DEVELOPING A REAL-TIME QUALITY PROGRAMME FOR DAIRY

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ABSTRACT

The Fonterra Advanced Process Control (APC) programme began in the mid-1990s, with the purpose of maximising plant efficiency and reducing operating costs through the implementation of technologies such as Model Predictive Control. This programme is now an integral part of Fonterra manufacturing operations in New Zealand. A new Fonterra APC initiative called Real-Time Quality is focussing on using online mathematical tools to actively manage product quality during processing as an alternative to traditional approaches of relying on post-manufacture testing. This work is being undertaken in conjunction with researchers from the University of Auckland and Auckland University of Technology as part of the Primary Growth Partnership (PGP) programme.

Process Analytical Technology (PAT) is a widely-accepted term to refer to the use of integrated systems that analyse and control the manufacturing process to assure acceptable end-product quality at the completion of the process. Our initial work has focussed on reviewing current PAT practises in other industries such as chemical and pharmaceuticals in order to identify areas of similarity and difference. Most large-scale dairy processing is continuous rather than batch so there are stronger parallels with chemical than pharmaceutical operations. Dairy processes typically have fewer inline analytical instruments than the other industries, so must rely on inferential modelling to determine product characteristics.

In this paper we evaluate PAT across different industries and describe the aims of the Fonterra Real-Time Quality initiative, in particular, outlining how the focus of our programme differs from the typical PAT research studies.

INTRODUCTION

Advanced Process Control has been a key technology within Fonterra (and its predecessor co-operatives) for more than 15 years. A centralised team of engineers develop, deploy and support APC solutions across manufacturing operations in New Zealand & Australia. The focus of this team is to improve processing efficiency through real-time modelling and control tools. Pavilion8 software from Rockwell Automation is the foundation of this programme. Using this toolset the APC group has developed Model Predictive Controllers as well as Real-Time Product Tracking, Optimisation & Process Monitoring solutions. Early on it became apparent that success could only be achieved with the right technology tools, a well-developed automation and IT infrastructure and a group of talented people. Most of the APC group's solutions focus on delivering benefits in terms of yield, energy efficiency and productivity. Pavilion8 is a logical platform for delivering a new quality initiative throughout Fonterra manufacturing.

Over the last few years, across a disparate group of processing industries, there has been a deliberate shift from controlling production to a focus on quality. In some industries, such as pharmaceutical, this shift has been explicit or even mandated. PAT has become the generally accepted acronym applied to the assessment and control of product quality, and has come to mean far more than the Process Analytical Technologies it was originally used to denote. One reason for this swing towards quality was that the US FDA (Food & Drug Administration), perhaps after a particularly candid assessment of their manufacturing industry, wanted to encourage mechanisms and promote good practice to improved quality and control (FDA, 2004; Munson *et al.,* 2006; Swarbrick, 2007) and hence recommended PAT philosophies be adopted by the pharmaceutical industry. PAT is dominated by a focus on the specifics of analytical technologies for measurement and quality assessment after the fact. PAT can tend to mean different things to different industries and as a result an alternative term - Real-Time Quality has been adopted for our purposes.

FONTERRA'S ADVANCED PROCESS CONTROL (APC) PROGRAMME

Since the mid 1990's Fonterra has had an APC programme running in partnership with Pavilion Technologies (now Rockwell Automation). The Fonterra APC team consists of 11 dedicated control engineers that develop and support APC solutions across Fonterra's manufacturing assets. This programme is underpinned by a Strategic Alliance with Rockwell.

Strategy

- Fonterra's APC strategy focuses on:
- Delivering real-time solutions that improve plant performance and support manufacturing decision-making
- Add value, not cost - implementing technologies to deliver sustained gains in manufacturing efficiency - yield, throughput, energy reduction
- Invest in manufacturing infrastructure as a technology enabler
  - site historians
  - flexible site & enterprise reporting systems
  - good network connectivity (both within and between sites)

The APC group's business model involves managing the lifecycle of APC applications from beginning to end:

1) *R&D activities identify new opportunities & develop new* solutions – prototype development and initial quantification of benefits.
2) *A deployment programme rolls out proven solutions across many plants* – generic solutions are developed from initial prototypes to streamline deployment
3) *Ongoing user support is provided using internal resources* – APC technologies will only generate sustained value when operators are well trained and have confidence in the applications.

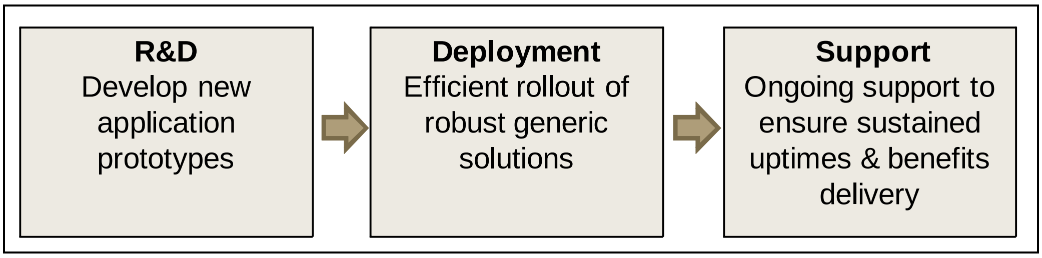

Figure 1: APC group's business model

Generally the focus of Fonterra APC solutions has been on problems where benefits are easily quantified (yield, capacity, energy), solutions with manageable complexity and situations where generic solutions can be efficiently deployed across multiple plants.

Success factors

The Fonterra APC programme has been highly successful, and continues to deliver significant financial benefits annually. The current state of the Fonterra APC programme sees:

- APC solutions running on approximately 40 factories across 16 sites
- Consistent level of IT infrastructure across all plants regardless of age
- Implementation of Information Systems & APC technologies into new plants is a given
- Stable team of talented staff who are skilled in real-time techniques and tools
- Mature engineering standards and formalised internal acceptance processes
- APC programme is now expanding into quality management

On the journey of developing an APC programme there are many aspects that have been learned, which are transferable to the area of Real-Time Quality. Success factors include:

- Strong support & unwavering commitment from senior management
- Having the right people. Good technology by itself won't guarantee success.
- An effective support programme to deliver sustained benefits
- Formalised application handover process for support
- Robust engineering standards to enable efficient solution deployment
- Transparency:
    - Demystifying the technology with the end users
    - Widespread visibility of plant performance and the benefits generated
- A desire to instigate change. Improvements are only achieved if people have a willingness to push the boundaries.

Focus on quality

Fonterra has recently initiated a 7-year project with University of Auckland and Auckland University of Technology. The intention is to leverage the university capability in process control & food R&D to accelerate the development and adoption of PAT tools within Fonterra manufacturing operations. Key deliverables include:

- Development of a PAT framework for food processing industries
- A systematic assessment that quantifies the impact of key flowsheet design attributes on product traceability.

- Tools for real-time estimation of product quality
- Automatic identification & visualisation of process exceptions
- Tools to continuously assess model accuracy

The first step was to review the application of PAT in other industries and to get an understanding of how PAT would fit Fonterra's manufacturing processes and quality management requirements.

REVIEW OF PAT ACROSS DIFFERENT INDUSTRIES

Process Analytical Technology is a multidisciplinary field that involves combining analytical chemistry, engineering, biology, process control and technology with multivariate data analysis. It has been described as "systems for analysis and control of manufacturing processes based on timely measurements of critical quality parameters and performance attributes of raw materials and in-process products, to assure acceptable end-product quality at the completion of the process" (Lopes *et al.,* 2004; Yu *et al.,* 2004; Munson *et al.,* 2006; Rathore *et al.,* 2010; Skibsted & Engelsen, 2010; Menezes, 2011)

With the shift in focus to controlling product quality there has been a rise in activity in the PAT space particularly in the pharmaceutical industry. This has been hastened by the FDA's decision to recommend that the pharmaceutical industry move towards a coherent system "for design, analysis and control of the manufacturing processes, based on timely measurements (i.e. during processing) of critical quality and performance attributes of raw and in-process materials and products to assure high quality final products." (FDA, 2004; Munson *et al.,* 2006; Swarbrick, 2007).

Traditional methods of manufacturing have many flaws that create obstacles for continuous improvements, quality by design (QbD), innovations, and efficiency improvement. These deficiencies are responsible for the high cost of products, lack of consistency in the quality of the finished products, large amount of sampling (including raw materials, intermediates and final products), increased testing time with batch release delays, the large numbers of Out of Specifications (OOS) and rejects. In traditional manufacturing, quality is tested and determined at the finished product and there is no strategy of continuous improvement of quality or quality designed into the product. In traditional manufacturing a specialised staff and laboratory equipment (i.e. HPLC, chemical regents) are required (Munson *et al.,* 2006).

After the publication of FDA's report about PAT introduction and implementation (FDA, 2004), a paradigm shift began to occur from traditional manufacturing to PAT-based manufacturing. PAT is based more on science and logic than specifications. Strict regulatory demands in terms of quality control, safety and traceability are mainly responsible for this move away from relying on post-production quality testing. In other words, under the PAT framework, the industry is gradually moving from inferential monitoring and control towards continuous measurement of quality parameters. PAT represents a silent revolution in industrial quality control and has focus on rapid final product evaluation, increased productivity and enhancing competitiveness (Skibsted & Engelsen, 2010; Van den Berg *et al.,* 2012).

It is not surprising that the meaning of PAT has evolved over the last decade depending on the focus and the specific industry. What is interesting about the FDA's PAT definition is the deliberate single focus on quality as opposed to say production, or the adherence to a control set point, or real-time optimisation, or even safety and sustainability. These latter objectives are of course not mutually incompatible with quality, but here they are simply implicitly assumed (Munson *et al.*, 2006; Rathore *et al.*, 2010; Read *et al.*, 2010; Chen *et al.*, 2011).

The pharmaceutical industry is of course not the only one that embraced PAT (Yu *et al.*, 2004; Moes *et al.*, 2008; Read *et al.*, 2010), although the penetration over other chemical processing and manufacturing industries is uneven. It is no surprise that the closely related food industry also has a long history of using PAT-type thinking (Karoui & De Baerdemaeker, 2007; Van den Berg *et al.*, 2012). The industry shares many characteristics with pharmaceuticals; they both manufacture material intended for human consumption that must meet stringent quality controls, often using batch processes. The material is shipped across country borders and international agreements regarding what constitutes an acceptable product is problematic.

A review of PAT definitions shows general similarities although closer inspection reveals differences between various industries as shown in Figure 2. The dairy and food industry have greatest similarities to the pharmaceutical and chemical industries. They tend to have a narrow range of process specifications like pharmaceutical industry but are similar to chemical industry in terms of process type (continuous or batch), process inputs (feed with variable properties), sample type (homogeneous or heterogeneous) and process control (control limit that gives the highest yield).

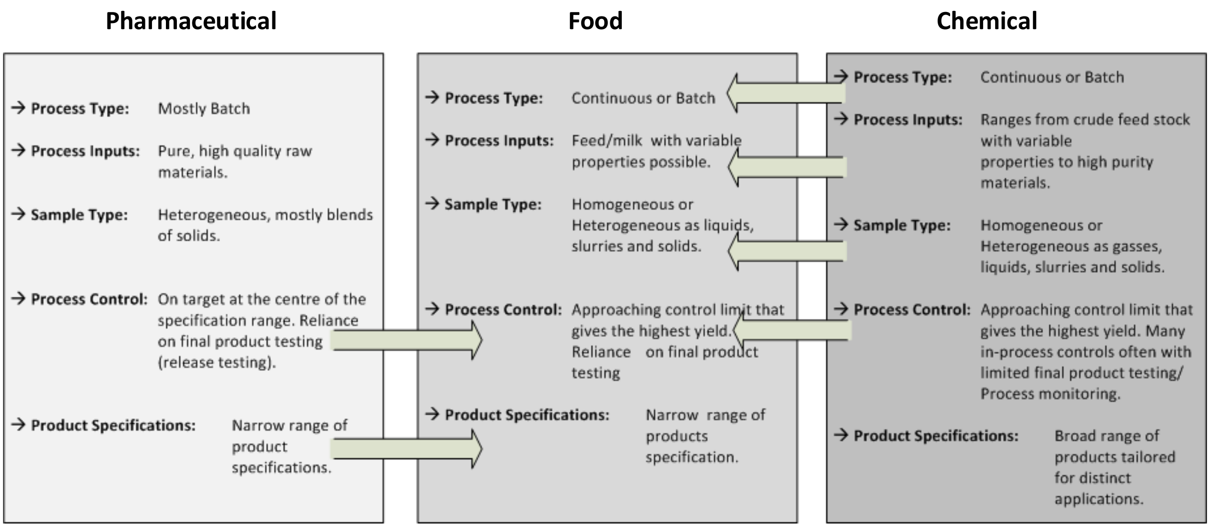

Figure 2: Variation of PAT definitions across different process industries

TECHNOLOGIES AND METHODOLOGIES ASSOCIATED WITH PAT

PAT tools and methods can be categorised as follows:

- Multivariate tools for design, data acquisition and analysis (chemometric approaches such as multivariate statistical and pattern recognition methods);

- Process analysers (at-line, in-line, or on-line measurement of process quality and performance attributes using a variety of instrumentation and measurement strategies such as near-infrared (NIR));
- Process control tools (Process monitoring and control strategies);
- Continuous improvement and knowledge management tools (Data collection and analysis over the life cycle).

Both the food and pharmaceutical industries have traditionally struggled to find ways to adequately measure key parameters in their products, let alone the critical quality attributes mentioned in the FDA definition. They have therefore resorted to sophisticated laboratory analytical instruments such NIR, UV, Raman and front face fluorescence spectroscopy. The underlying common factor is that all of these analytical techniques involve handling of spectra which is essentially a large number of measurements that are highly correlated, and whose relation to the critical quality parameters is obscure. These, we term high-dimensional measurements. The accepted way to manage these sorts of measurements in a numerically robust manner is to essentially reduce the dimension down to a more manageable level using PLS and PCA algorithms derived from statistics and linear algebra. This then introduces a potential confusion. Because PLS/PCA strategies are so common in the treatment of spectroscopic data, and spectroscopic data is so crucial in the production, PAT, or more accurately "PAT tools" have become synonymous with multivariate PLS/PCA techniques applied to NIR data (Eriksson *et al.*, 2006; Skibsted & Engelsen, 2010).

When surveying the varying interpretations of PAT, it is interesting to note that it is not until one looks at the chemical industry that there is an explicit focus on process dynamics and the distinction between dynamic and stationary samples. While multivariate techniques such as chemometrics are highlighted as important components in the PAT toolset, there is also acknowledgement of the more traditional statistical process control techniques that are primarily univariate along with standard process control techniques such as supervision, data reconciliation and gross error detection. What is evident from our preliminary survey is that those industries whose economics are dominated by the production of bulk chemicals are slower to embrace the thinking behind PAT or at least the multivariate-centric interpretation of PAT. Traditionally online or inline spectroscopic instruments are rare in bulk chemical plants, perhaps because the standard pressure/flow/temperature sensors deliver robust information often in an aggressive operating environment in order to characterise the key quality variables. If they fall short, soft sensors such as the extended Kalman filter may be used to fill in the missing information. However when compared to spectroscopic measurements, these traditional lean process sensors deliver relatively modest numbers of variables (the degrees of freedom are small) which are comparatively uncorrelated with each other. Hence multivariate tools are less useful in this environment. In fact it is rare to find a reported application of PAT outside spectroscopic applications.

Whilst PAT is undoubtedly a worthwhile concept, its proponents can get a little over-enthusiastic about what one can realistically achieve. For example, some maintain that the PAT framework leads to process understanding where key sources of process variability are identified and explained, and that one subsequently can then manage the process variability. This is a good example of confusing modelling with controllability. Process understanding might lead to good models, but it does not in itself necessarily lead to good control.

While PAT is concerned with analytical techniques, the associated data processing and the subsequent control, it is really about quality and for that reason the thinking needs to be compared to other quality concepts such as 6-sigma, ISO 9000 or the Toyota Way. Of these latter three, the holistic viewpoint of the Toyota Way with its focus on creating an adept and enabling culture and addressing problems as they occur throughout the entire manufacturing process shares the most with the underlying PAT philosophy (Karoui *et al,*. 2003; Liker, 2004; Karoui & De Baerdemaeker, 2007; Lander & Liker, 2007; Schroeder *et al,*. 2008).

REAL-TIME QUALITY AN ALTERNATIVE TO PAT

In our view, there is something missing from PAT given its dominant focus on the specifics of analytical technology and quality assessment after the fact. Likewise process control thinking can lose sight of quality issues. We have coined the term Real-Time Quality, in an attempt to marry the clear benefits of Advanced Process Control (such as utilising dynamic models to synthesise timely optimal strategies to mitigate against disturbances) with an explicit focus on quality (including ways to quantify and improve it in real-time). The definition of Real-time Quality that has been adopted for our purposes is - Real-time tools for manufacturing that allow desired quality to be reliably attained at lesser cost than existing post-manufacture approaches. The Real-Time Quality thinking is holistic, and therefore needs considerable support from the upper echelons of the organisation. A key performance metric such as the cost of quality failure may not be known until well after the material has left the production site so good record keeping and the closing of the financial information loop is essential. Optimising the whole (what we want) is typically better than optimising the parts separately which is certainly easier to implement. The opportunity is significant but so too are the challenges of sustainable implementation.

To achieve the Real-Time Quality goals, we propose both a structured approach accompanied by a set of key tools. Perhaps due to our own past experiences and comfort zone, our tools will be in the dynamic process modelling and data processing space as oppose to specific algorithms tailored for spectroscopic instruments. Real-Time Quality expresses the desire to focus on product quality assessment and control in a timely manner. This combines on-line measurements, real-time data analysis and modelling techniques that provide the quality assessment together with suitable process control and decision-making tools that provide the real-time management of the product quality. In time, the Real-Time Quality assessments could be used within a product grading system to supplement or replace some of the traditional final product quality tests. Thus the real-time tools will not only assist in making good product during manufacture but also help with the decision-making process around assessment of final product quality.

CONCLUSIONS

The goal of PAT is to enhance the understanding and control of a manufacturing process. The principle is that quality cannot be tested into products; it should be built-in or present by design. The goal of our Real-time Quality initiative is no different. However we have adopted the term Real-Time Quality to clarify the focus of our development aims. PAT has become a broad field but tends to have an emphasis on the use of spectroscopic instruments and multivariate statistical analysis for better process understanding. Our Real-time Quality programme is clear in its deliverables:

- real-time assessment of plant stability and operating region relative to specific bounds
- real-time measurements or inference of product quality attributes
- real-time assessment of product quality
- real-time control or decision-making tools including:
    - automatic process regulation or
    - visual displays or alerts for plant staff
- the association of real-time quality metrics and assessments to defined units of finished products
- the use of real-time quality metrics and assessments within an accepted product grading system

These could be considered ambitious aims however with a focussed and well-managed programme of development, the technology and techniques exist to successfully achieve these outcomes. Having an existing and successful APC programme provides the necessary foundation for this undertaking.

REFERENCES

Chen, Z., D. Lovett and J. Morris (2011). "Process analytical technologies and real time process control a review of some spectroscopic issues and challenges." Journal of Process Control **21**(10): 1467-1482.

Eriksson, L., E. Johansson, N. Kettaneh-Wold, J. Trygg, C. Wikstrom and S. Wold (2006). Multi- and Megavariate data analysis: Basic principles and applications (Part I). Umeå, Sweden, Umetrics AB.

FDA (2004). PAT — A framework for innovative pharmaceutical development, manufacturing, and quality assurance. Rockville, MD, U.S. Department of Health and Human Services. Food and Drug Administration Center for Biologics Evaluation and Research.

Karoui, R. and J. De Baerdemaeker (2007). "A review of the analytical methods coupled with chemometric tools for the determination of the quality and identity of dairy products." Food Chemistry **102**(3): 621-640.

Karoui, R., G. Mazerolles and É. Dufour (2003). "Spectroscopic techniques coupled with chemometric tools for structure and texture determinations in dairy products." International Dairy Journal **13**(8): 607-620.

Lander, E. and J. K. Liker (2007). "The Toyota Production System and art: making highly customized and creative products the Toyota way." International Journal of Production Research **45**(16): 3681-3698.

Liker, J. K. (2004). The Toyota Way—14 Management Principles from the World's Greatest Manufacturer New York, NY, McGraw-Hill.

Moes, J. J., M. M. Ruijken, E. Gout, H. W. Frijlink and M. I. Ugwoke (2008). "Application of process analytical technology in tablet process development using NIR spectroscopy: Blend uniformity, content uniformity and coating thickness measurements." International Journal of Pharmaceutics **357**(1–2): 108-118.

Munson, J., C. Freeman Stanfield and B. Gujral (2006). "A Review of Process Analytical Technology (PAT) in the U.S.Pharmaceutical Industry." Current Pharmaceutical Analysis **2**(4): 405-414.

Rathore, A. S., R. Bhambure and V. Ghare (2010). "Process analytical technology (PAT) for biopharmaceutical products." Analytical and Bioanalytical Chemistry **398**(1): 137-154.

Read, E. K., J. T. Park, R. B. Shah, B. S. Riley, K. A. Brorson and A. S. Rathore (2010). "Process analytical technology (PAT) for biopharmaceutical products: Part I. concepts and applications." Biotechnology and Bioengineering **105**(2): 276-284.

Read, E. K., R. B. Shah, B. S. Riley, J. T. Park, K. A. Brorson and A. S. Rathore (2010). "Process analytical technology (PAT) for biopharmaceutical products: Part II. Concepts and applications." Biotechnology and Bioengineering **105**(2): 285-295.

Schroeder, R. G., K. Linderman, C. Liedtke and A. S. Choo (2008). "Six Sigma: Definition and underlying theory." Journal of Operations Management **26**(4): 536-554.

Skibsted, E. and S. B. Engelsen (2010). Spectroscopy for Process Analytical Technology (PAT). Encyclopedia of Spectroscopy and Spectrometry (Second Edition). L. Editor-in-Chief: John. Oxford, Academic Press**:** 2651-2661.

Swarbrick, B. (2007). "Process analytical technology: A strategy for keeping manufacturing viable in Australia." Vibrational Spectroscopy **44**(1): 171-178.

Van den Berg, F., C. B. Lyndgaard, K. M. Sørensen and S. B. Engelsen (2012). "Process Analytical technology in the food industry." Trends in Food Science & Technology(Accepted).

Yu, L. X., R. A. Lionberger, A. S. Raw, R. D'Costa, H. Wu and A. S. Hussain (2004). "Applications of process analytical technology to crystallization processes." Advanced Drug Delivery Reviews **56**(3): 349-369.