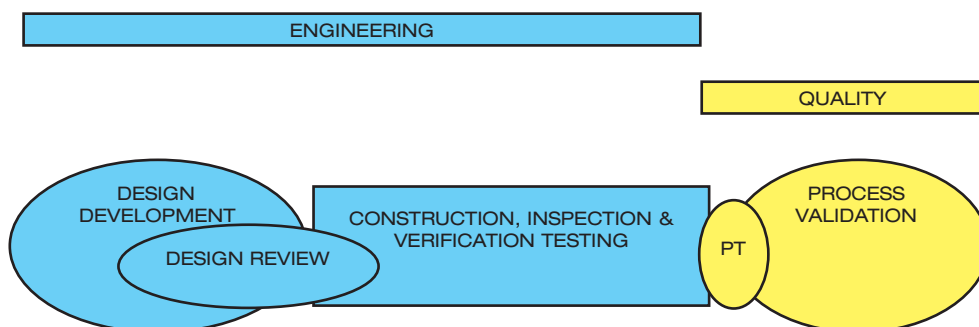
## Current Standards Vs Proposed Standards

- ISPE Baseline Guide 5
  - Design Inputs
  - Impact Assessment
  - Design Qualification
  - Commissioning
  - Multiple Trial Runs to Get Things Right
  - IQ, OQ, PQ and Acceptance Criteria
  - GEP scope and QA scope overlapped
  - Focused on Documentation Deliverables
  - Rigid Change Management
- ASTM E2500
  - Design Inputs
  - Design Review
  - Risk Mitigation
  - Critical Control Parameters Define Acceptance Criteria
  - Verification Testing
  - Performance Testing
  - GEP scope and QA scope have clear boundary
  - Process, Product Quality and Patient Safety
  - Quality by Design, Design Space and Continuous Improvement

### Current Standard validation model



### Proposed Standard.



# Design, Specification and verification.

