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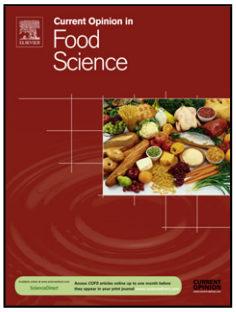

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Real-Time Product Release and Process Control Challenges in the Dairy Milk Powder Industry

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Abstract

Real-time release testing in the dairy milk powder industry may potentially be achieved by implementing process analytical technology. Research advances have focused on the application of spectroscopic sensors and multivariate data analysis, while neglecting suitable process control strategies and decision-making tools to control critical quality attributes. Due to the unique characteristics of this industry, real-time release, and process control challenges need to be considered before achieving the goal of real-time product release. For example, complex quality attributes can be inferred using proxy measurement; the dependence of advanced analytical sensors can be minimised by using standard pressure/flow/temperature sensors; and investment is required in additional resources and skills for advanced analytical sensors, multivariate models, and control strategy development.

Keywords: Process analytical technology, real-time release, process control

1. Introduction

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This paper discusses process analytical technology research activities, prominent trends, real-time release and process control challenges in the milk powder processing industry. In this study, the milk powder industry based on bovine milk feed only was considered.

Like other process industries (e.g. pharmaceuticals), the dairy processing industry likes to release their products in real-time. Real-time release testing is defined as “the ability to evaluate and ensure the quality of in-process and final product based on process data” [1]. There are several benefits of using real-time release testing for manufacturers such as shorter business cycle time, decreased analytical testing, and reduced inventories. The shorter business cycle time attainable through real-time release testing is because manufacturers do not need to wait for quality results to finish their production cycle and distribute their batch(es). However, other real benefits of real-time release testing for the process industries include increased process and product understanding.

The facilitating approach or system that can achieve real-time release testing in the process industry is known as process analytical technology (PAT). Process industries implement PAT for real-time release testing. The concept of PAT was originally introduced for the pharmaceutical industry in 2004 by the US Food and Drug Administration (FDA). The FDA has described PAT as “systems for design, analysis, and control of manufacturing processes based on real-time process monitoring 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” [2]. The term PAT is now applied in various other industries such as chemical, dairy processing, and other food industries [3]**.

The concept of PAT is based on process understanding, science, and a risk-based approach. Under the PAT approach, process industries are not required to validate processes by providing repeatable quality. Instead, the approach focus is a science-based understanding of how critical process parameters impact critical quality attributes. The design of experiments approach [4] and multivariate data analysis are usually employed to determine relationships between critical process parameters and critical quality attributes (i.e. how variations in critical process parameters affect critical quality attributes), and the boundary limits of critical process parameters for desired product quality.

2. PAT components

According to the US Food and Drug Administration (FDA) [2], the PAT approach has three main components: process analysis, multivariate data analysis, and process control. At – line, in – line, or on – line process analysers are required to measure and monitor critical process parameters and critical quality attributes. Multivariate data analysis tools are used to understand critical process parameter' relationships with critical quality attributes, identify values of critical process parameters needed to achieve desired critical quality attributes, and identify dominant patterns in the data sets, such as groups, trends, and outliers. Process control tools (e.g. statistical process control performance monitoring) are used to monitor and execute control actions [5, 6] based on critical process parameters and critical quality attribute measurements.

3. PAT in the dairy industry

This section briefly summarises recently published literature about real-time release testing or process analytical technology (PAT) activity in the dairy industry. Prior to commencing it is interesting to note that the dairy industry has unique characteristics which are quite different from other industries (e.g. pharmaceuticals) already implementing PAT. For example, the dairy industry raw materials (e.g. milk) are highly variable and heterogeneous in nature [7, 8]. Critical quality attributes include multi-array functional properties which are hard to measure (e.g. taste and flavour). The dairy milk powder industry also uses mostly semi-continuous processing [9] and has a high-volume to low-value product ratio. It is important to consider these unique characteristics before implementing PAT in the dairy milk powder industry.

In the dairy industry, real-time release testing or PAT activity is mainly dominated by spectroscopic technologies for process analysis, the first of the three main PAT components [3] **. This observation might be due to the fact that spectroscopy can be used to predict product quality after statistically relating a measured signal to a reference signal. Spectroscopic technologies such as mid-infrared spectroscopy, near-infrared [10], and front-face fluorescence spectroscopy [11] have been applied in the dairy industry. Spectroscopic techniques are routinely applied in the dairy industry for compositional control to standardise the fat, protein and moisture content of the powder [12, 13]. However, this is generally not reported on, as aspects of it are commercially sensitive.

Other than for compositional control in the process, one example of the application of spectroscopic PAT techniques is for monitoring the adulteration of infant formula. Melamine (2,4,6-triamino-1,3,5-triazine) addition to infant formulas in small amounts (up to 2.5 ppm) increases the apparent protein content reported by standard post production tests as because it is high in nitrogen. However, a high dose is toxic, and a recent incident of melamine contamination in infant formula resulted in more than 300,000 children being affected with renal complications in China [14, 15]. Mauer et al. [16] evaluated the ability of near- and mid-infrared techniques to detect and quantify melamine in infant formula rapidly. Models of spectral data of infant formula containing between 0.1 – 40 % melamine were correlated with melamine concentration using partial least-squares models with regression coefficients, R^2, of more than 0.99. Furthermore, factorization analysis of spectra was successfully used to differentiate between unadulterated infant formula from samples containing 1 ppm melamine. Mauer et al. [16] concluded that near- and mid-infrared techniques are non-invasive, require little or no sample preparation, and can rapidly detect and quantify melamine in infant formula powders.

PAT applications in the dairy milk powder industry are not restricted to spectroscopic analyses or to compositional characteristics only. Milk powders are also quality tested for functional performance, sensory and microbiological attributes. These quality tests tend to be highly labour intensive and, often, as in the case of sensory and functional performance, subjective. Furthermore, they are usually carried out post-production with a significant time delay [17]. Nonetheless, it is still possible to implement PAT with these characteristics. For example, using particle size as a proxy measurement for inferring the dispersibility of powder during manufacture [18] **. The dispersibility test is one of a number of tests that measure the dissolution ability of instant whole milk powder, and is very labour and time intensive and often carried out post manufacture [18, 19]. However, the dispersibility of milk powder is largely dependent on the particle size distribution [19, 20]. Thus Boiarkina et al. [18] ** have proposed the use of particle size distribution measurement to infer whether the powder dispersibility specification is being met during manufacture. Boiarkina et al. [18] ** found that particle size distribution measurement could be used for this purpose, however, due to the subjective nature of the dispersibility test itself, false-positive and false-negative test rates have to be factored in when using this proxy test. Particle size distribution of powder can be measured on-line, at-line or in-line, and a number of industrial instruments are available on the market, such as the MYTA® online particle size measurement (by Buhler Group) or the Insitec device (by Malvern). This creates the opportunity for large scale industrial plants that rely on post-production testing to be able to correct poorly dispersing powder during manufacture [18] **.

However, from the review of the published literature about real-time release testing or PAT activity, it is evident that the implementation of PAT is heavily biased towards discussion of spectroscopic analysis. Many manufacturers are introducing advanced spectroscopic instruments to reduce outmoded laboratory systems but without closing the control loop. This can lead to a potential confusion and an incorrect perception that PAT is just a spectroscopic sensor integrated into a process.

Multivariate data analysis tools and applications also dominate PAT research activities in the dairy industry. This might be due to the fact that multivariate data analysis tools are required to be used in combination with spectroscopic technologies, which are the most common analysis methods. Mathematical tools such as principal component analysis, and partial least squares regression are therefore commonly employed in the dairy industry to manage high dimensional data, building relations between critical process parameters and critical quality attributes, and improving process understanding [21, 22].

There appears to be limited research activity on closing the control loop to achieve real-time product release or successful PAT implementation in the dairy industry. Most of the studies about process control in real-time release testing or PAT primarily focus on constructing critical quality attributes from the raw materials and do not explain what is subsequently done with critical quality attributes. A few exceptions do however exist such as the use of multivariate statistical process control for automatic control in API manufacturing [23] and regressing a data-driven model from operating data to estimate milk powder function properties [24][*].

4. Challenges to implementing real-time release testing in the dairy industry

Both real and perceived challenges hinder real-time release testing or process analytical technology (PAT) implementation in the dairy industry.

4.1. Subjectivity of Quality Parameters

One key challenge of incorporating PAT into the dairy industry is that a number of the quality tests are highly subjective (such as sensory attributes [25]) or labour intensive and difficult to measure [18] **. This means that for some tests it is a physical impossibility to make the test on-line or even off-line, such as the use of sensory panels for flavour evaluation. Tests that could conceivably be automated to at least off-line measurement are often highly discretized and defined by the test procedure itself, such as the measurement of rehydration properties [18] **. This makes it very difficult to create robust automated measurements based directly on these quality tests.

If alternative, proxy measurements are sought then this creates additional questions as different physio-chemical properties can result in changes to a single functional or sensory attribute. For example, changes in the wettability of instant milk powder can be caused by changes in both the particle size and lecithination [20], which are very different powder characteristics. This means that more than one type of on-line measurement might be required to be able to resolve a single functional or sensory characteristic.

The complexity of the quality attributes in dairy powders inherently creates a large challenge for the implementation of PAT.

4.2. Requirement of advanced analytical sensors and data management

The first real challenge is to collect precise, accurate and reliable critical process parameter and critical quality attribute data in real-time in an industrial environment. Spectroscopic analyzers have been used in pharmaceutical industry labs for this purpose. Although most dairy plants also make use of inline near-infrared for standardisation purposes, spectroscopic techniques are not appropriate for all quality parameters, especially given the cornucopia of sensory and functional properties. And unlike the pharmaceutical industry, the critical quality attributes in the dairy industry are difficult to measure using a single instrument, as discussed in Section 4.1. This means that novel instruments and novel methods are necessary to be able to measure these properties, which requires further research. Furthermore, the use of advanced instruments in the industry is always fraught with practical issues, including complex implementation (in terms of sampling), reliability and maintainability, and safety [26].

Once an instrument is installed, the data coming from it needs to be stored somewhere so that it can be used. Given that most of the quality parameters measured in the dairy milk powder industry are not measured on-line, or in real-time, the information technology infrastructure often is not yet set up for capturing data that is designed to be captured in real-time. Creating an ad-hoc system for dealing with the data may complicate the implementation of the technology, as it may not be stored in the right form to be made the most use of. This creates an additional expense when considering the implementation of a new analytical sensor.

4.3. Requirement of calibration models

There are two types of models that are required for the successful implementation of PAT: 1) a model for calibrating the analyser to the critical quality parameter of interest, and 2) a model for calibrating the plant process parameters to the on-line analyser.

Calibration models are required to transform analyser measurements into a critical quality attribute of interest. However, the development of these calibration models initially has to be done at the laboratory scale. Depending on the type of data coming from the instrument, the models may need to be multivariate, in order to handle multiple data from different instruments, or spectral data from a single instrument. However, there is a large knowledge gap in the dairy milk powder industry around how to calibrate different analysers to the subjective quality attributes.

Furthermore, although novel sensors are being investigated, often these are not being calibrated against the industrially relevant tests, making the transformation from research to the industrial application more challenging. For example, the use of focused beam reflectance measurement for studying the rehydration of dairy powders [27], may not be calibrated against the relevant industrial wettability, dispersibility, and solubility tests.

The second type of calibration model that is needed is one that connects the on-line measurement to the process data [28]. This is needed for closing the process control loop, such that it is clear what process levers need to be pulled to effect a desired change in this attribute. It should be noted, that although this type of model of process parameters can be calibrated against a novel analyser, it can also be calibrated against the quality attribute of interest directly (e.g. using the process data as a soft sensor). For example, Rimpallainen et al. [24][*] looked at the development of a black-box model to predict sediment test results at a milk powder plant from the process variables and showed that the ability to predict poor sediment results was challenging. These models are difficult to develop as they generally require significant plant understanding and either historical data [29] or the ability to perform plant trials to evaluate the effect of operational parameter changes to be successful.

4.4. Ensuring process control is not forgotten

Another real challenge is closing the control loop to achieve real-time release testing or successful PAT implementation in the dairy industry. Process control component of PAT for real-time product release has lagged behind the other two core components (process analysis, and multivariate data analysis). Measuring critical process parameters and critical quality attributes in real time, and understanding their relationships without feed-back or feed-forward control actions provides little value to the real-time release testing aim of the dairy industry. Furthermore, real-time execution of multivariate calibration models needs to integrate control strategies, process and quality data to keep the process within control limits. As a result, PAT implementation adds more challenges that require understanding the process dynamics and knowledge of process control methods. The dairy industry will not get full benefits of PAT until there is an explicit focus on process control for real-time product release [3] **.

4.5. Requirement of systems integration

Systems integration is one of the biggest real challenges to deploying real-time release testing or PAT in the dairy industry. A successful PAT implementation integrates PAT software and hardware systems in a way that enables real-time monitoring and control.

4.6. Fear of the unknown and regulatory approval

"Fear of the unknown" is perceived as the biggest challenge because some manufacturers have never used the PAT approach before. They are unsure about how the PAT system will work on their plant and how that will affect their normal operations and plant scheduling. There is also a need of 'customer acceptance' of using PAT as a real-time release mechanism, as the aim is to release the product before any customary quality results have become available. Customers may need to be convinced that data used for real-time release is a robust indication of the product meeting their specification needs. This comes back to the necessity of calibration models, discussed in Section 4.3, that are industrially relevant, such as ones that are calibrated against the International Dairy Federation Standards.

5. Conclusions

The dairy milk powder industry has unique characteristics which are quite different from other process industries already implementing real-time release testing or process analytical technology (PAT). These unique characteristics need to be considered before implementing real-time release testing or PAT on any dairy plant.

When real-time release testing or PAT research activities in the dairy industry were surveyed, it was clear that spectroscopic analyzers and multivariate data analysis tools have enjoyed the widest application in the PAT implementation. On the other hand, suitable process control strategies, and decision-making tools to control critical quality attributes are not prominent in literature.

The dependence of advanced analytical sensors can be minimised by using the standard pressure/flow/temperature sensors which deliver robust information often in an aggressive operating environment to characterise the key quality variables. Buying spectroscopic analysers needs to be encouraged as well. Additional resources and skills are required for advanced analytical sensors, multivariate models and control strategy development. Software, hardware, and data management tools are also needed for implementing real-time release testing or PAT in the dairy milk powder industry.

The dairy milk powder industry cannot get the full benefits of real-time release testing or PAT approach until real-time closed loop process control is integrated with process analysers and multivariate data analysis tools. The combination of real-time critical quality attributes measurements, suitable mathematical tools, and automated control schemes is needed to achieve the real benefits of real-time release testing or PAT in the dairy milk powder industry.

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Highlights

- Real-Time Product Release and Process Control Challenges in the Dairy Industry
- The dairy milk powder industry has unique characteristics
- Unique features of dairy industry need to be considered before PAT implementation
- An explicit focus on process control for real-time release testing is needed