

Abstract

Quality by Design is a science and risk-based approach to pharmaceutical development and manufacturing technologies. The **De Montfort University MSc in Pharmaceutical Quality by Design** is based on the application of product and process sciences, from early to late stages of the product development cycle. The course equips graduates with the relevant knowledge and skills to compete for global jobs in the pharmaceutical and healthcare sectors and academia. We believe that JMP provides the capability to help students accelerate experiential learning.

Organisational Memory

When I left GlaxoSmithKline to set up **Insight by Design**, it occurred to me that one of the severe consequences of the downsizing, restructuring and outsourcing that takes place in the Pharmaceutical industry, is the loss of organisational memory associated with data driven decision making. The churn of personnel is even greater in academia. Each year, a new cohort of De Montfort students investigates the preparation of tablets and oral dose suspensions. How can I, along with other lecturers, help the current cohort access the experience and knowledge gained by past students?"

Exploiting JMP functionality

The Aim

- To access prior information in order to perform more efficient and effective experimentation.

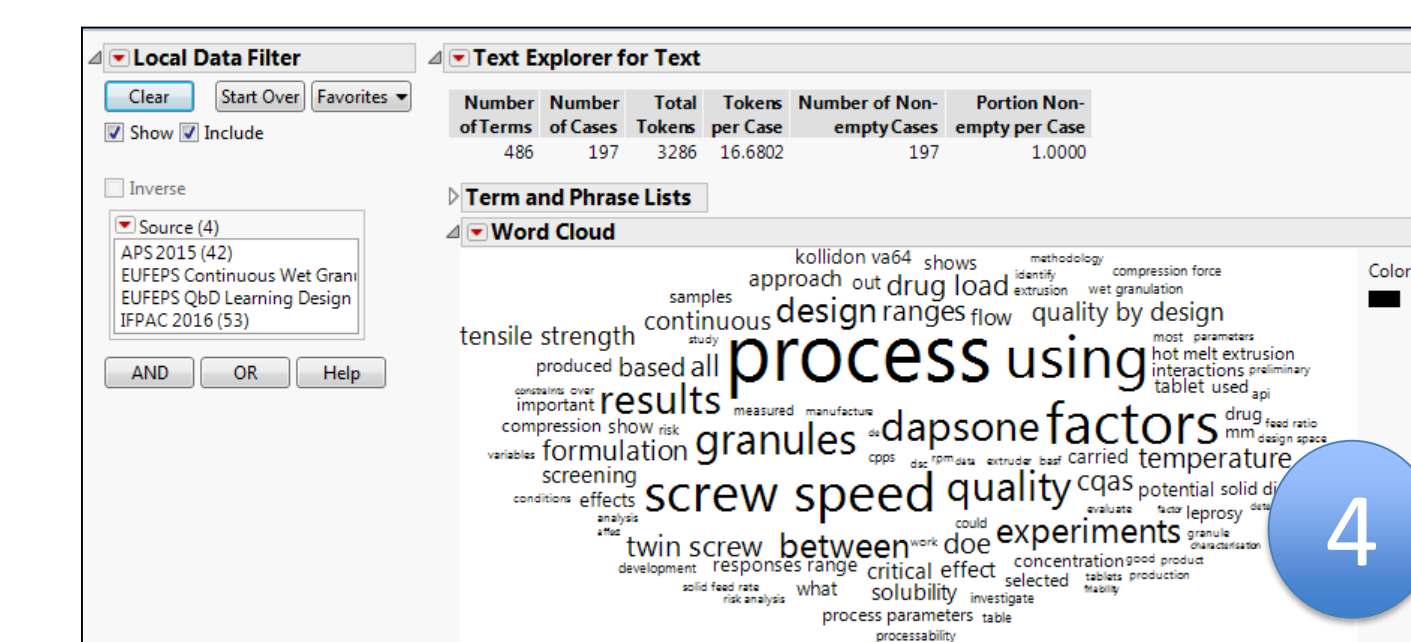
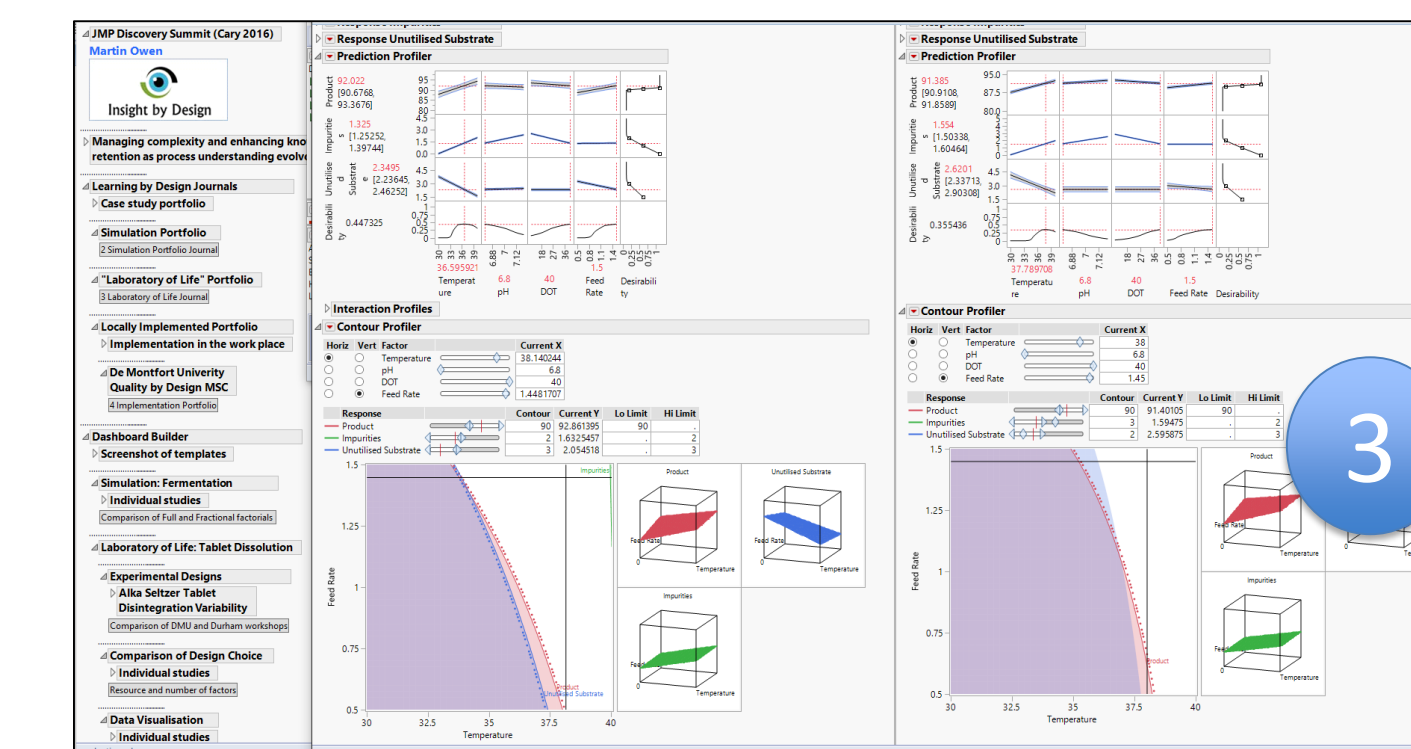
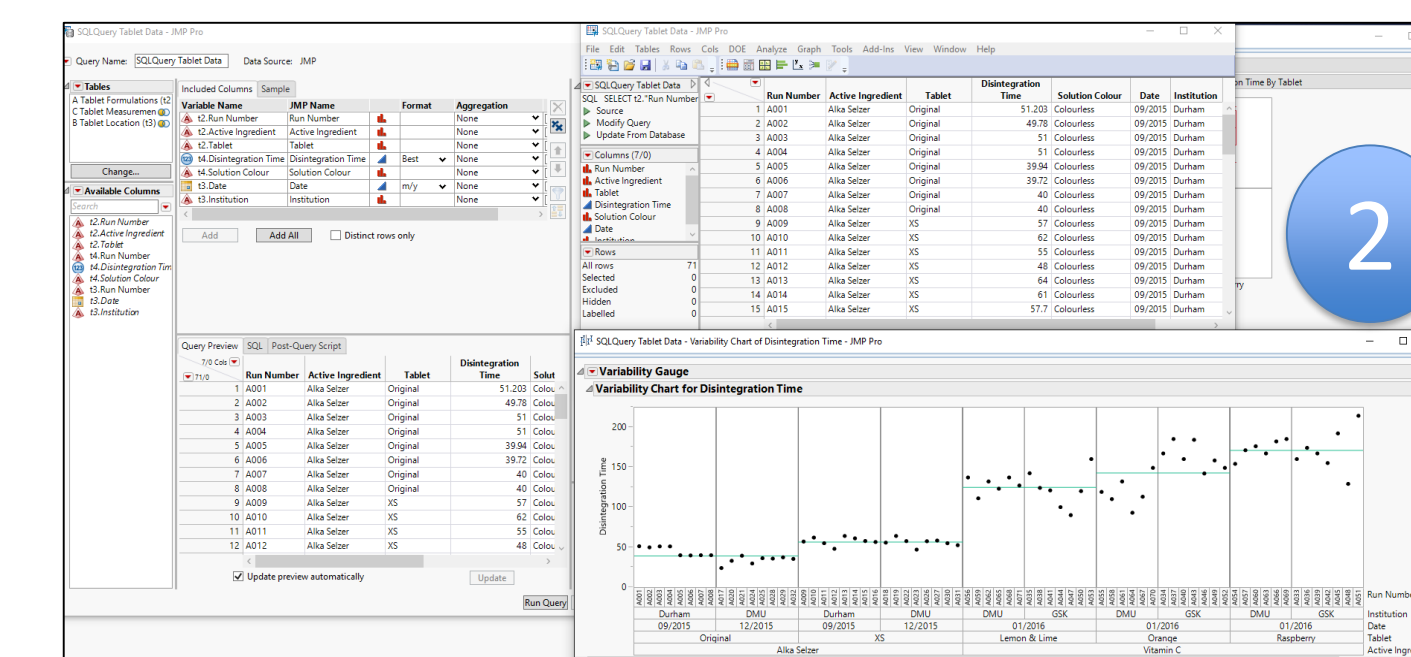
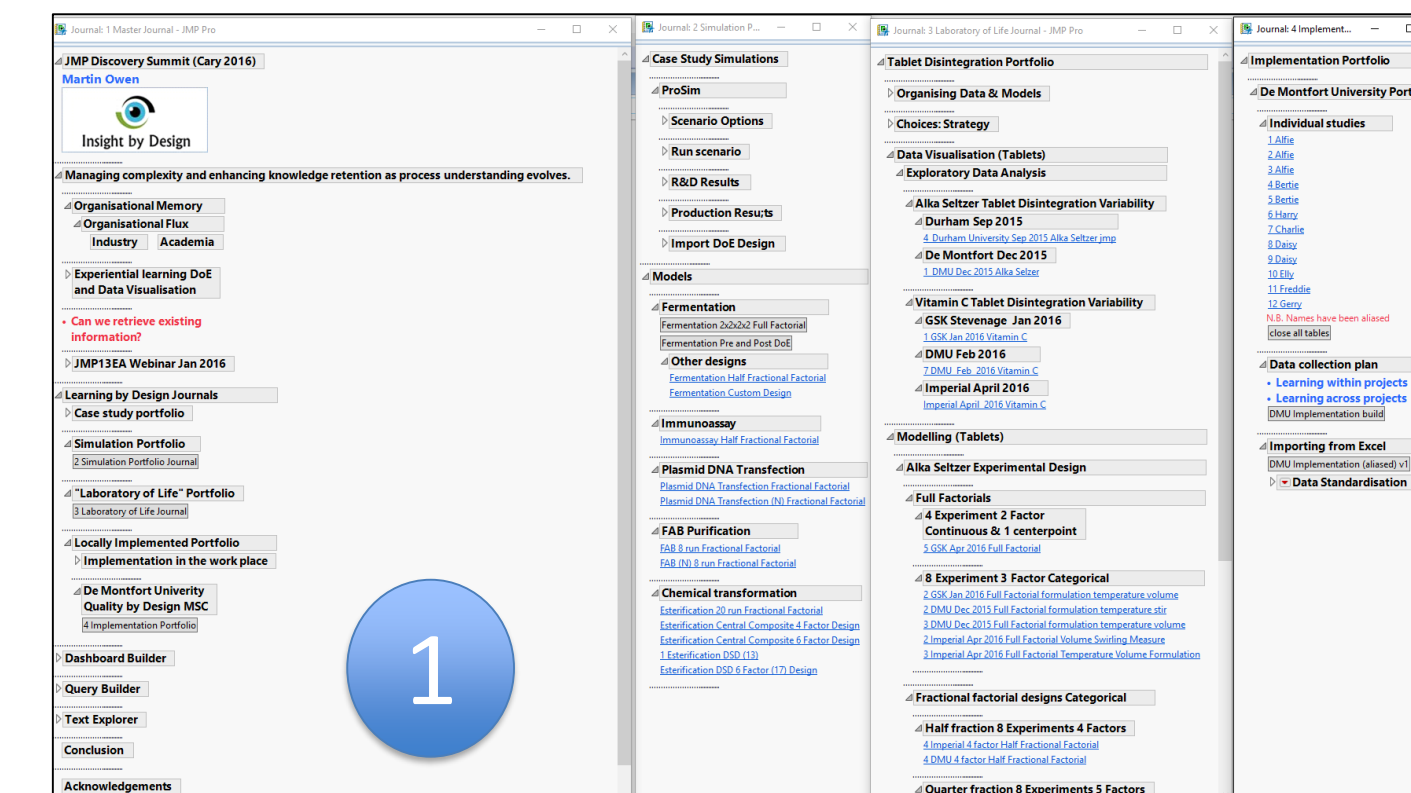
The Challenge

- To provide a flexible and efficient solution for structuring historical data.
- To share key concepts and important insights by using dynamic dashboards to communicate key messages.
- To gain new insights by combining data sets, in order to provide a bigger picture and exploit the “wisdom of crowds” disconnected over time and space.
- To supplement data and visualisations by summarising free text in documents and presentations.
- To show the value and importance of good data stewardship.

How?

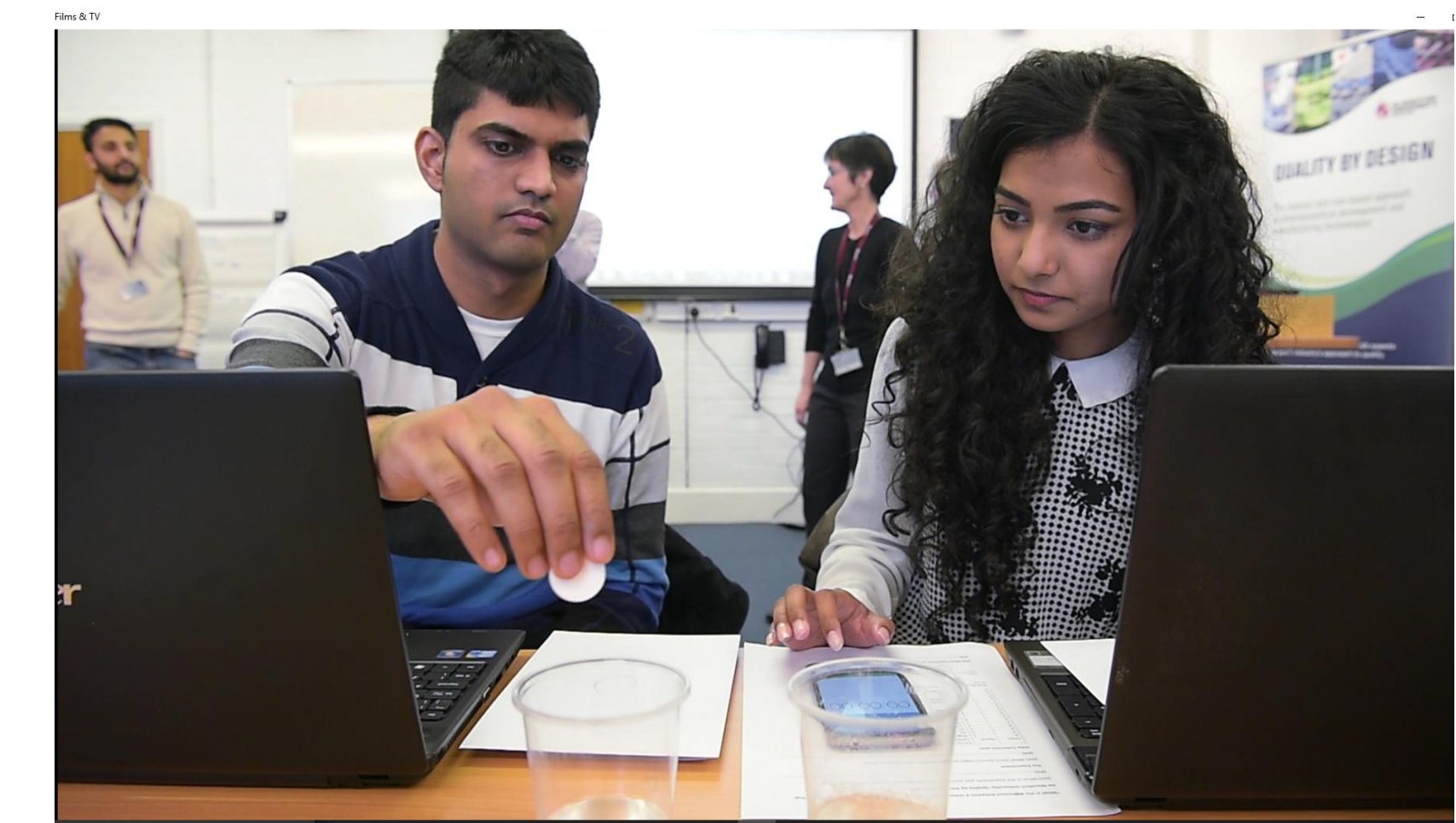
By exploiting existing and new functionality in JMP13:

- Journals:** Provide flexible structure and immediate access.
- Query Builder:** Combine data tables to see the bigger picture.
- Dashboard Builder:** Build compelling stories by bringing together key information on one screen.
- Text Explorer:** Supplement data and visualisations by summarising free text in documents and presentations.



[Click here for more information on Journals and Query Builder](#)

[Click here for more information on Dashboard Builder and Text Explorer](#)



Results

By utilising JMP functionality we were able to store information in a structured way and access prior knowledge in just a few clicks. Students value the application-based approach to the learning design of the MSc program over and above traditional theory-based lectures.

Conclusions

JMP enabled students to explore their own data, and provides a mechanism for accessing and communicating results from colleagues and previous cohorts of students.

[Click here for more information on the De Montfort Quality by Design MSc Slide 4](#)

If you would to discuss the themes in this poster, contact martin.owen.insight@gmail.com

Creating and Sustaining an Organisational Memory: Communicating New Insights

Martin Owen and Walkiria Schlindwein

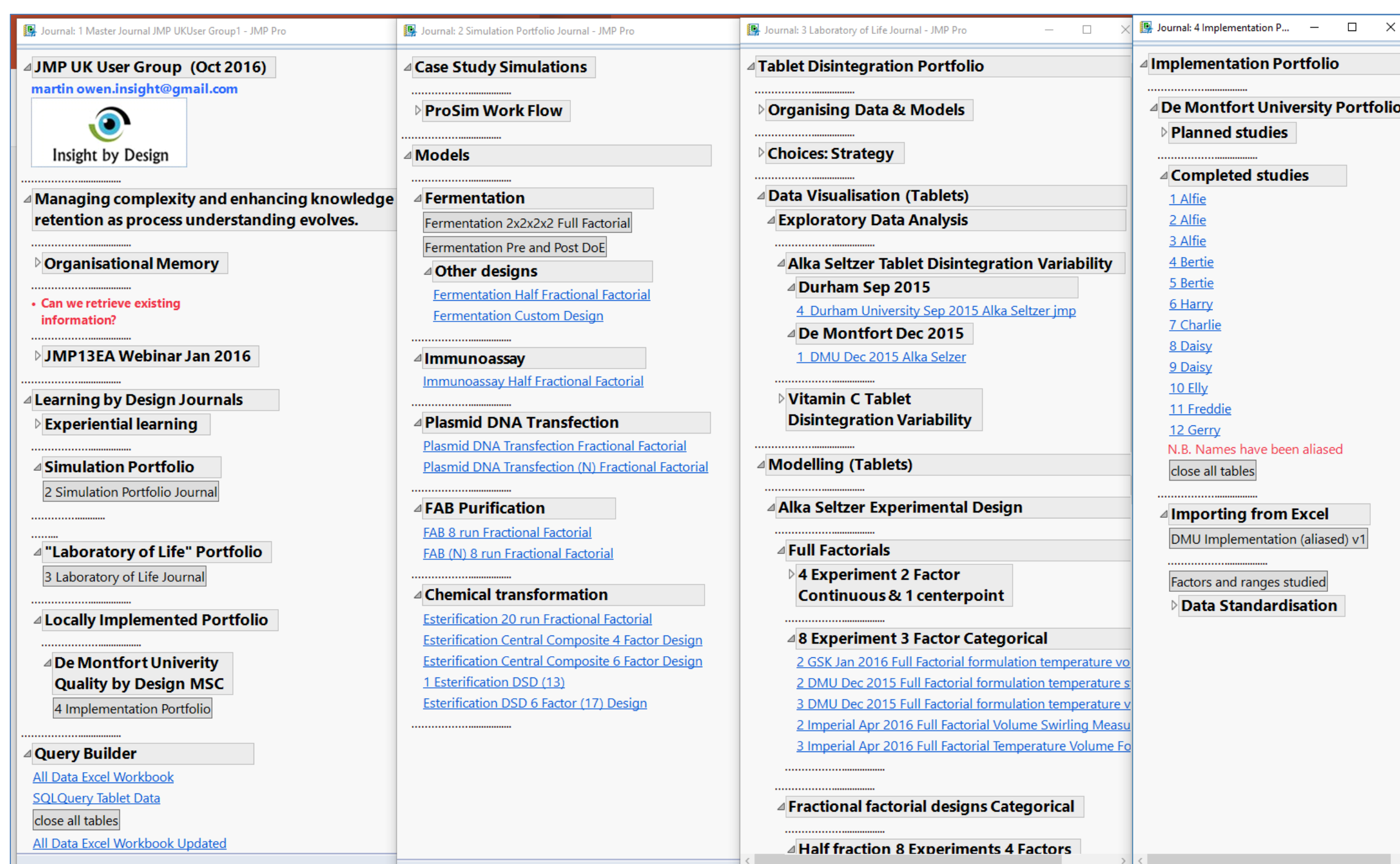


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Journals

The Journal provides a flexible way for:

- creating master files;
- structuring filing system and
- retrieving data files efficiently.



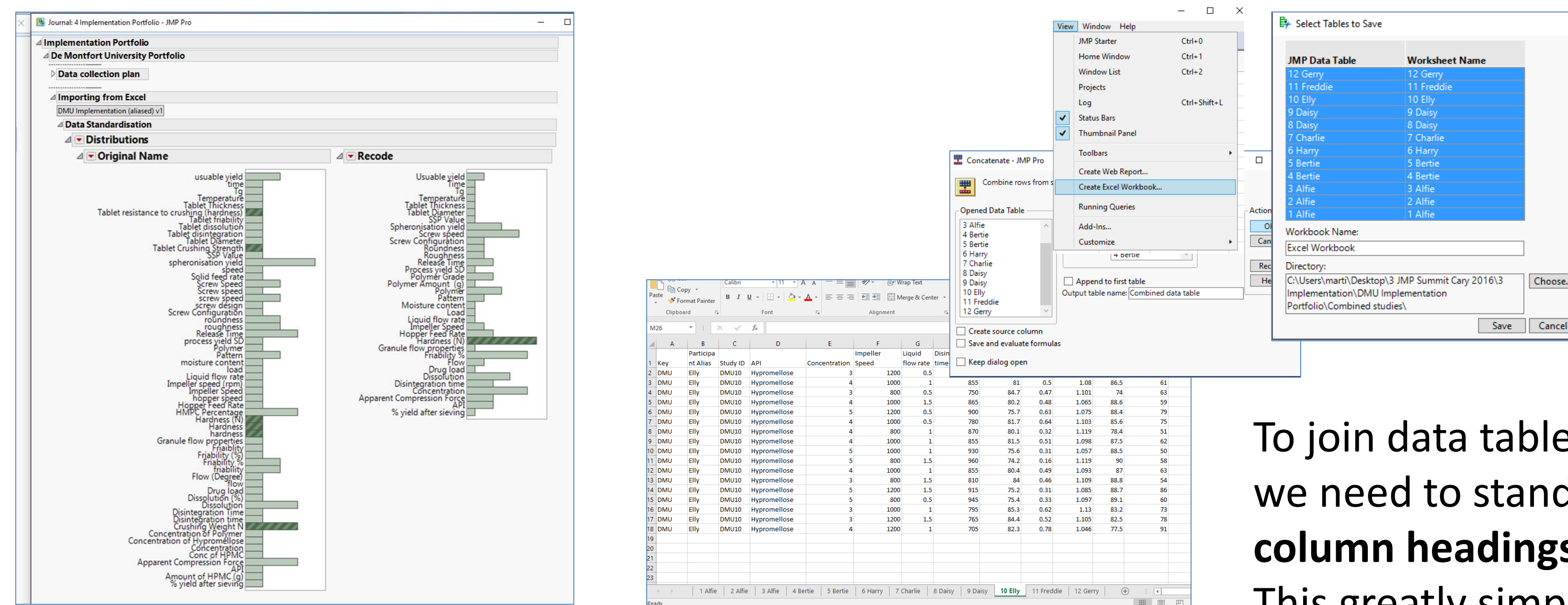
One of the fundamental principles of our workshop design is to help participants, new to experimental design, take the “leap of faith” to progress from the classroom to implementation in science laboratories.

We usually use a mix of **case-studies, simulations and “laboratory of life”** practical sessions to help participants rapidly build experience. This provides an environment where they are able to explore different tactical approaches and see the consequences of their decision-making.

One of the themed Journals used allows us to access our portfolio of simulated results. Prism’s Process Simulator, **ProSim**, provides a way to experience and try out different designs and strategies for many different applications “in the safety of the classroom”.

www.prismtc.co.uk

Tables and Query Builder



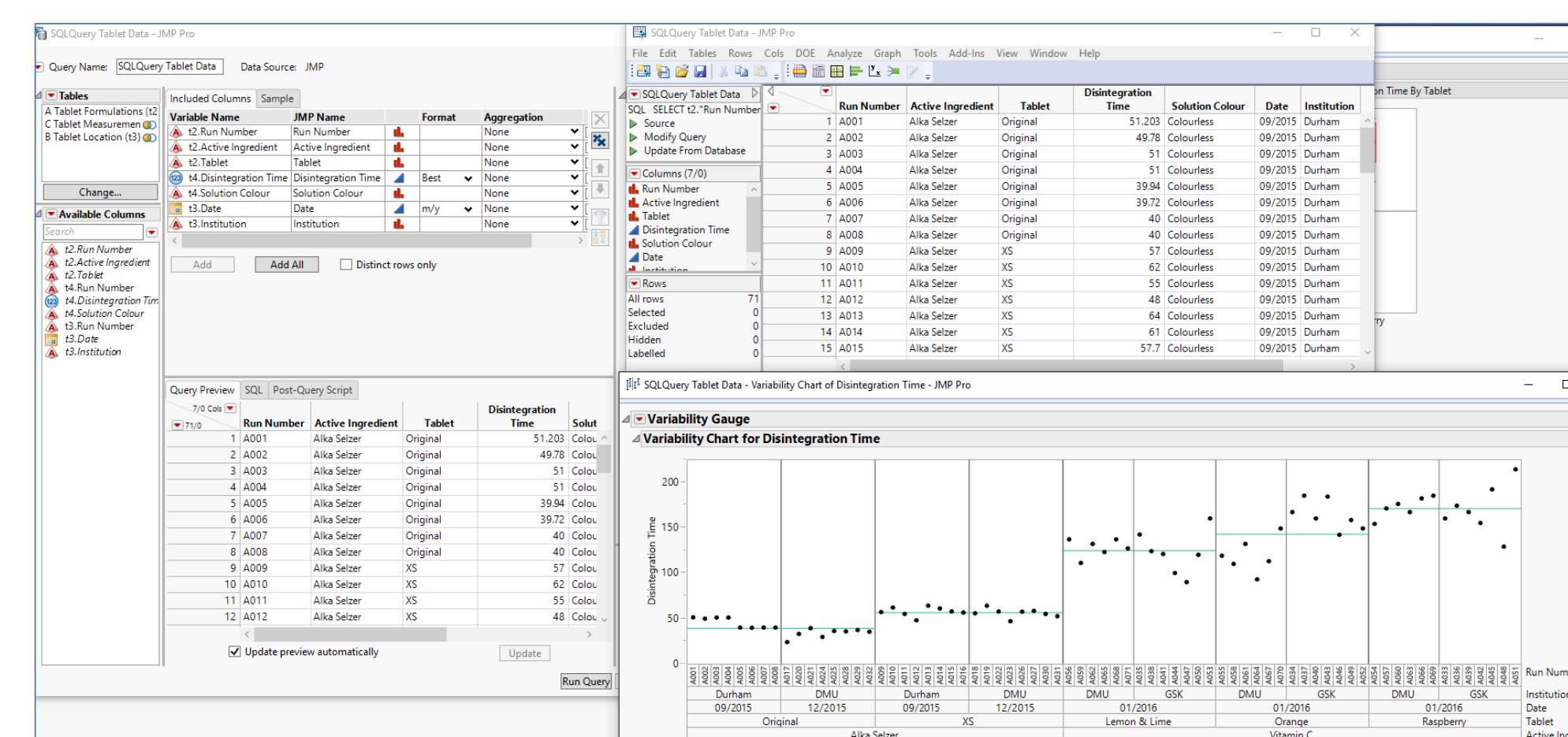
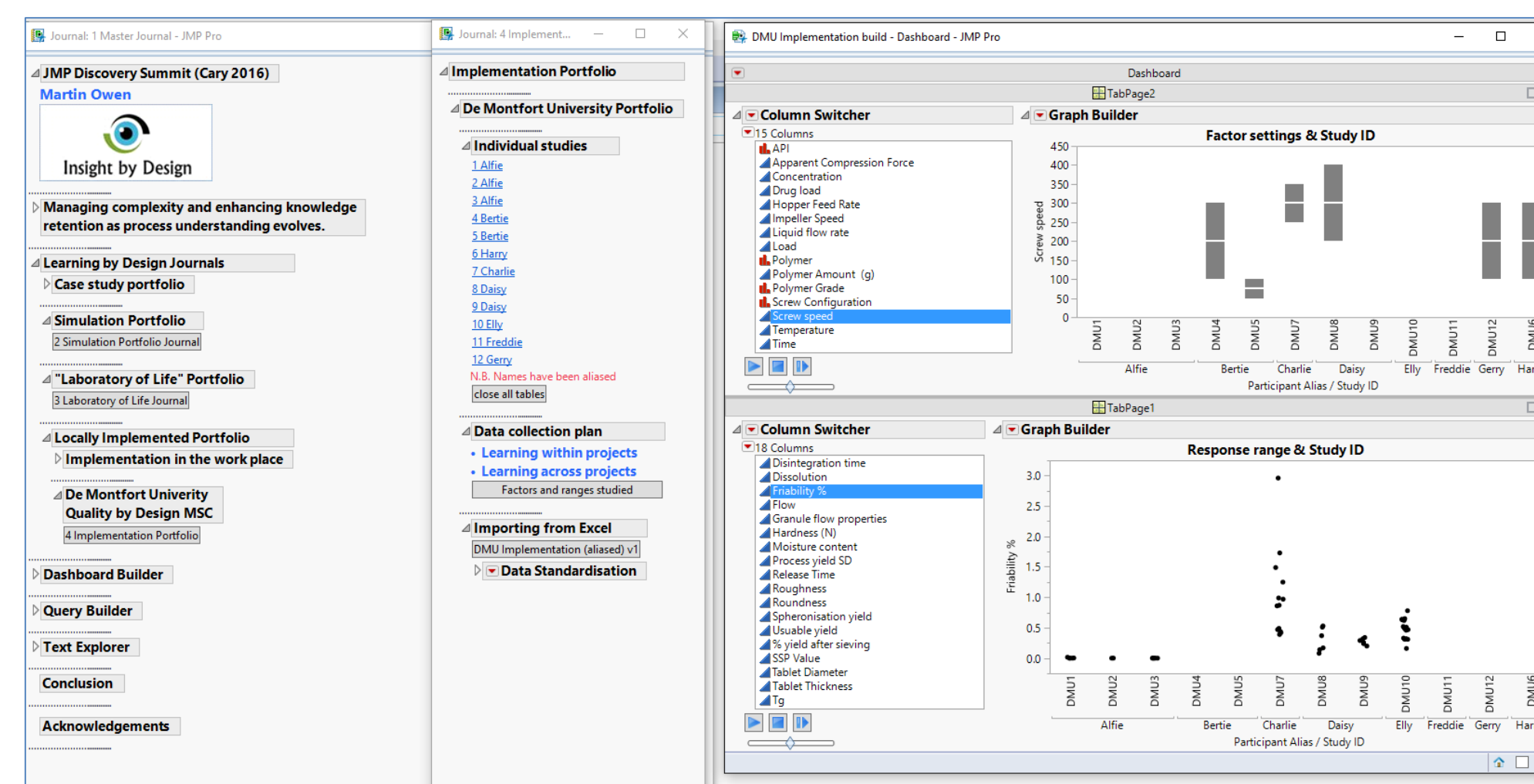
To join data tables efficiently we need to standardise on **column headings**. This greatly simplifies the task in hand.

Once the data headings are standardised, it is very easy to concatenate tables to **build a combined data set**.

We can also save range open JMP tables back into a tabbed Excel workbook.

The **Query Builder** now enables JMP tables to be loaded and manipulated (e.g. reordered and filtered).

Scripts can be incorporated so that as new data becomes available, visualisations are updated.





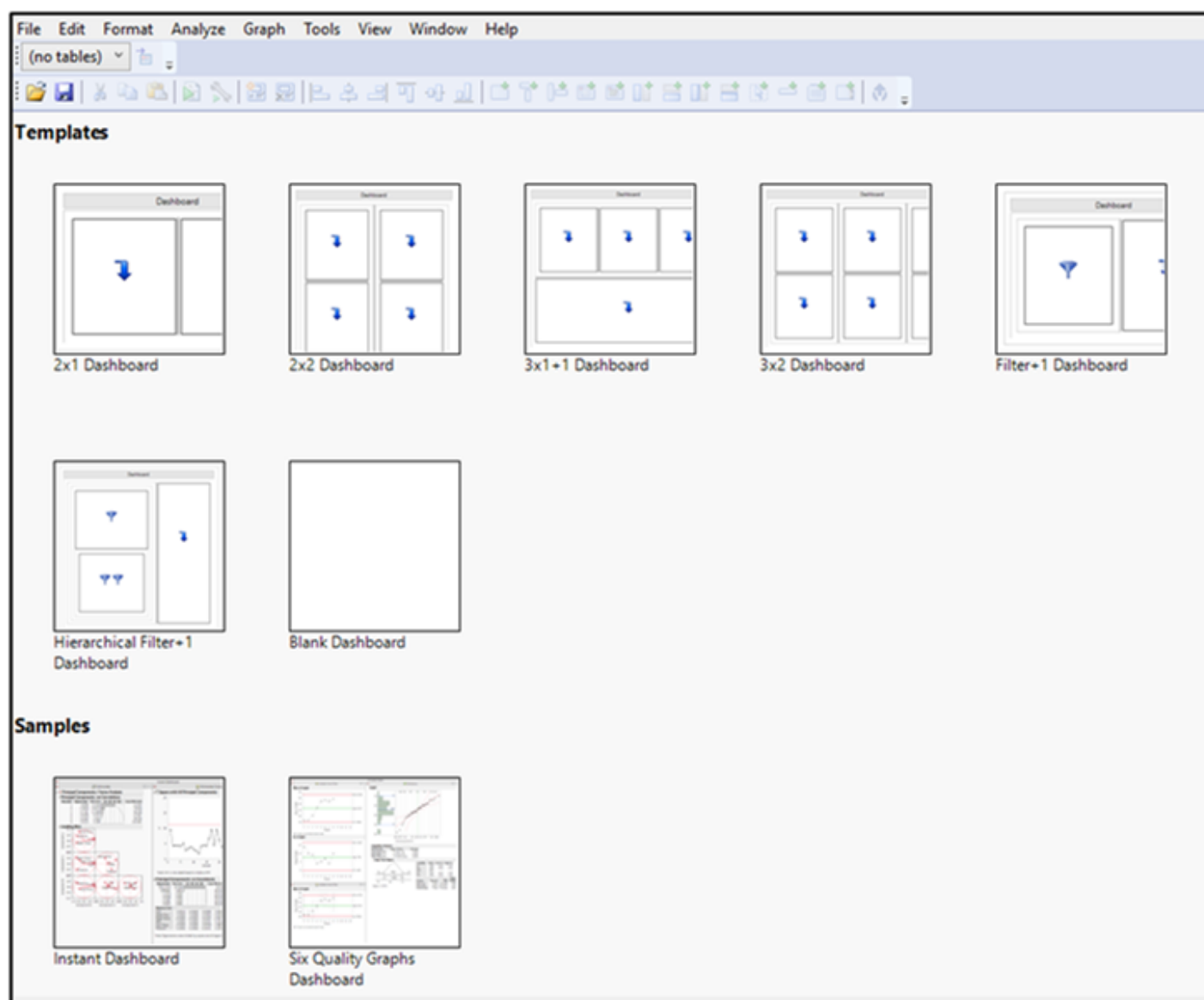
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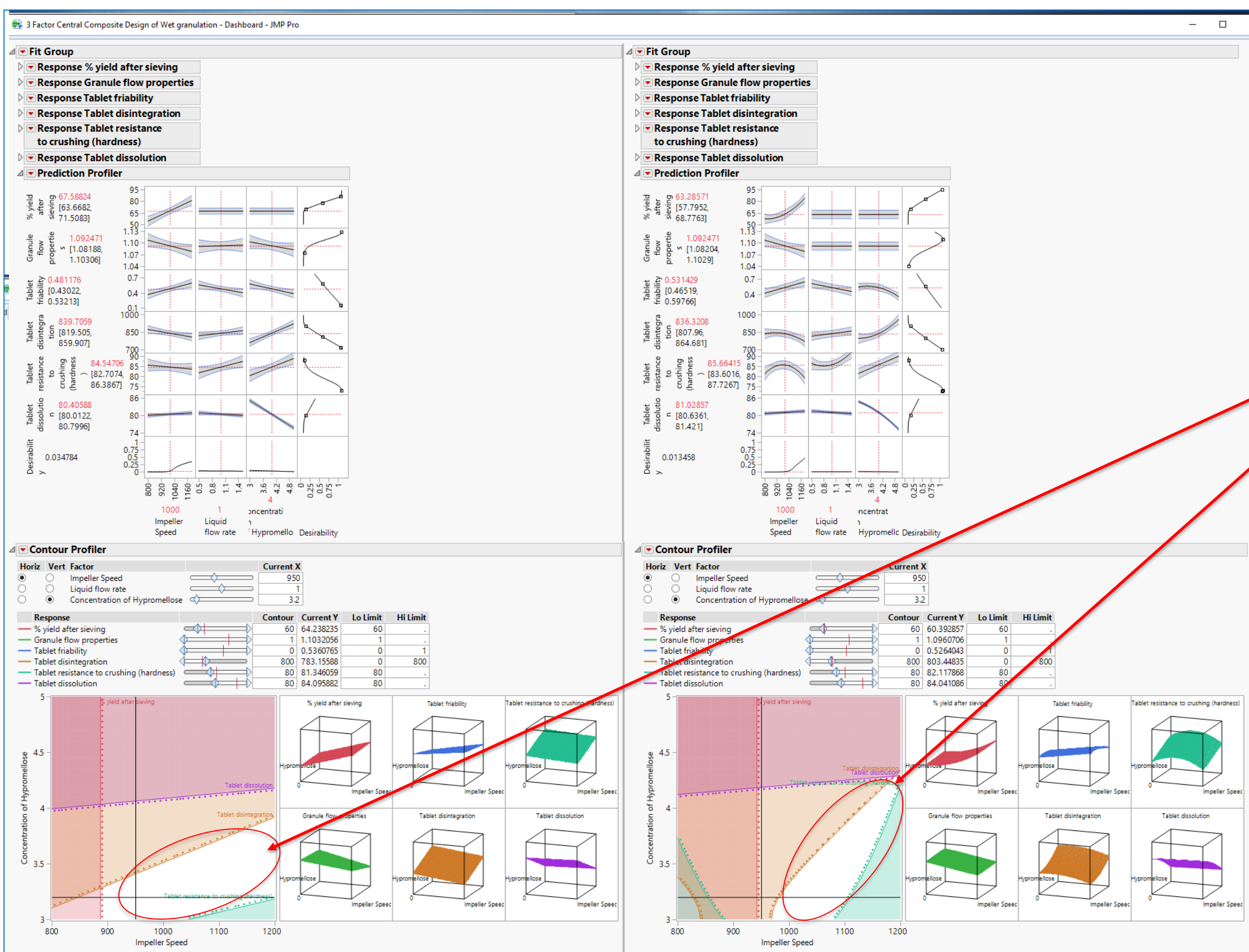
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Dashboard Builder



We use the **Dashboard builder** to reinforce learnings. It is easy to construct interactive dashboards, which can be used to quickly illustrate and summarise important concepts.

For example, we can show case studies where very similar models are generated, even though one design required 8 experiments and the other required 20 experiments. Conversely, as in the example below, the extra resource gives a more predictive model.



Participants new to Quality by Design often fall into the trap of believing the model is absolute".

The **white space** in the contour plot represents the settings where the model predicts the responses will pass specification.

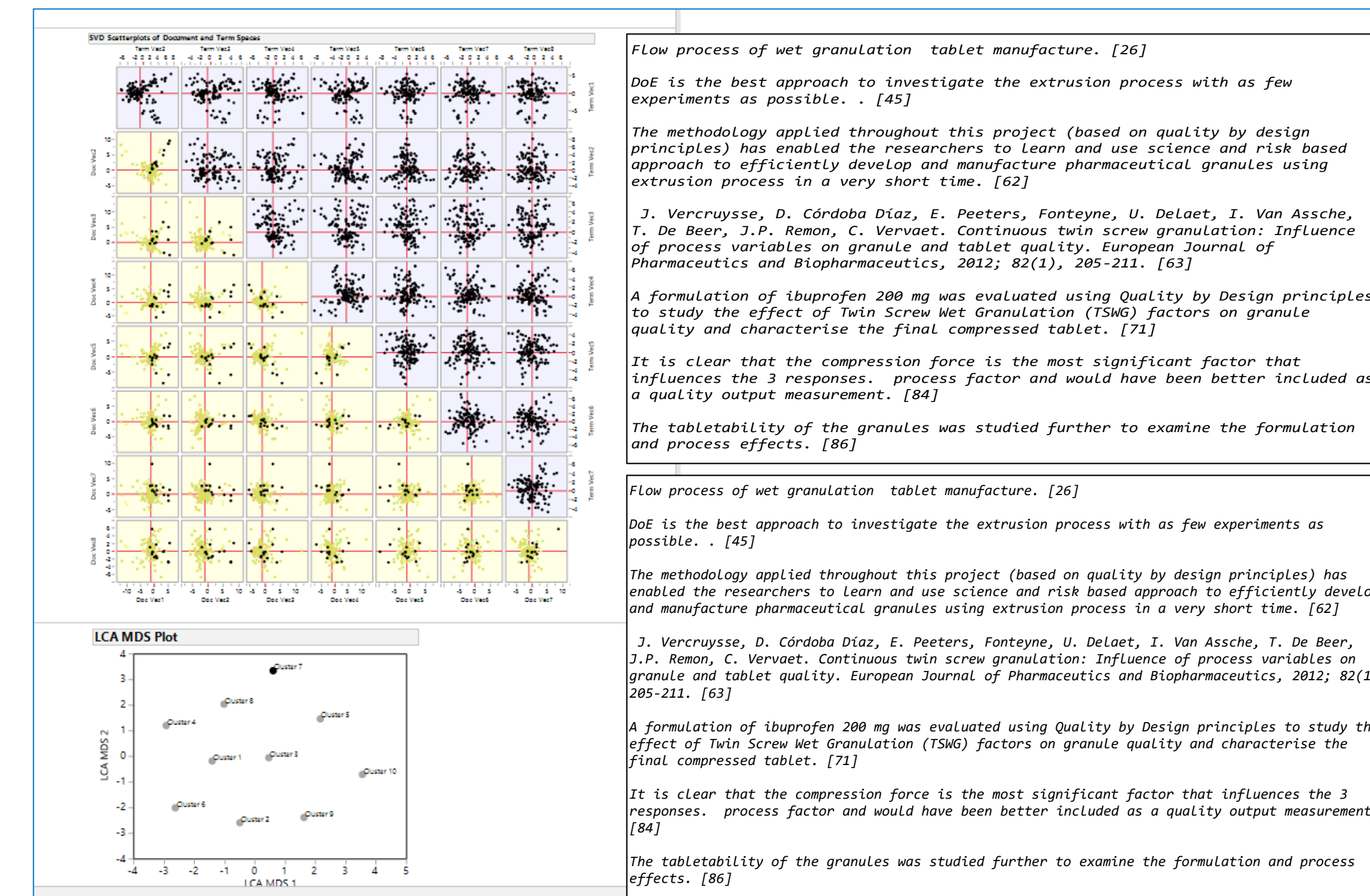
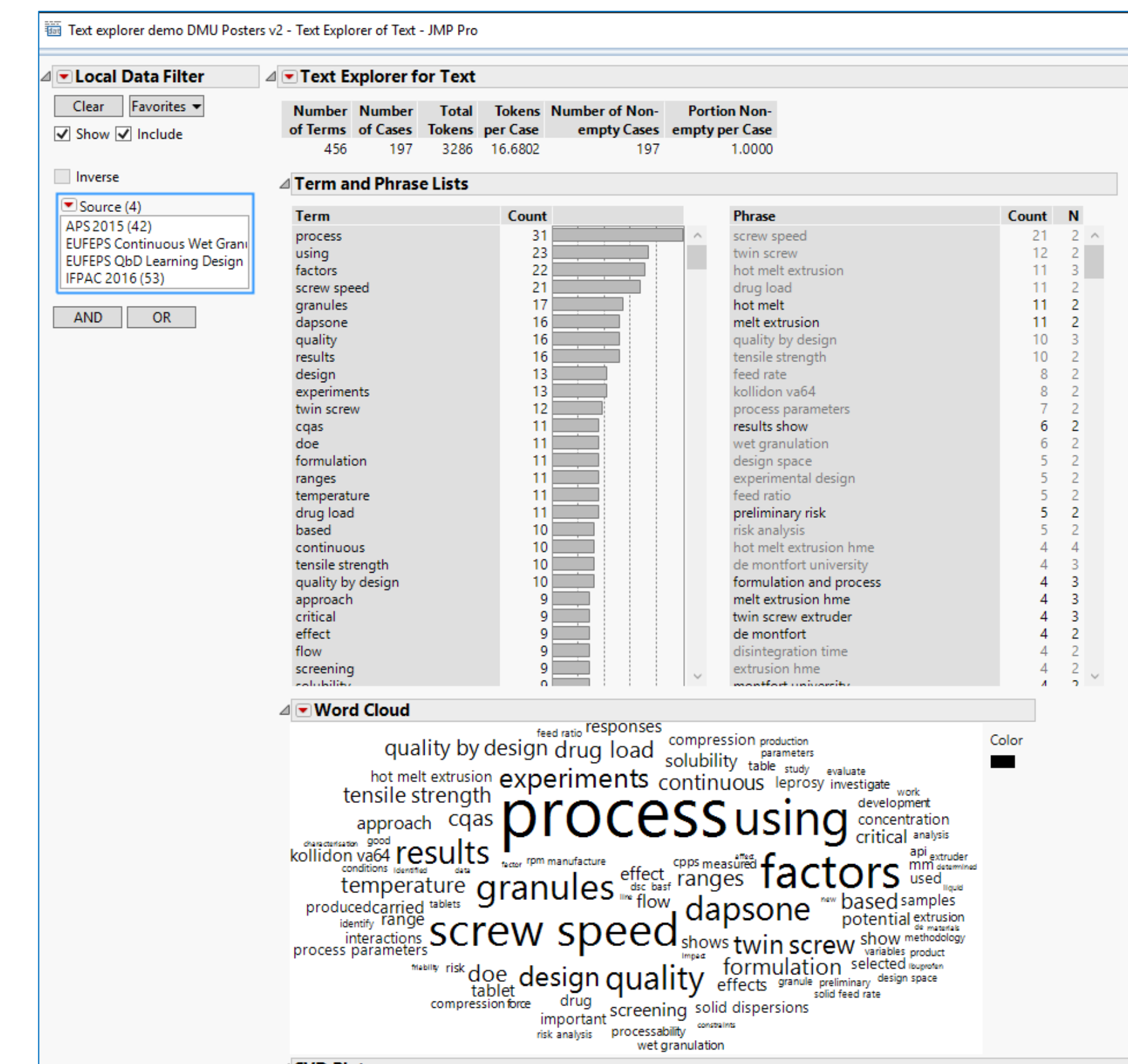
In this case, we can show that the **initial model** predicts a pass with settings that fail in the more predictive model. it is good practice to follow-up with verification studies.

Text Explorer

Not all information is captured in tables. A lot of information is stored as free text in reports, journal articles, posters and presentations. To illustrate the utility we took four posters describing prior work by DMU students and used the Text Explorer functionality to see what would emerge.

The **Text Explorer** helps to:

- efficiently clean unstructured data,
- visualise data relationships and
- find themes.

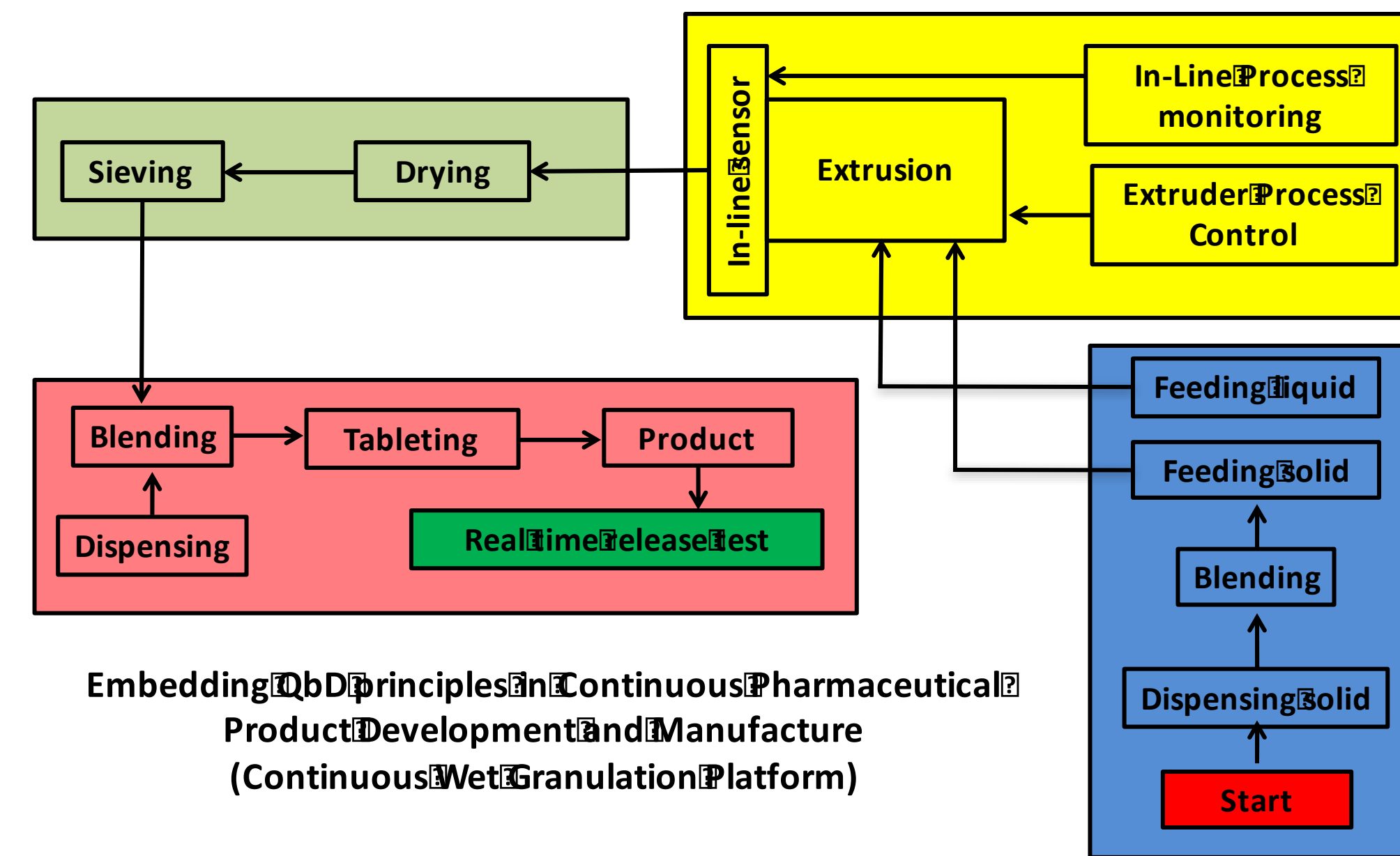
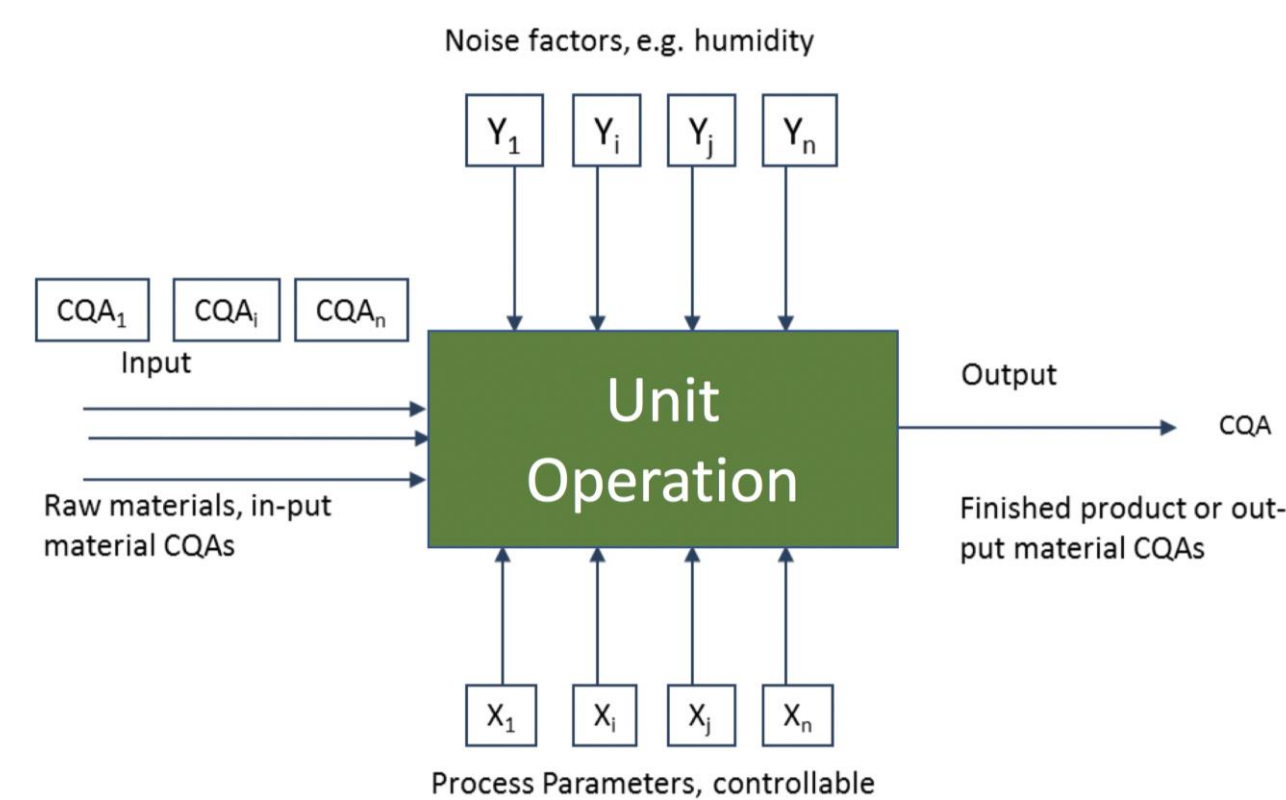


Flow process of wet granulation tablet manufacture. [26]
DoE is the best approach to investigate the extrusion process with as few experiments as possible. [45]
The methodology applied throughout this project (based on quality by design principles) has enabled the researchers to learn and use science and risk based approach to efficiently develop and manufacture pharmaceutical granules using extrusion process in a very short time. [62]
J. Vercauteren, D. Córdoba Díaz, E. Peeters, Fonteyne, U. Delaet, I. Van Assche, T. De Beer, J.P. Remon, C. Vervaeke. Continuous twin screw granulation: Influence of process variables on granule and tablet quality. *European Journal of Pharmaceutics and Biopharmaceutics*, 2012; 82(1), 205-211. [63]
A formulation of ibuprofen 200 mg was evaluated using Quality by Design principles to study the effect of Twin Screw Wet Granulation (TSWG) factors on granule quality and characterise the final compressed tablet. [71]
It is clear that the compression force is the most significant factor that influences the 3 responses. process factor and would have been better included as a quality output measurement. [84]
The tabletability of the granules was studied further to examine the formulation and process effects. [86]
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Quality by Design methodology

Quality by Design (QbD) methodology is becoming more established in the Pharmaceutical sector and is also recognised by the regulatory authorities at a time when the industry is under pressure to deliver efficiencies in manufacturing and drug development.

The production of tablets is a sequence of unit operations. The output of one unit operation is the input into the subsequent unit operation. The example here is for continuous wet granulation.



De Montfort QbD Teaching Laboratory



De Montfort University is supporting the creation of a centre for “Embedding QbD principles in Continuous Pharmaceutical Product Development and Manufacture”. The centre will offer unique hands on experience to the students in areas such as process analytical technologies (PAT), process improvement and life cycle management of medicines. (visit www.qbd-dmu.co.uk)

Blending

Feeding solid

Feeding liquid

Extrusion (Screw configuration)

Extruder Process Control

“Dial-a-granule!”



The formulation is mixed in a Tubula shaker mixer



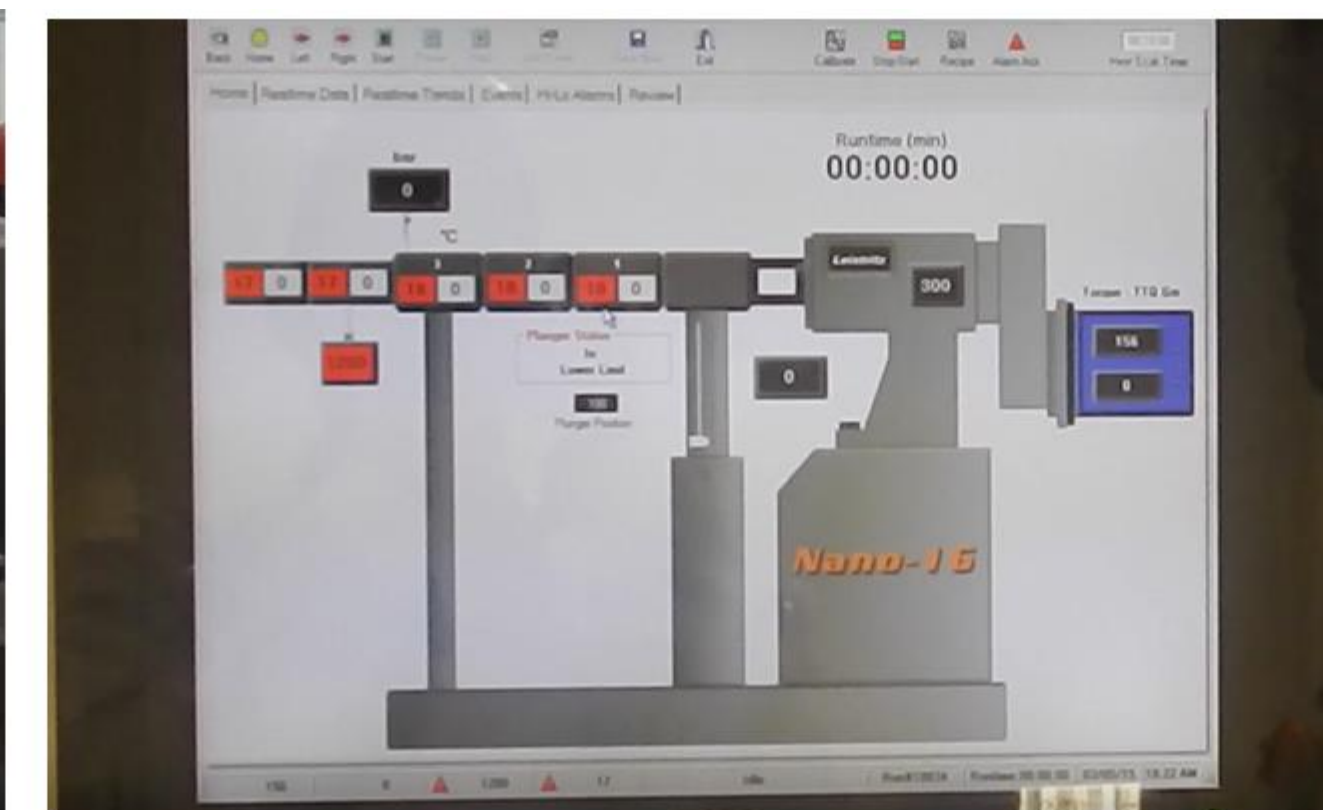
Twin screw solid feeder is kept between 30-70% of full capacity. Feed rate is set to desired throughput



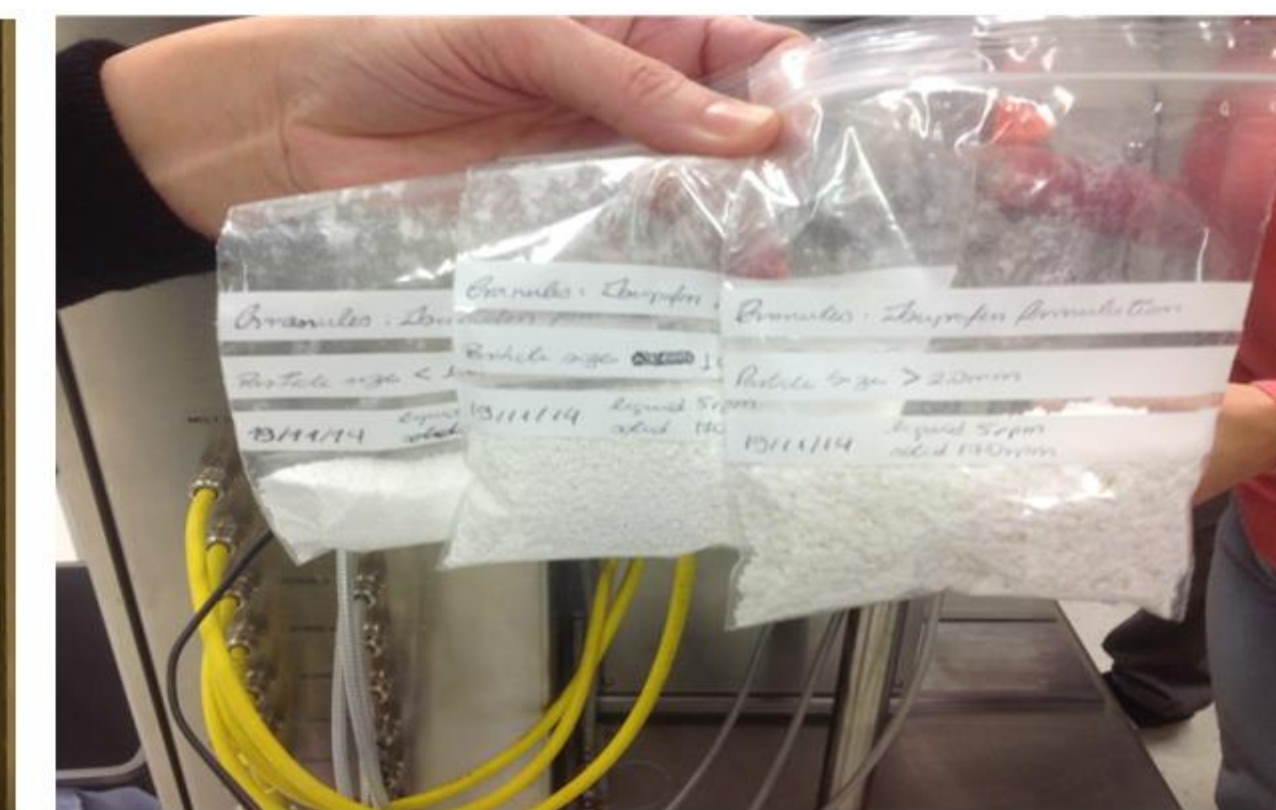
The binder feed rate is selected. The operation conditions are checked to provide a continuous feed.



The screw elements are assembled for wet granulation configuration.



Process temperature is controlled by real time feedback. Screw speed is set to desired value. Torque and pressure are continuously measured.



The DoE model is used to predict settings which produce granules of desired particle size distribution.