



## Process Analytical Technology (PAT): Recommendations for Statistical Software to Support PAT

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# Process Analytical Technology (PAT): Recommendations for Statistical Software to Support PAT

## Introduction

Process Analytical Technology (PAT) and Quality by Design (QbD) guidance from the FDA stresses the importance of manufacturing process understanding and control. Integral in those efforts is the utilization of proper statistical analysis processes and platforms. Over the years, StatSoft has been in numerous relevant collaborations with Pharmaceutical and Bio-Pharmaceutical manufacturers and has learned about a number of factors that are important in applying the statistical software to support PAT and QbD projects. This paper outlines and discusses those factors.

## Background

This paper is not an exhaustive coverage of Process Analytical Technology (PAT) or Quality by Design (QbD). StatSoft points you to the FDA guidance as good sources of information about the detailed recommendations. Instead, what is important are the major themes in terms of the guidance and the recommended tools: Both PAT and QbD have the potential to change the approach to quality in Pharmaceutical and Bio-Pharmaceutical manufacturing by focusing on process understanding and monitoring as tools for repeatable quality outcomes. The FDA makes it clear that each of these initiatives has important components such as experienced people (including process engineers, quality professionals, and statisticians), processes, and tools (including sensors and multivariate statistical software).

## Recommendations

In our years of experience, StatSoft has worked with a number of companies, large and small, both Pharmaceutical and Bio-Pharmaceutical, at differing stages of adoption of PAT and QbD, and across a range of project types.

Through this experience, we have accumulated a set of five best practices in our area of expertise, that is, statistical software and its applications:

### 1. Think Holistically and Long Term

We encourage our colleagues, when considering how to equip their organizations with the proper statistical software tools, to think globally and long term about the needs for these initiatives, and to think of them together and across departments, rather than focusing on niche applications. In the past, sometimes we have seen companies consider individually their needs for Principal Components (PCA)\Partial Least Squares (PLS) or their needs for Design of Experiments (DoE) as individual and wholly separate endeavors. In contrast, it is our

recommendation to consider these needs and the other statistical analysis needs together. Unfortunately, we have encountered companies that licensed software for niche needs and then faced the issues that they lacked software for comprehensive graphical data analysis that would allow robust querying of their databases, that would provide flexible general linear models (GLM), that would provide recursive partitioning (“tree” methods such as CART, CHAID, Random Forests) or neural networks methods for when PCA or PLS is not a fit for the particular process/data. In addition, it is sometimes the case that there are countless hours invested in determining how to share data between the applications and how to implement a common framework for importing data from the various data repositories in a format that all of the various statistical software applications can share.

In contrast, an alternative approach is to evaluate the statistical software needs holistically, both in terms of short-term (immediate) and long-term needs, “future proofing” your company as additional tools are needed as the PAT and QbD efforts grow and change and are applied to other sites and processes.

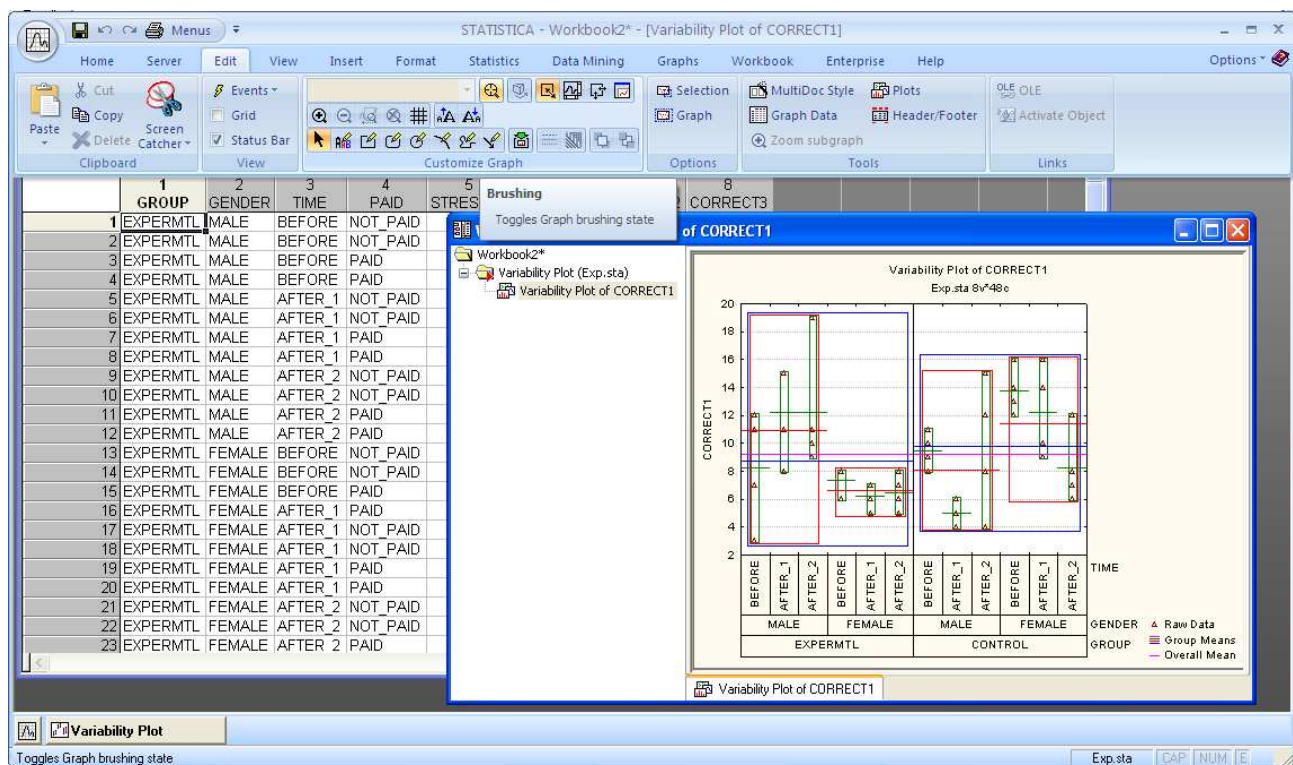


Figure 1: Graphical Data Analysis as one important component

For example, *STATISTICA Enterprise* provides an analysis platform for both ad hoc interactive and exploratory applications and for the configuration of workflows and analysis applications. It provides a rich assortment of data analysis and predictive modeling tools, data management and data transformation options, and graphical data analysis capabilities.

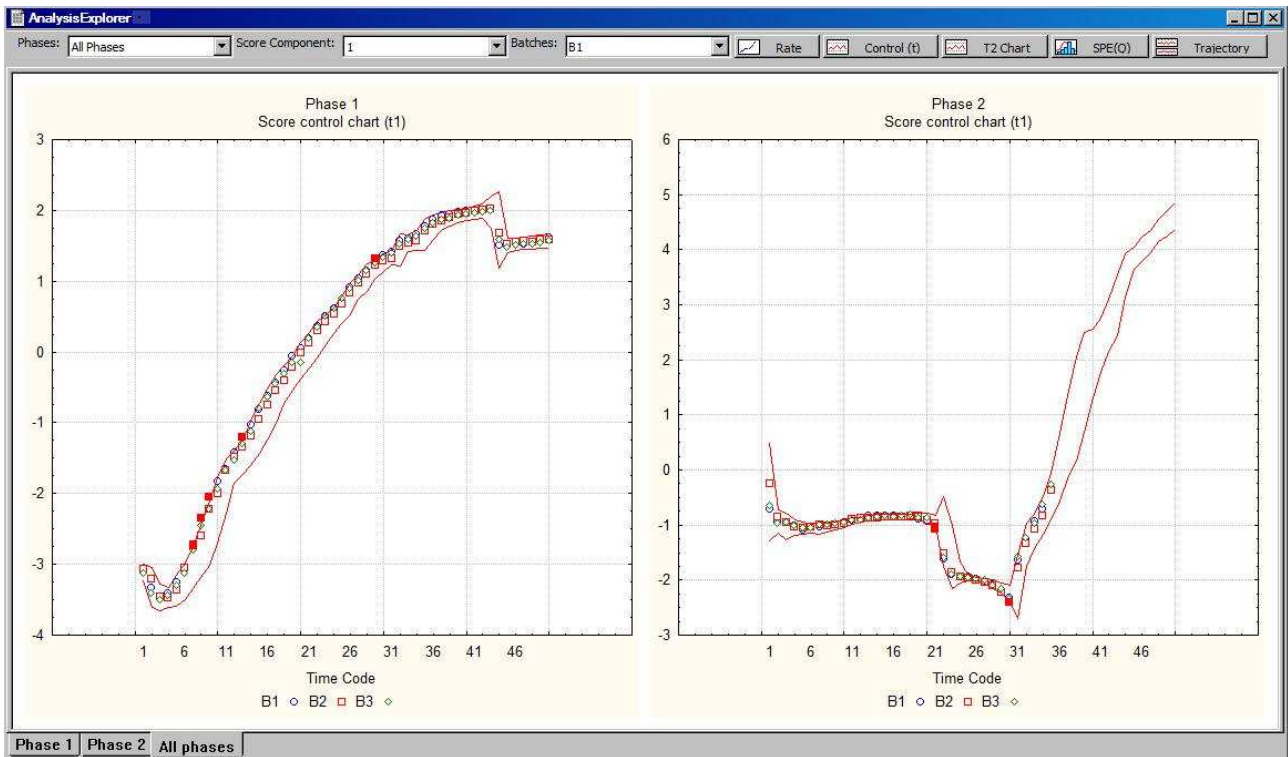


Figure 2: STATISTICA Enterprise for Online Multivariate Analyses (PCA)

Lastly, the PAT needs are both offline and online, for both the analysis of historical batches and for the monitoring of current batches as they mature. Even if the immediate process needs are such that they are offline, it is important to consider that these needs will grow and that other sites and processes may need online multivariate analysis (MVA).

## 2. Think Across Departments and Sites

PAT and QbD efforts surely do not involve individual people working in isolation, using stand-alone applications. Instead, they are project- and team- based and are constantly evolving and growing as new personnel are added.

It is important that the software fit that context of use by empowering users to work together and collaborate, while also respecting their various roles and responsibilities.

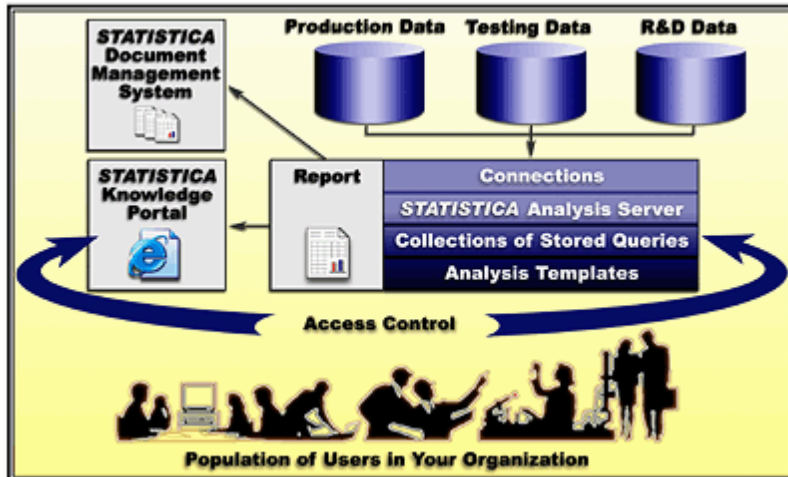


Figure 3: STATISTICA Enterprise Multi-User Features

From this perspective, the following items become important considerations:

- Users/Groups and Roles/Permissions
- Central configuration and management of the user interface organization, connections to data repositories, queries to data and metadata about these data
- Features for users to share reports, results, and data in a secure and flexible way
- Multiple approaches to deployment to meet various needs including client/server, workstation, and Web-based architectures

### 3. Think About the Data Sources

Much of the work in PAT and QbD applications is in the planning stages and the data acquisition and understanding tasks. Often, the difficult and time-consuming part is getting access to, aggregating, organizing, and understanding the relevant data.

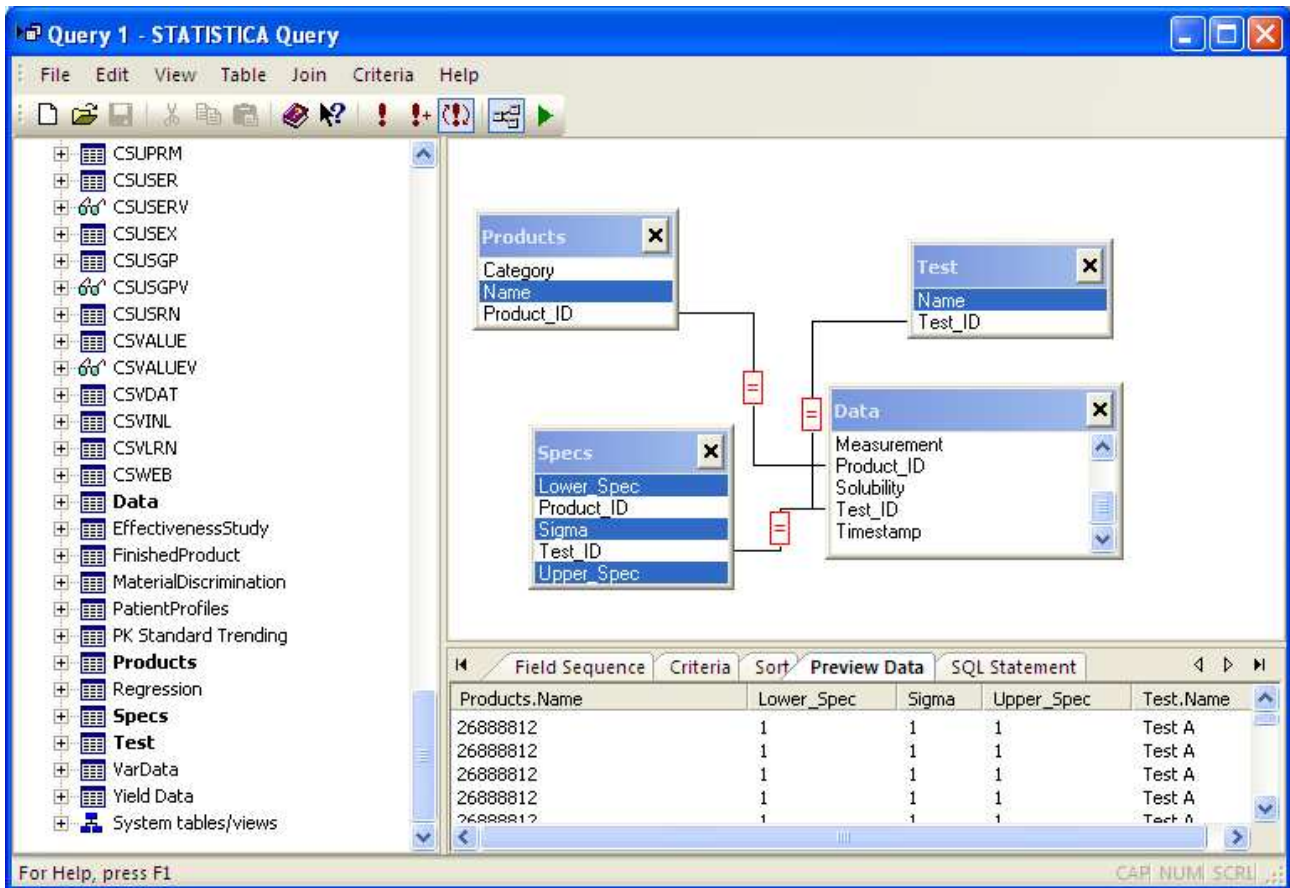


Figure 4: Querying capabilities in STATISTICA Enterprise

It is important to consider all of the relevant data sources for the successful and streamlined access to these data, as required ongoing for PAT and QbD initiatives.

#### 4. Think Compliance

At some stage in your company’s adoption of PAT and QbD, the process understanding and monitoring will be used for decision making, will impact consumer safety, and will be relevant to GMPs (Good Manufacturing Practices). It is important to consider the compliance features of the software platform and how easy it will be to validate, when that becomes relevant.

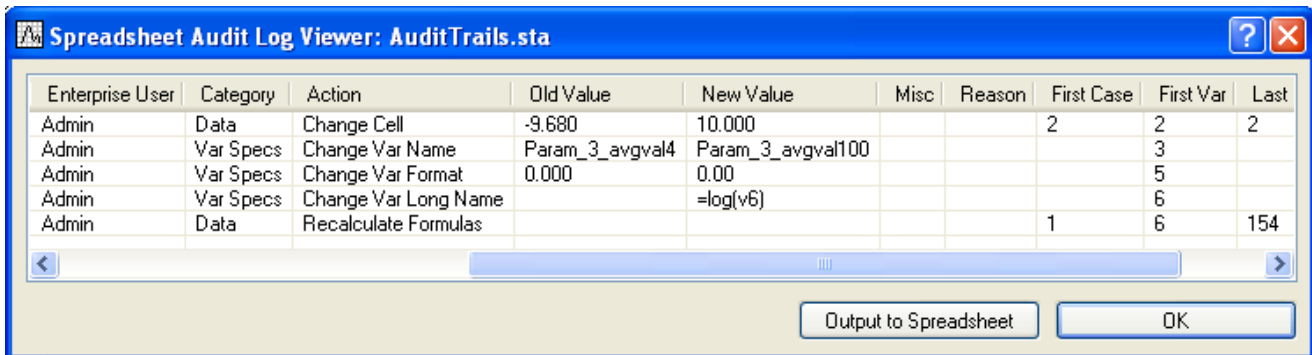


Figure 5: Audit Trails on Data Changes in STATISTICA Enterprise

## 5. Think Ease-of-Use

Many people will be involved in PAT and QbD efforts. They will have different levels of experience and knowledge of statistics. How easy will it be to train them on the software? Does the software have the tools for the “power users?” Does the software provide the option for a more streamlined user interface for the bulk of the users who are making decisions based on the results? How easy is it to automate routine tasks by recording macros?

## Summary

In summary, based on our experience in collaborating with companies to support their PAT and QbD initiatives, we recommend thinking about the following critical items when considering how to support the statistical software needs of your company’s initiatives:

- Think Holistically and Long Term
- Think Across Departments and Sites
- Think About the Data Sources
- Think Compliance
- Think Ease-of-Use