



# Quality control from the very start

Because the pharmaceutical industry is highly regulated, final products are required to meet very strict specifications. According to Professor Staffan Folestad, Senior Principal Scientist at AstraZeneca in Mölndal, Sweden, however, this does not mean that the industrial process is optimised.

A customer case study presented by Umetrics

“There is only one way to achieve this: quality control must be integrated into the process”. To achieve this, AstraZeneca uses software from Umetrics.

As with the manufacturing industry's Total Quality Management, Staffan Folestad would like a quality control tool that is integrated into the production line using strict requirements and measurement techniques. By using Process Analytical Chemistry (PAC), the pharmaceutical industry has made some progress in this effort. The development of chemometrics and multivariate data analysis (which uncovers extensive information from previously thought unmanage-

able data sources) has also helped in this process. The process, however, has focused on measurement data from traditional parameters: time, temperature, pressure, and flow. These parameters, according to Professor Folestad, are physical factors and only indirectly relate to chemistry.

“What is really new are measurement methods that allow us to measure chemical content. This is something that is much more difficult”.

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*Chemical processes are like ‘black boxes’. You cannot just start measuring; you have to know that you are measuring the right parameters.*”

## The go ahead for PAT

Professor Folestad compares chemical processes to ‘black boxes’. You cannot just start measuring; you have to know that you are measuring the right parameters. This is where Umetrics software for both design of experiments and multivariate data analysis is useful. For example, Folestad notes that the parameters that industry has to measure to meet the requirements of regulatory authorities, such as content, effect, and therapeutic

results, are all linked to the patients. These parameters, however, are not necessarily the parameters that should be measured in manufacturing.

Process Analytical Technologies (PAT) are now being developed to help in this effort. The PAT model will be used increasingly now that the FDA has begun encouraging the pharmaceutical industry to use it. This is despite the fact that PAT is currently only being used by about 5% of companies according to the FDA.

## Design of experiments is the key

According to Professor Folestad, the most important tool for increased understanding of chemical processes (and thereby being able to efficiently produce drugs) is design of experiments.

"This is the only way to quantify relations between the product's properties and how it is processed. Although you may know the theory behind drug manufacturing and use, reality is often more complex, especially since every drug is based on a new chemical substance".

Design of experiments is a systematic approach. A mathematical model is developed based on a hypothesis on the optimal way of processing. This model can be optimised through design of experiments.

"Design of experiments is regularly used at AstraZeneca in Mölndal. Naturally it is most important for researchers and engineers when developing new products, but we also see it as a way of structuring our experiences and minimising the number of experiments".

This is why MODDE® for design

of experiments is used throughout the entire product chain, from R&D to production and quality control, as part of routine monitoring. When problems are found, the tools help find the causes.

## Assured quality and reduced product waste

Money can be saved by making production more effective (i.e., less product waste). Design of experiments also shortens lead times for producing new drugs and thereby limits the long development times, which often are between 10 and 20 years. Professor Folestad emphasises the value of design of experiments to create better understanding of the chemical processes "to avoid problems later". This helps avoid late set backs in the process when costs can skyrocket.

"This is both an active tool and indirect support for assuring customers of quality".

Professor Folestad points out that good design of experiments also means simpler systems can be used for quality control.



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## Umetrics knows the entire chain

It is important to provide structure to development work, from the start to the finish. Professor Folestad sees this as something of a paradigm shift, and he believes that the entire pharmaceutical industry will adopt this approach in the coming years to ensure uniform quality and uniform production. AstraZeneca isn't waiting around for the stragglers.

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Since 2000, AstraZeneca in Sweden, is a client of Umetrics' Enterprise Platform (EP), complete with software, training in design of experiments and multivariate data analysis, and consulting services. Today, the EP concept is increasingly used throughout AstraZeneca. Professor Folestad notes that although "there is other software for the design of experiments and multivariate data analysis, none is as complete as Umetrics". ■

### AstraZeneca

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