SPREITZENBARTH CONSULTANTS

PLA 2017

WORKSHOP DIGITAL DATA CONVERGENCE, REGULATORY AUDIT SUPPORT AND THE DEVELOPMENT OF PAT AND QBD

Barcelona April 4, 2017

A holistic approach to tactical and strategic information

Agenda

1. plantex introduction
2. The PAT & QbD Business case
3. plantex live in a PAT & QbD environment
4. Q&A

Matthias Spreitzenbarth

Moritz Pflaum

Marc Vorderman

SPREITZENBARTH CONSULTANTS

A holistic approach to tactical and strategic information

- data science
- simulation
- mathematical optimization
- visual communication
- collaboration

- A holistic approach will make certain that your business is running at its full potential, building an environment of “real” continuous improvement as opposed to simply having strong and weak areas.
- The holistic approach to business information is meant to look beyond your operational data.
- Considering all available data, business, operational and scientific data, internal and external data sources and find information; actionable insights…
- … previously impossible to find due to the limitation of the source.

SPREITZENBARTH CONSULTANTS

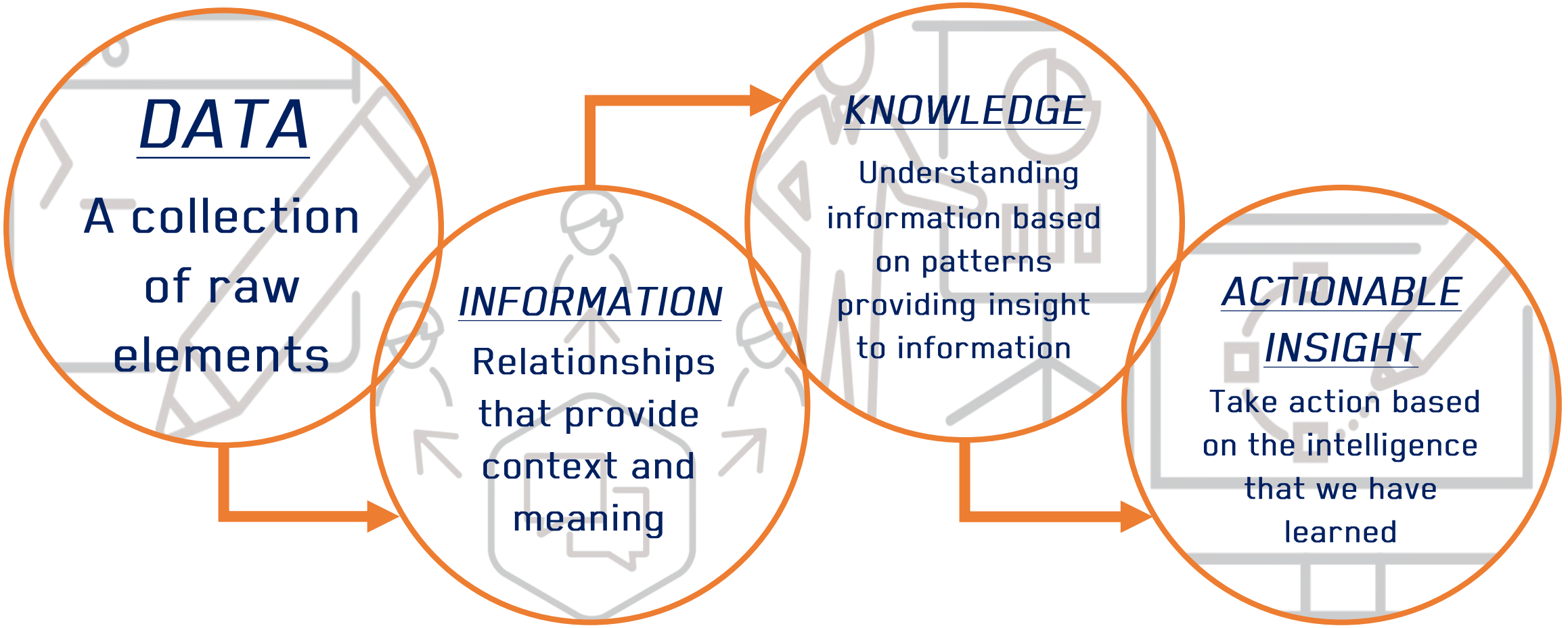
Discovering Actionable Insights

The complexity of discovering actionable knowledge grows in lock-step with the volume of data!

SPREITZENBARTH CONSULTANTS

Knowledge

From Data to an Actionable Insight



SPREITZENBARTH CONSULTANTS

The Analytics Spectrum

… AS THE ANALYTICAL FUNCTIONALITY INCREASES THE "BUSINESS CLIENT" GAINS MORE INSIGHT INTO THE MECHANICS OF OPTIMIZATION

Operational ***Strategic***

insight into existing conditions and performance, comparing existing activities to expectations

THE NOTION OF USING DATA TO BOTH RUN AND IMPROVE THE BUSINESS SUGGEST A DIFFERENT APPROACH TO THINKING ABOUT THE VALUE OF INFORMATION

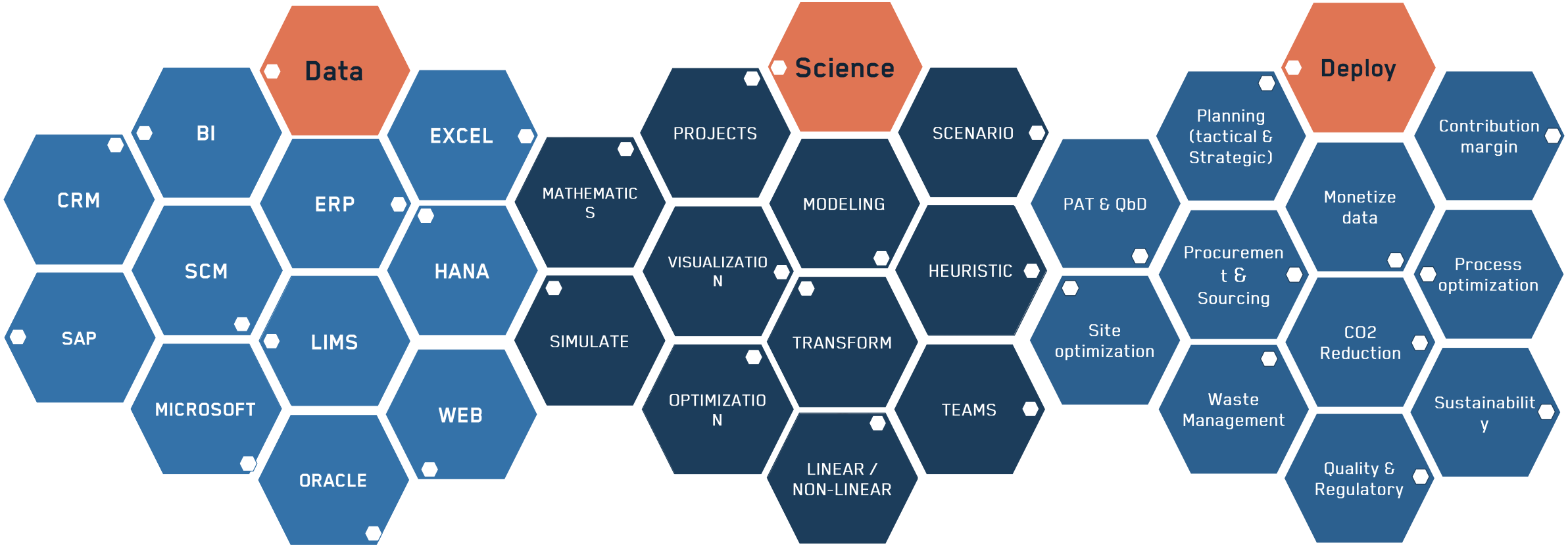
evaluate the degree to which any potential measurements impact future corporate value

plantex covers the full spectrum

SPREITZENBARTH CONSULTANTS

Reports | Ad Hoc | Search | Dashboards | Statistical Analysis | Forecasting Models | Planning | Predictive Models | Optimizing models

What Happened | Why | What if | What next | How



Operational

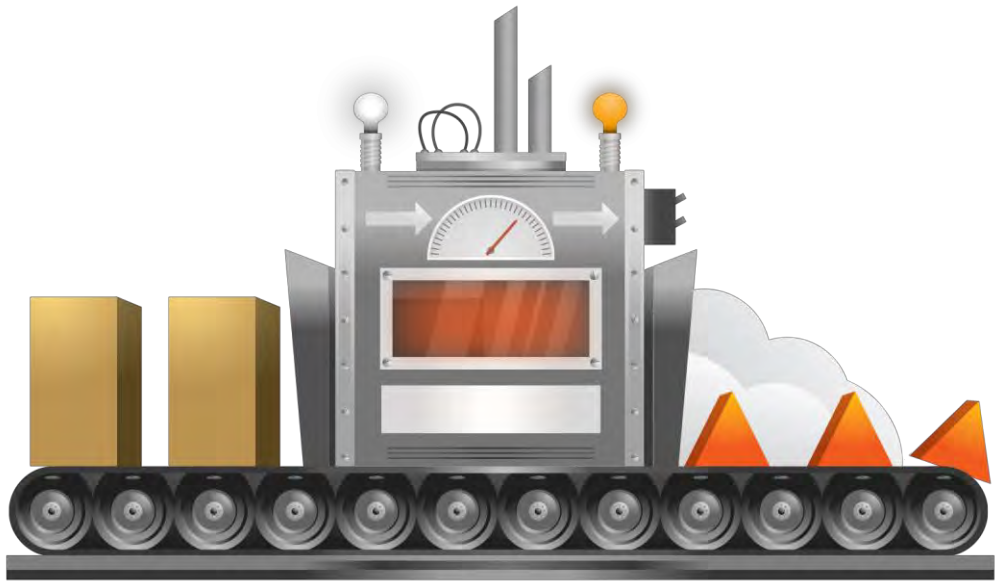
Strategic

Plantex and PAT & QbD

SPREITZENBARTH CONSULTANTS

A HOLISTIC APPROACH TO INFORMATION

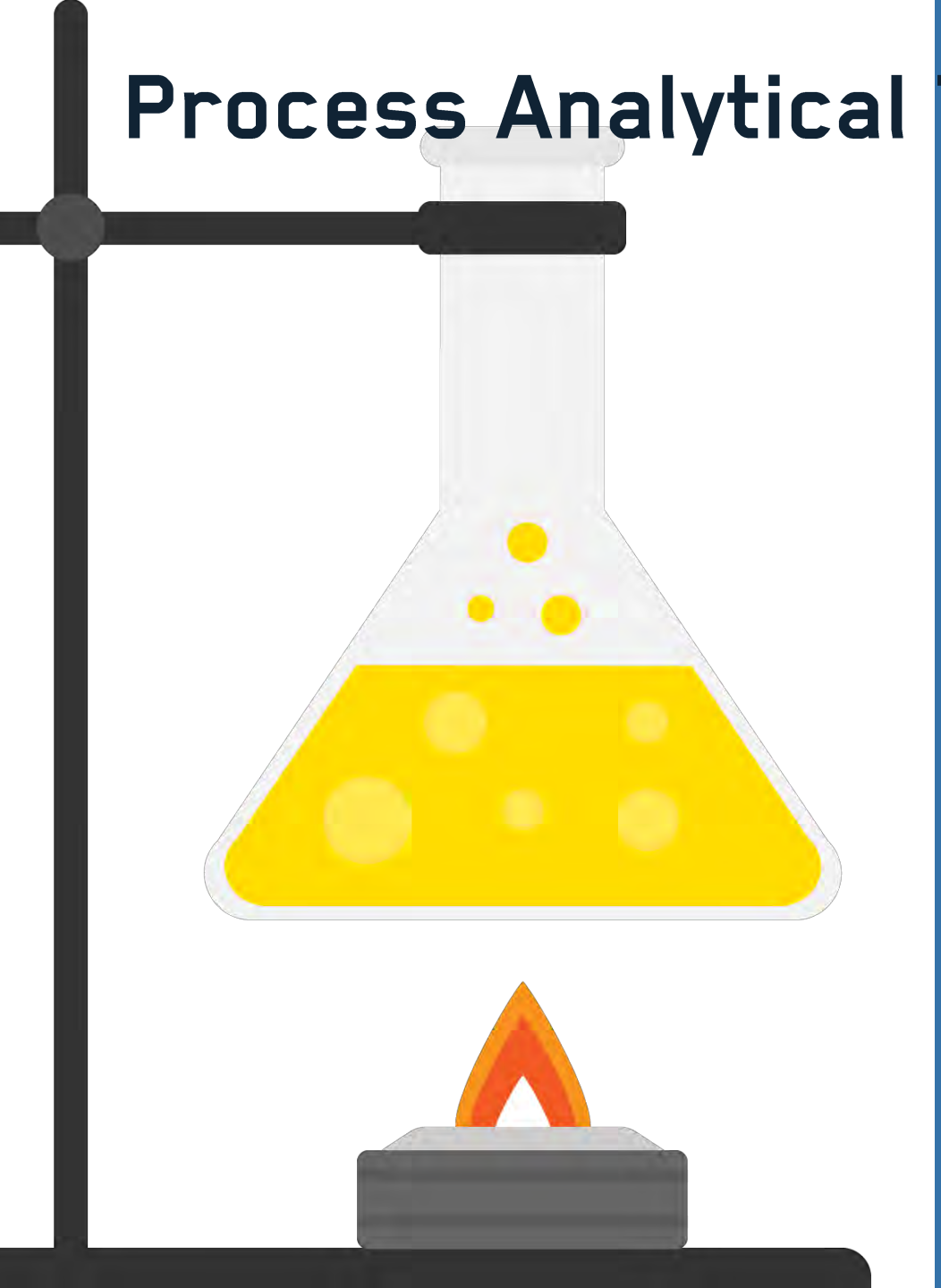
A chapter in the process of developing a new formulation using PAT & QbD.



- With plantex we will combine process, quality and scientific data.
- Analyzing experimental, process and related quality data to identify the critical process parameters and their influence on quality attributes.
- The actionable insights found will make it possible to create a mathematical model to predict how changes in critical material attributes or process parameters will influence the product quality.

Process Analytical Technology (PAT)

SPREITZENBARTH CONSULTANTS



- Used to design, analyze and control processes
- Critical Process Parameters (CPP)
- Critical Quality Attributes (CQA)

It is necessary to:

1. Acquire and analyze data to understand the process
2. Use in- or on-line analytical instruments, calibrate them
3. Provide a basis for continuous improvement

Quality by Design (QbD)

SPREITZENBARTH CONSULTANTS

Using a thorough understanding, it is possible to:

- predict quality attributes,
- instead of measuring them.

<u>Quality is guaranteed by design.</u>

When approved it can:

- Save resources
- Reduce time to market
- Make processes more efficient

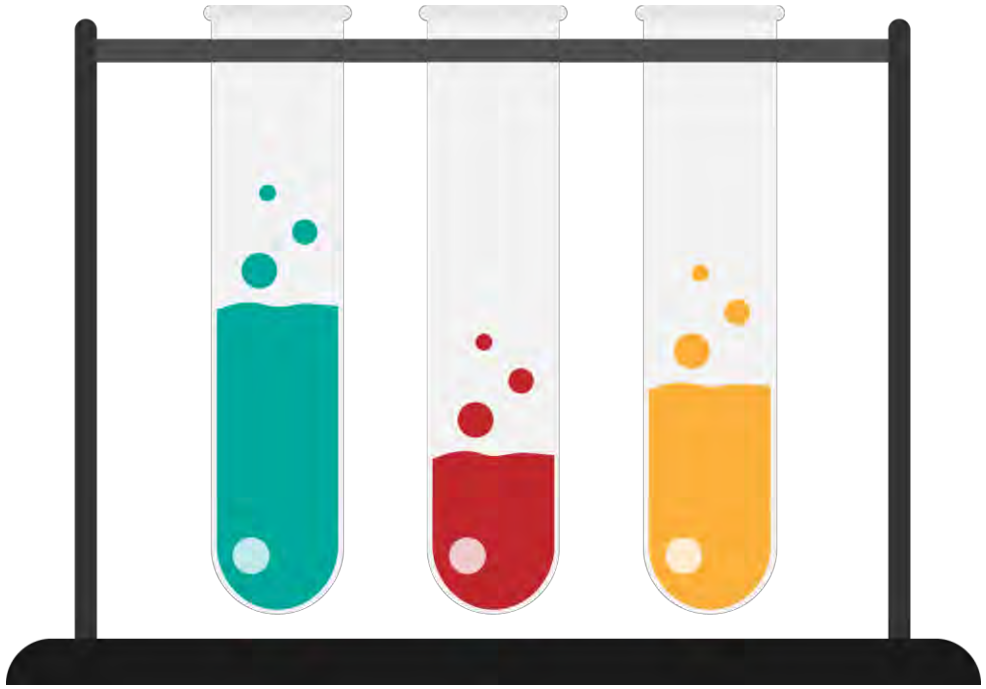
Sources

SPREITZENBARTH CONSULTANTS

- QbD study: ACE-Tablets
  (https://www.ispe.org/pqli/case-study-ace-tablets.pdf)
- Implementation of ICH Q8, Q9, Q10
  (http://www.ich.org/fileadmin/_migrated/content_uploads/Q-IWG_Web_Case_Study.pdf)
- FDA QbD example
  (https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM304305.pdf)

The data model used

SPREITZENBARTH CONSULTANTS



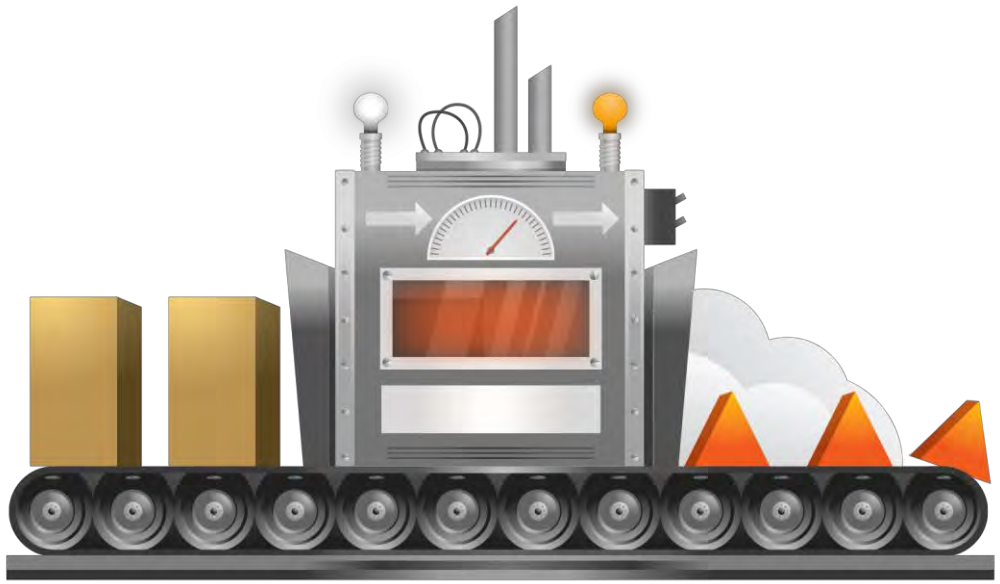
- Laboratories and suppliers
- Drugs (APIs)
- Formulations (i.e. “Metabene 20mg tablets”)
- Production processes
- Batches
- Process data
- Other data sources
  (EM, experimental data, etc.)

Plantex and PAT & QbD

SPREITZENBARTH CONSULTANTS

A HOLISTIC APPROACH TO INFORMATION

A chapter in the process of developing a new formulation using PAT & QbD.



- With plantex we will combine process, quality and scientific data.
- Analyzing experimental, process and related quality data to identify the critical process parameters and their influence on quality attributes.
- The actionable insights found will make it possible to create a mathematical model to predict how changes in critical material attributes or process parameters will influence the product quality.

SPREITZENBARTH CONSULTANTS

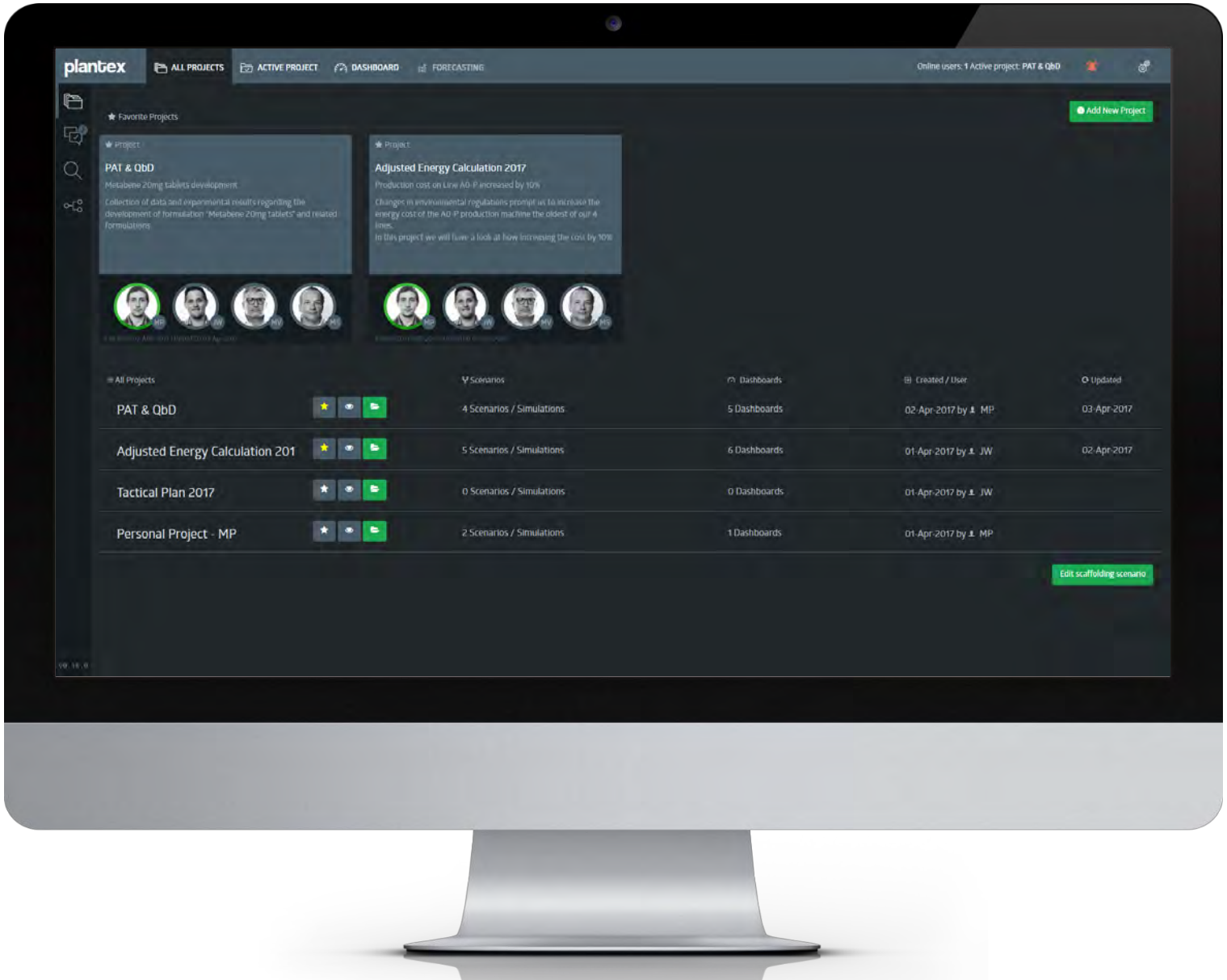
plantex

We will step right into the application for the next part of the workshop.

At first, we see a list of available projects to choose from.

Projects provide the means to easily group topics/tasks and teams.

For this workshop, we will open the “PAT & QbD” project.



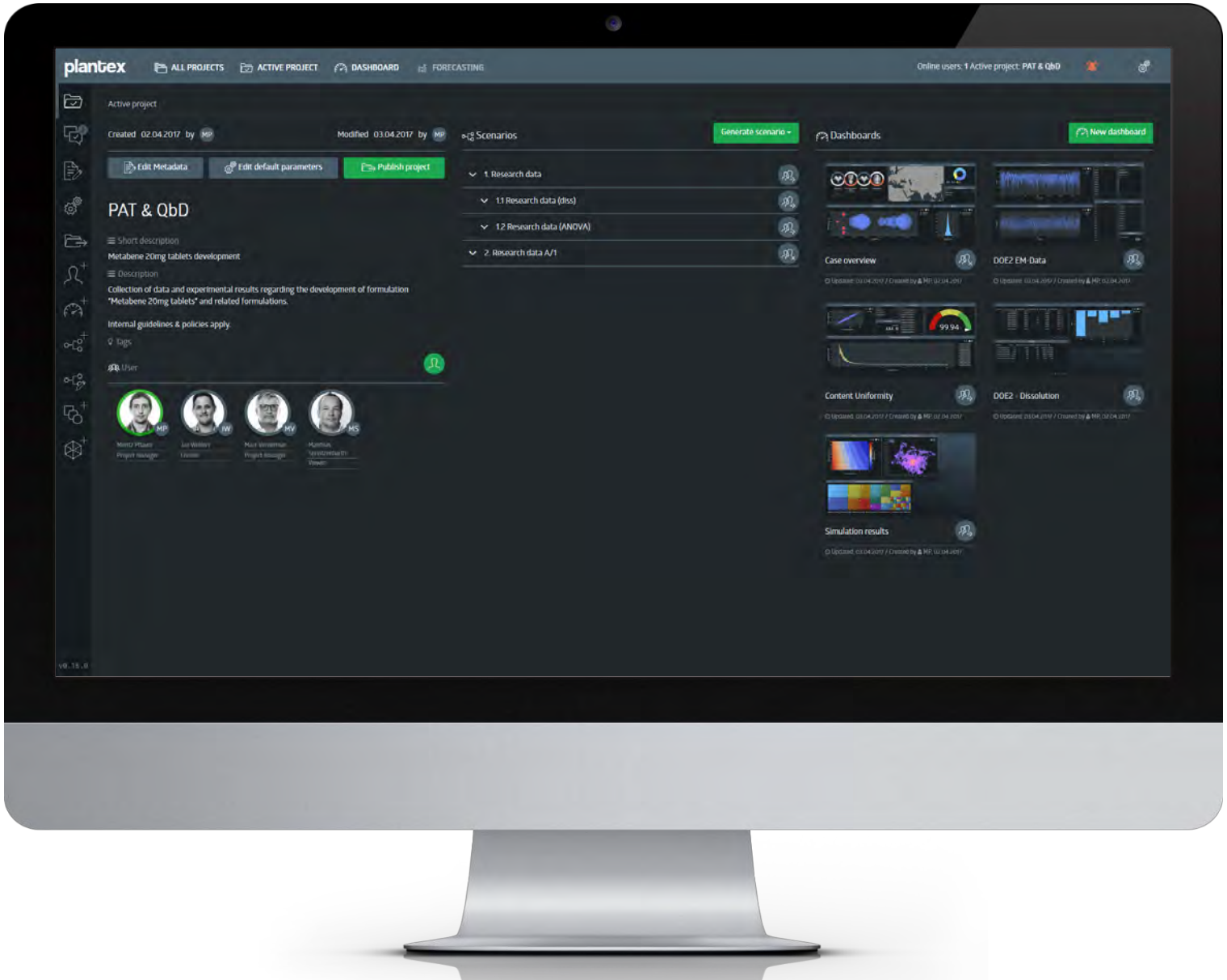
SPREITZENBARTH CONSULTANTS

Project view

In the project view, there is a lot of information, which we will look at in detail a bit later.

First, we want to provide a overview of the process and model that we will see.

The screen on the next slide shows the “case overview” dashboard, at which we will look more closely.




plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Production process
Blending
(diffusion mixer)
Dry Granulation & Milling
(roller compactor)
Lubrication
(diffusion mixer)
Compressing
(rotatory press)
Metabene (API)
Lactose
Microcrystalline Cellulose (MCC)
Croscarmellose Sodium (CCS)
Magnesium Stearate
Laboratories & suppliers
Kazakhstan
Mongolia
Turkey
People's Republic of China
Libya
Egypt
Saudi Arabia
India
Niger
Sudan
Malaysia
Labs by total production
BNL5
DE04
FR3X
Formulation types
Search ...
Experimental
Production
Page # 1 of 1
Batch timeline
Experimental
Production
API.ParticleSize.D90 [µm]
ProductionDate
Jul 2014
Jan 2015
Jul 2015
Jan 2016
Jul 2016
Jan 2017
EM-Data
Temperature histogram
Normal distribution
Temperature [°C]
v0.16.0

SPREITZENBARTH CONSULTANTS

Production process

The widget in the top left corner shows a visualization of the production process to produce the tablets.

In this workshop, we are looking at the development of a new formulation: “Metabene 20mg tablets”

Metabene is the fictional drug (API) we chose for this example case.

SPREITZENBARTH CONSULTANTS

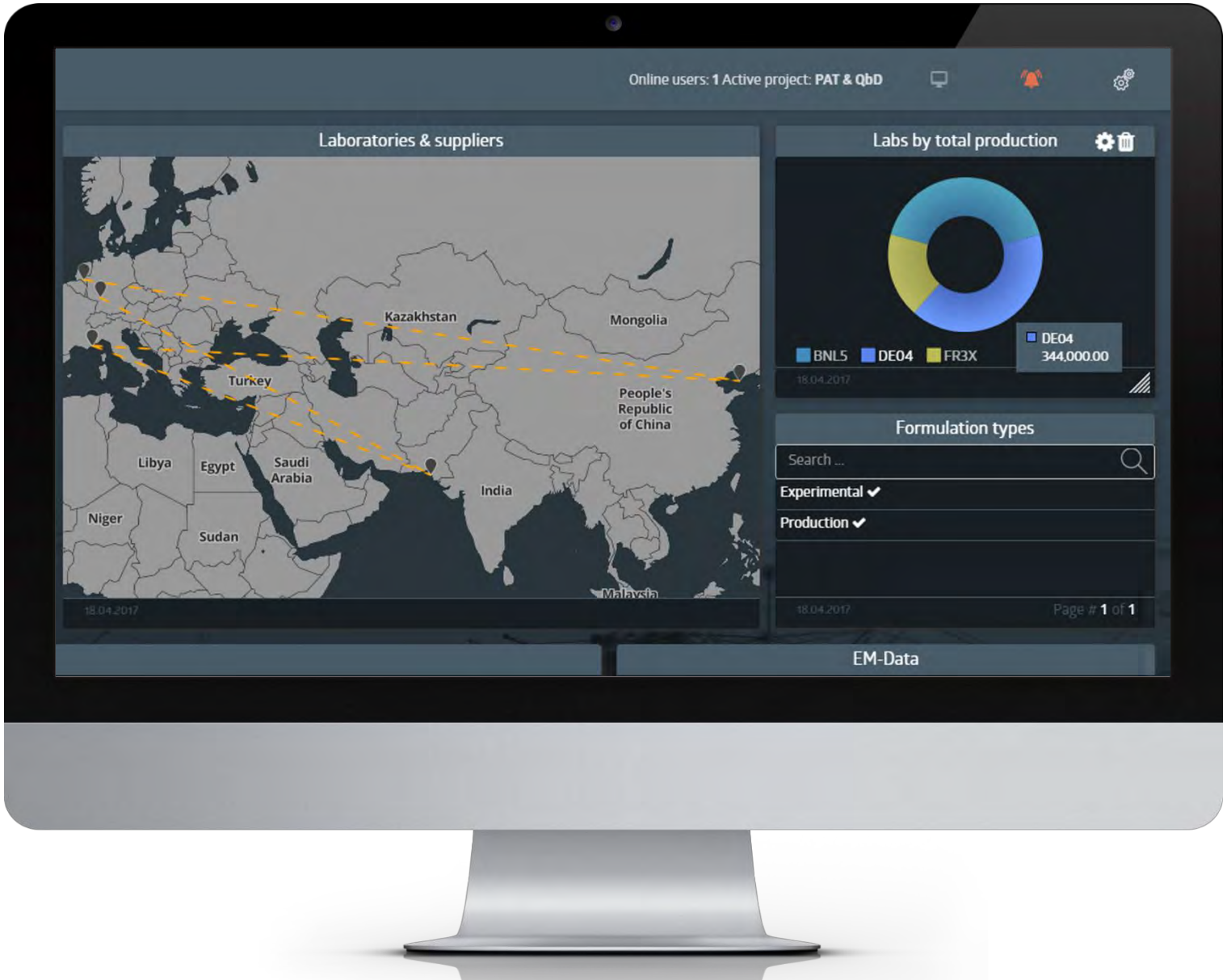
Laboratories

On the map widget, we can see three laboratories:

- France (FR3X)
- The Netherlands (BNL5)
- Germany (DE04)

The yellow supply lines indicate their suppliers in China and Pakistan.

Clicking the pie chart allows us to filter just the German lab, which we will see in the next slide.




plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Production process
Blending
(diffusion mixer)
Metabene (API)
Lactose
Microcrystalline Cellulose (MCC)
Croscarmellose Sodium (CCS)
Dry Granulation & Milling
(roller compactor)
Lubrication
(diffusion mixer)
Magnesium Stearate
Compressing
(rotatory press)
Laboratories & suppliers
Germany
Hungary
Italy
Greece
Turkey
Kazakhstan
Uzbekistan
Turkmenistan
Libya
Egypt
Saudi Arabia
Labs by total production
DE04
Formulation types
Search ...
Experimental
Production
Page # 1 of 1
Batch timeline
Experimental
Production
(Apr 9, 2015, 20)
BatchAmount: 50000
Production
API.ParticleSize.D90 [µm]
ProductionDate
Jul 2014
Jan 2015
Jul 2015
Jan 2016
Jul 2016
Jan 2017
EM-Data
Temperature histogram
Normal distribution
Temperature [°C]
v0.16.0

SPREITZENBARTH CONSULTANTS

Batches

In the timeline chart in the lower left, we can see batches by production date (X-axis).

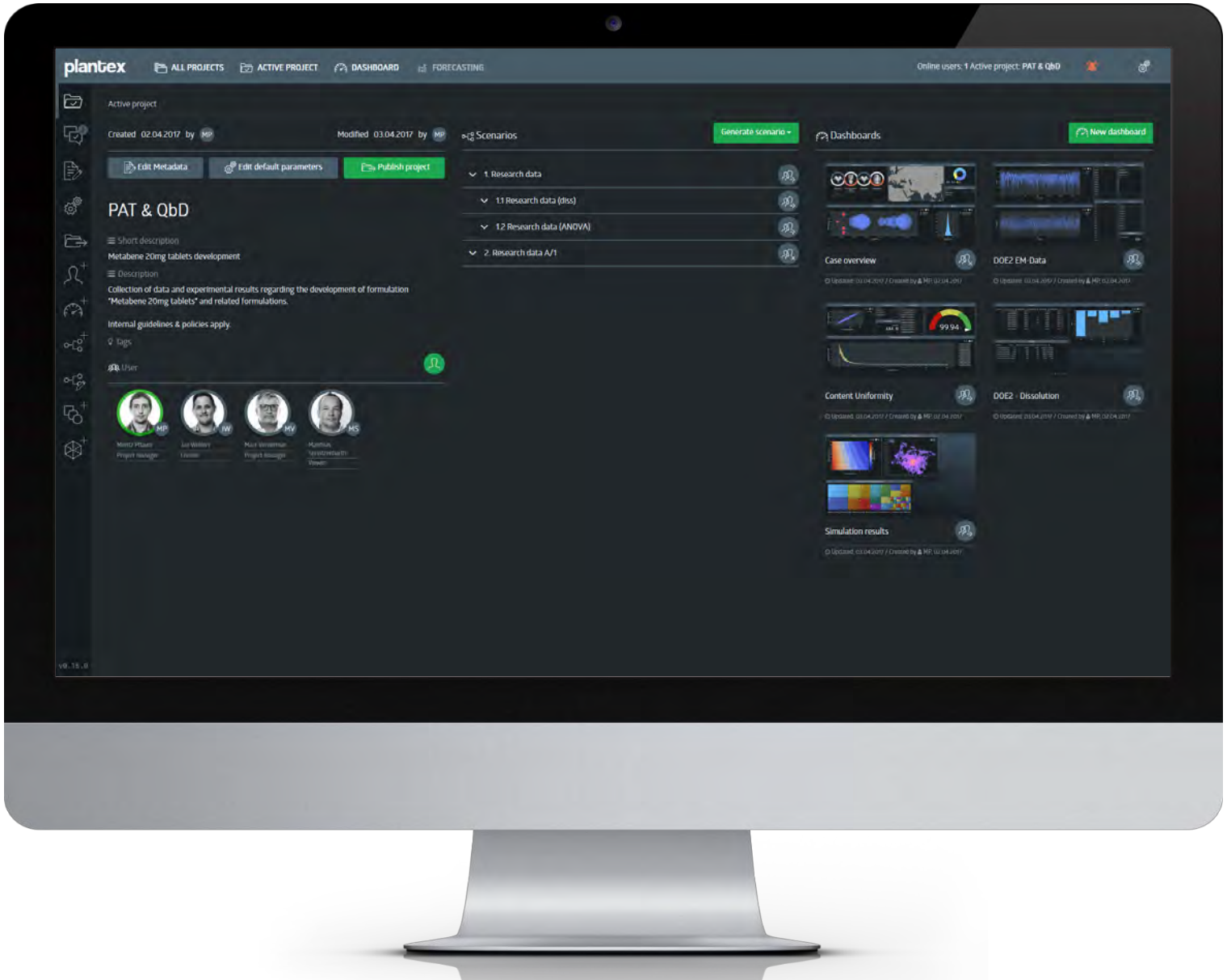
Experimental batches are colored red, production batches blue. The bubble size indicates the batch size.

We can also see the *API particle size* (Y-axis) was varied in some of the experimental batches.

SPREITZENBARTH CONSULTANTS

Project view

From the dashboard, we navigate back to the project overview page and take a look at the different elements on here.

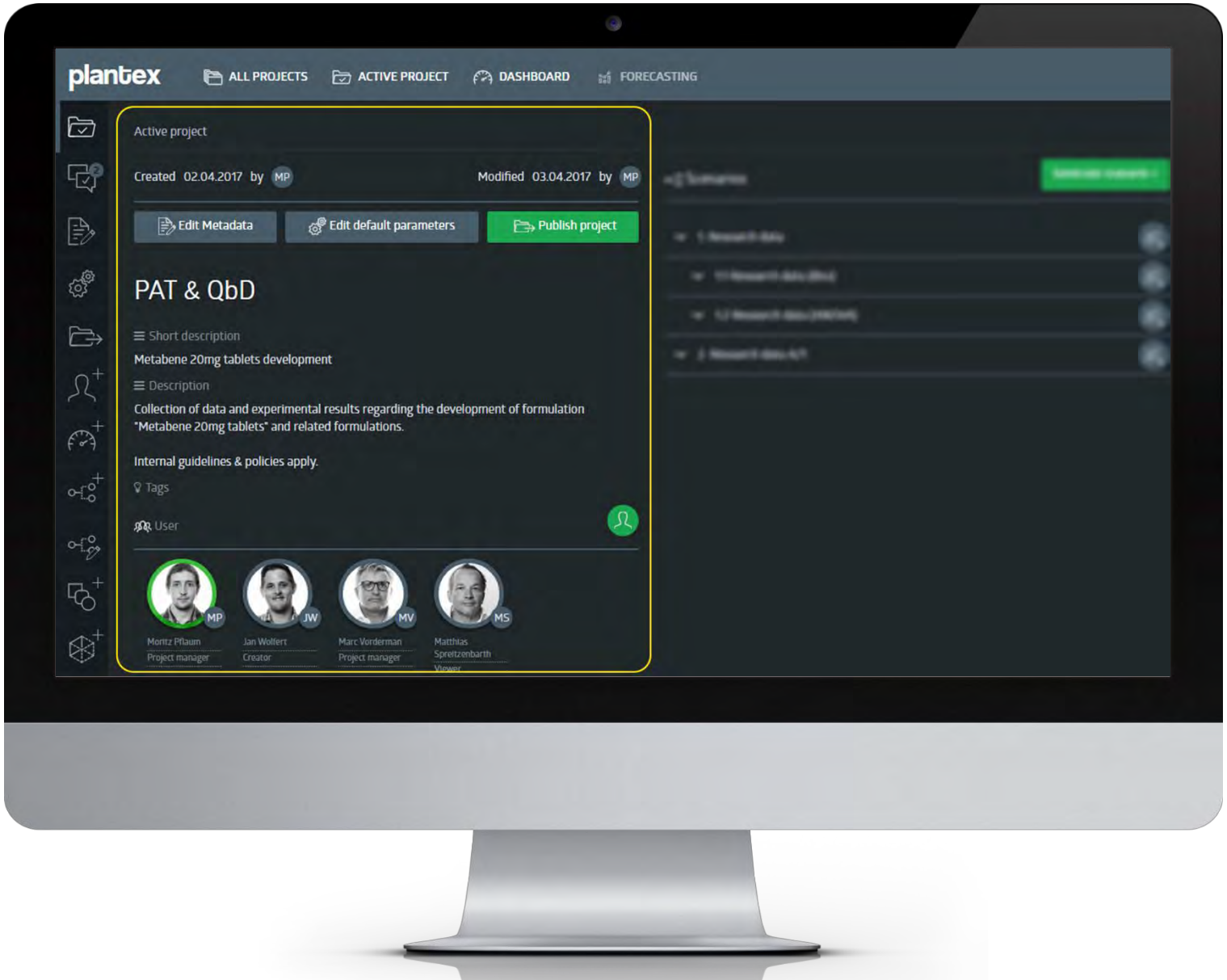


Project metadata

This section contains information about the project itself, like the name “PAT & QbD” and a short & detailed description.

Here you can also see the members of the project and their roles.

A green circle indicates an online user.



SPREITZENBARTH CONSULTANTS

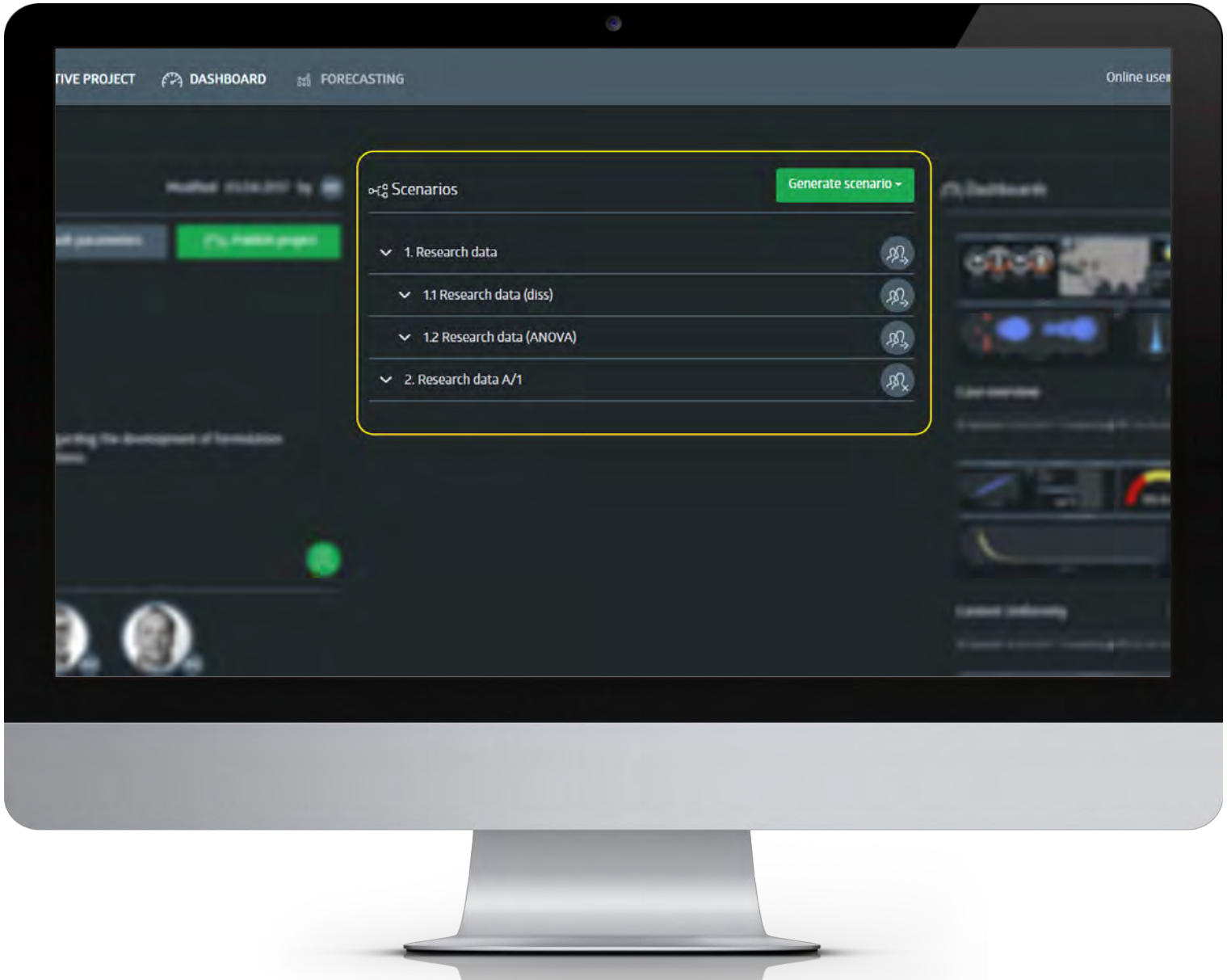
Scenarios

The middle section contains the project scenarios.

A scenario in plantex is a selection of the data you currently work with.

Once a scenario is created, it is fixed.

It is possible to create unlimited scenarios using either new data imports or methods such as **transformations** or **simulations** etc.



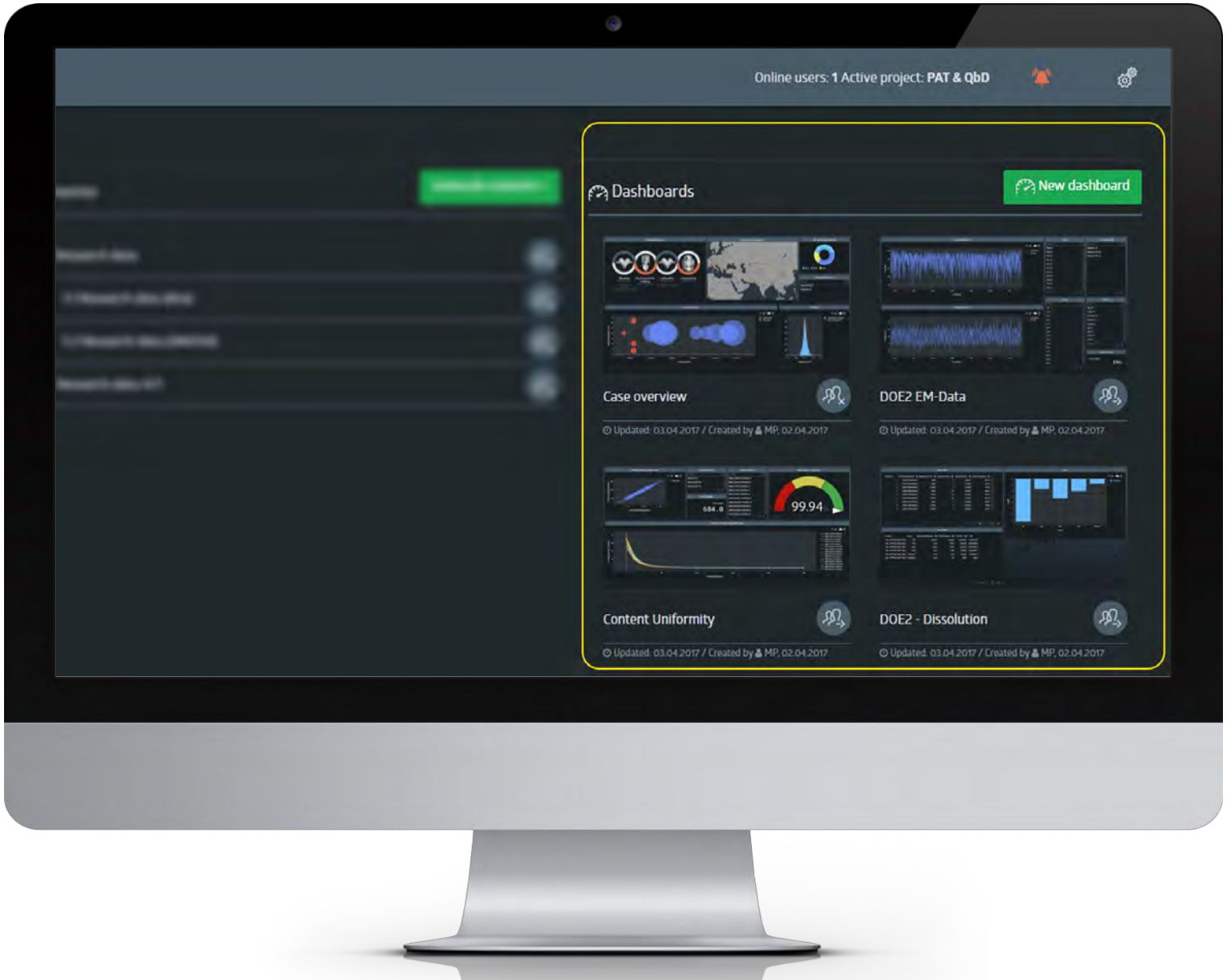
SPREITZENBARTH CONSULTANTS

Dashboards

The rightmost section shows the available dashboards, including a small preview picture.

These are either private dashboards the user created or public dashboards shared by someone in the project.

Clicking on a dashboard will navigate to the dashboard view.



Content uniformity

Next, we will look at the "Content Uniformity" dashboard.

Content uniformity is affected by the blend uniformity of the blend in the first step of the process.
Blend uniformity is measured by a *near infrared spectroscopy probe* (NIRS).

We can see the measurements in the lower half of the dashboard.


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
684.0
99.94
Blend uniformity during blending
BlendUniformity [% RSD]
BlenderRevolutions
0
100
200
300
400
500
5
10
15
20
25
bbnL5/64847-20150406
bbnL5/68144-20150326
bbnL5/71257-20150417
bbnL5/74352-20161101
bbnL5/74921-20161130
bdE04/66363-20160708
bdE04/68340-20150409
bdE04/69259-20150108
bdE04/70038-20161010
bdE04/73693-20161011
bdE04/74537-20160421
bdE04/EXP1.0-20140515
bdE04/EXP1.10-20140515
bdE04/EXP1.1-20140515
bdE04/EXP1.2-20140515
bdE04/EXP1.3-20140515
bdE04/EXP1.4-20140515
bdE04/EXP1.5-20140515
v0.16.0

Assay

If we filter to just a single batch, we see only one line remaining in the lower half.

The upper left chart shows the **tablet weight** (X-axis):

100% means the value is exactly what it is supposed to be. 105% means its 5% heavier, but still in the acceptable range (95% - 105%).

The Y-Axis displays the **label claim** (% of target assay, in our case 20mg).

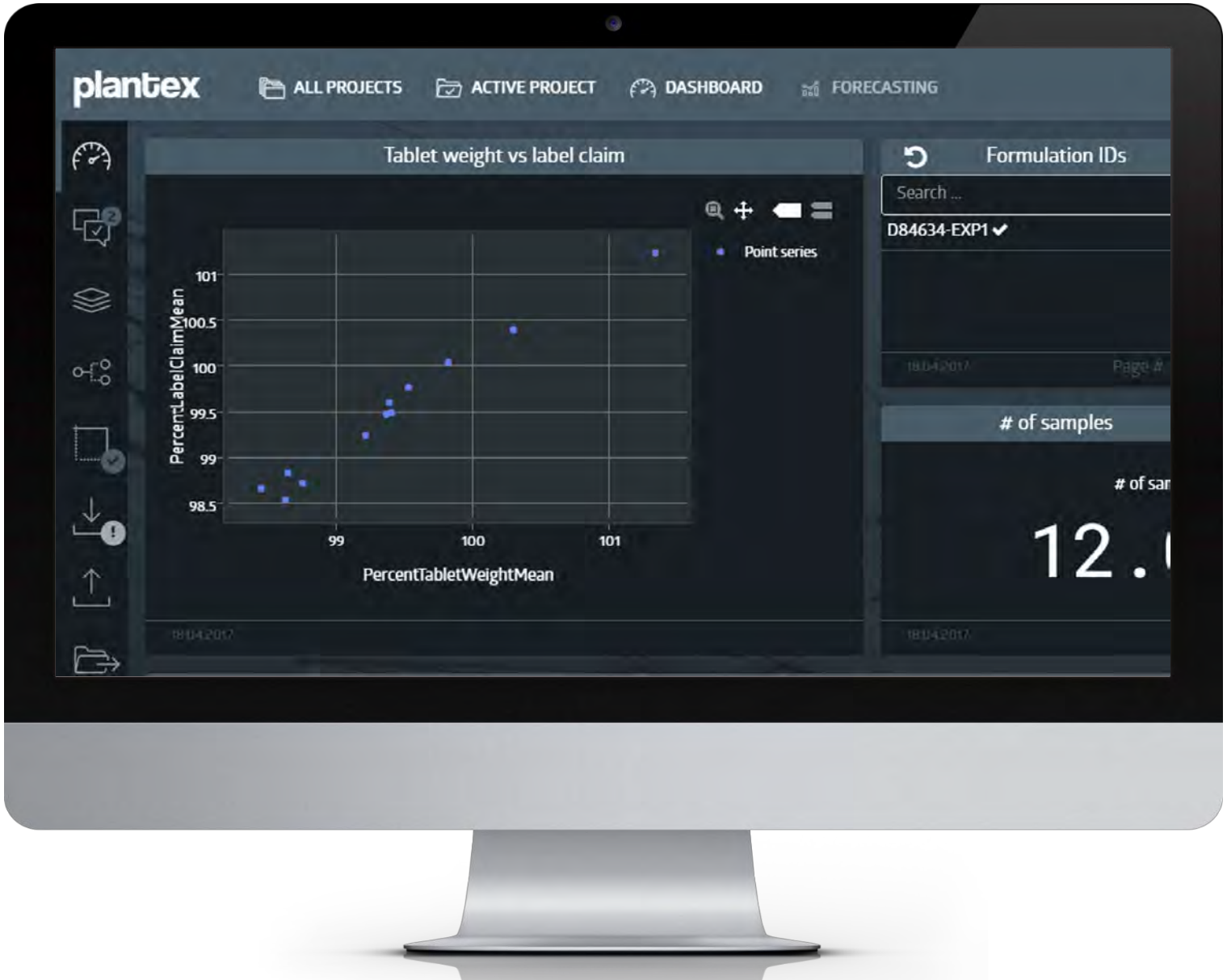
SPREITZENBARTH CONSULTANTS

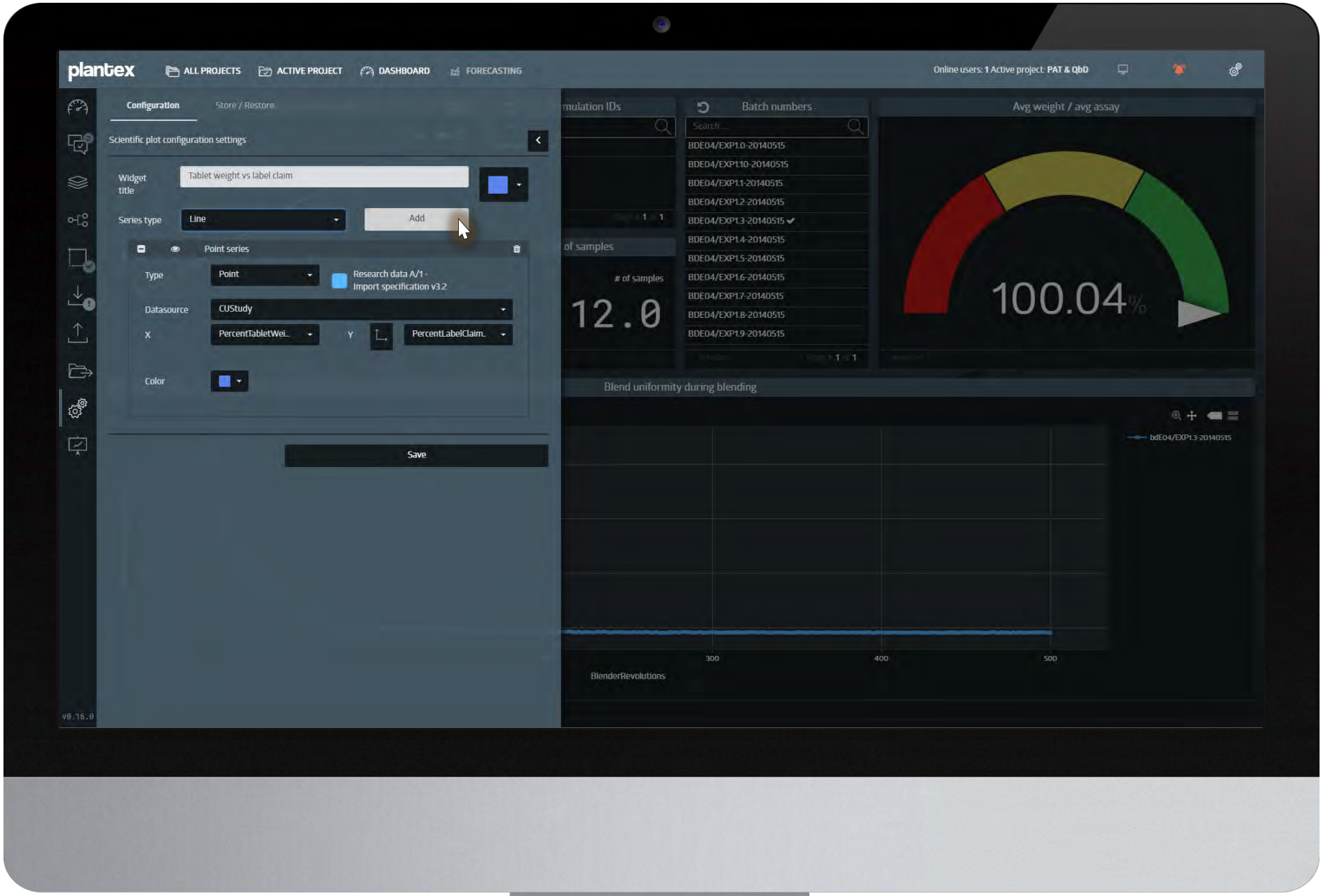
Assay

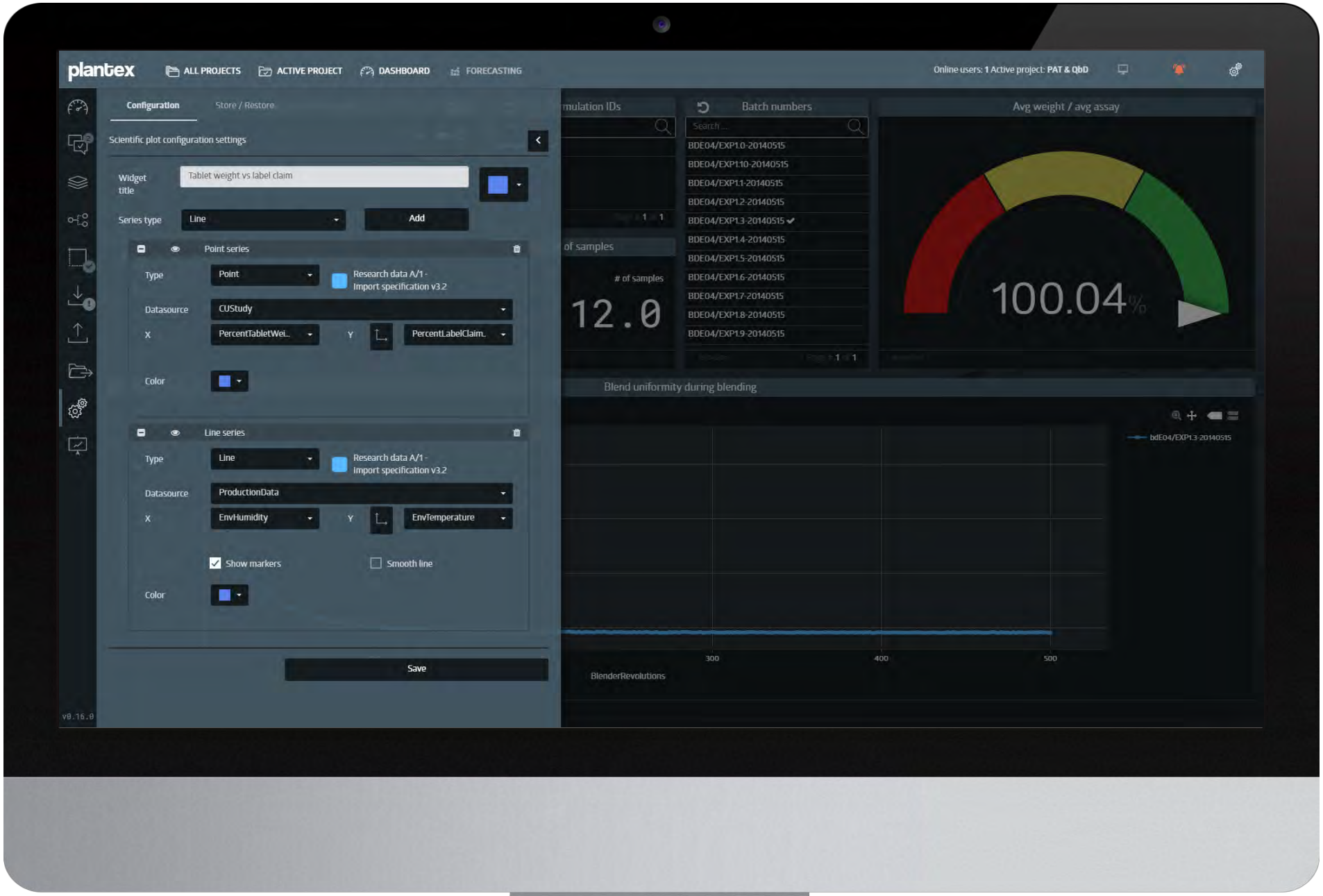
As we can see, there seems to be a linear relationship.

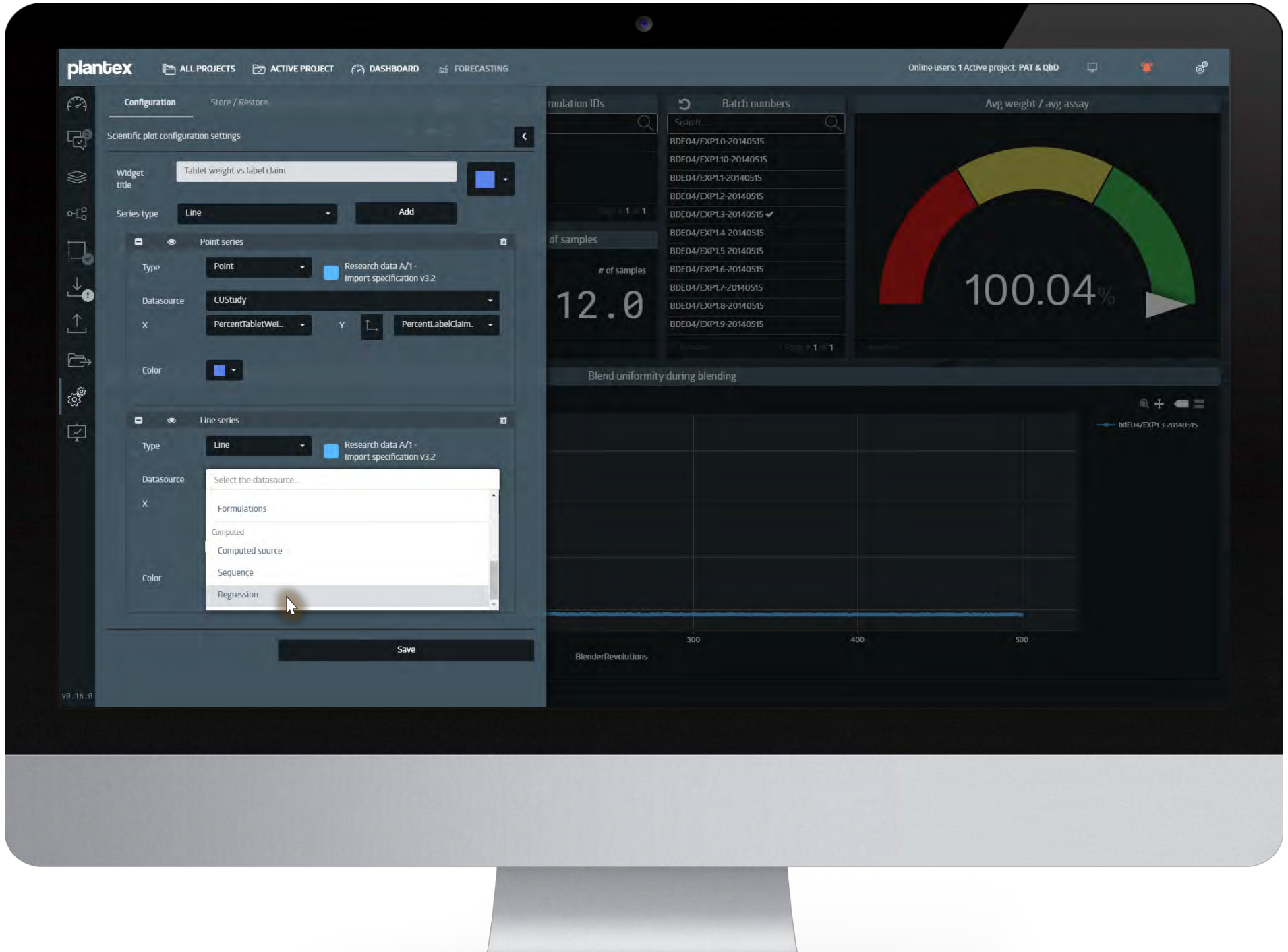
This implies, that if a tablet weighs 103% of what it is supposed to weigh, it likely also contains 103% of the API it is supposed to contain.

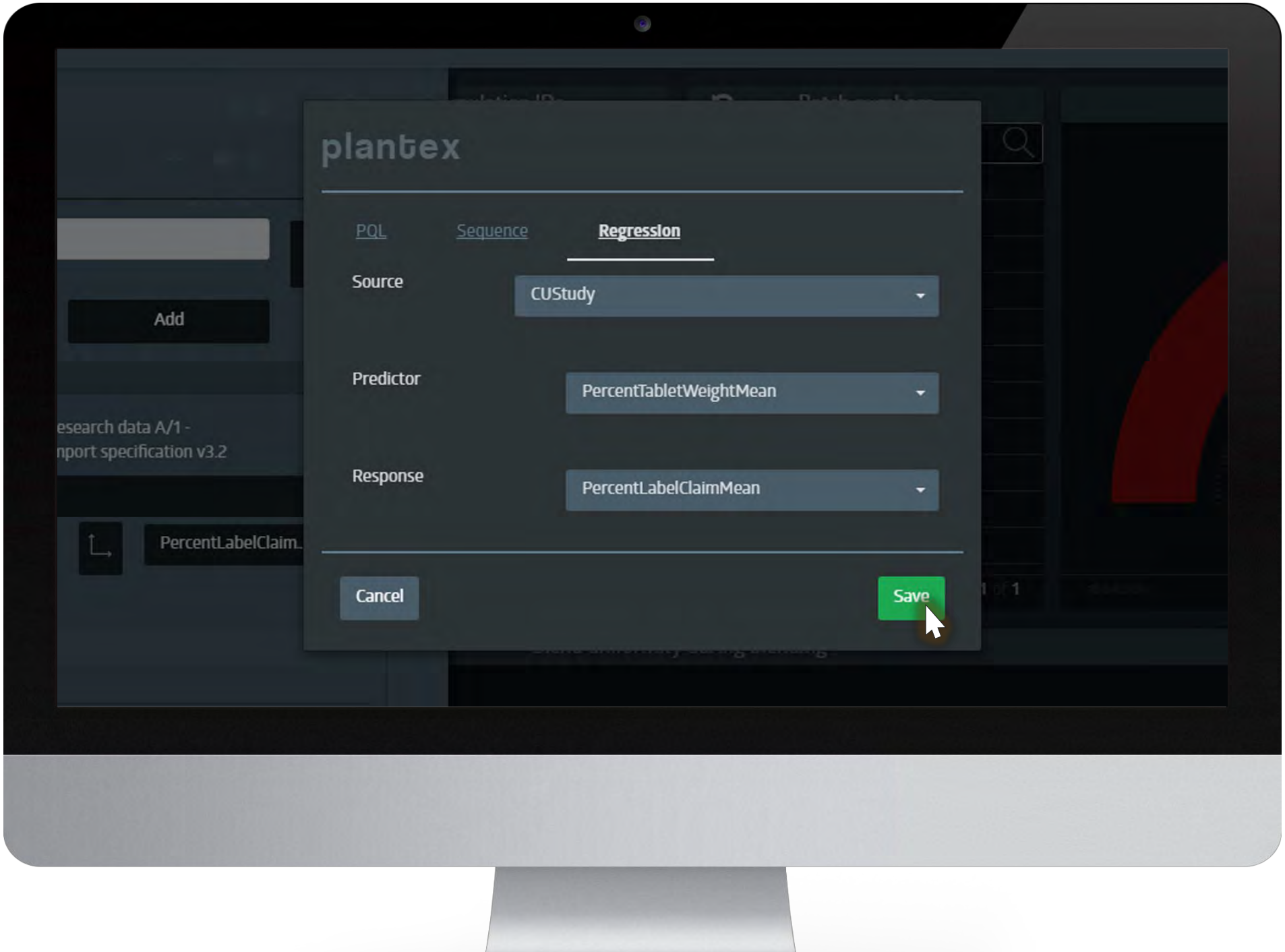
To emphasize this, we can use the *configure widget* dialog to add a calculated regression line, as seen in the next slides.

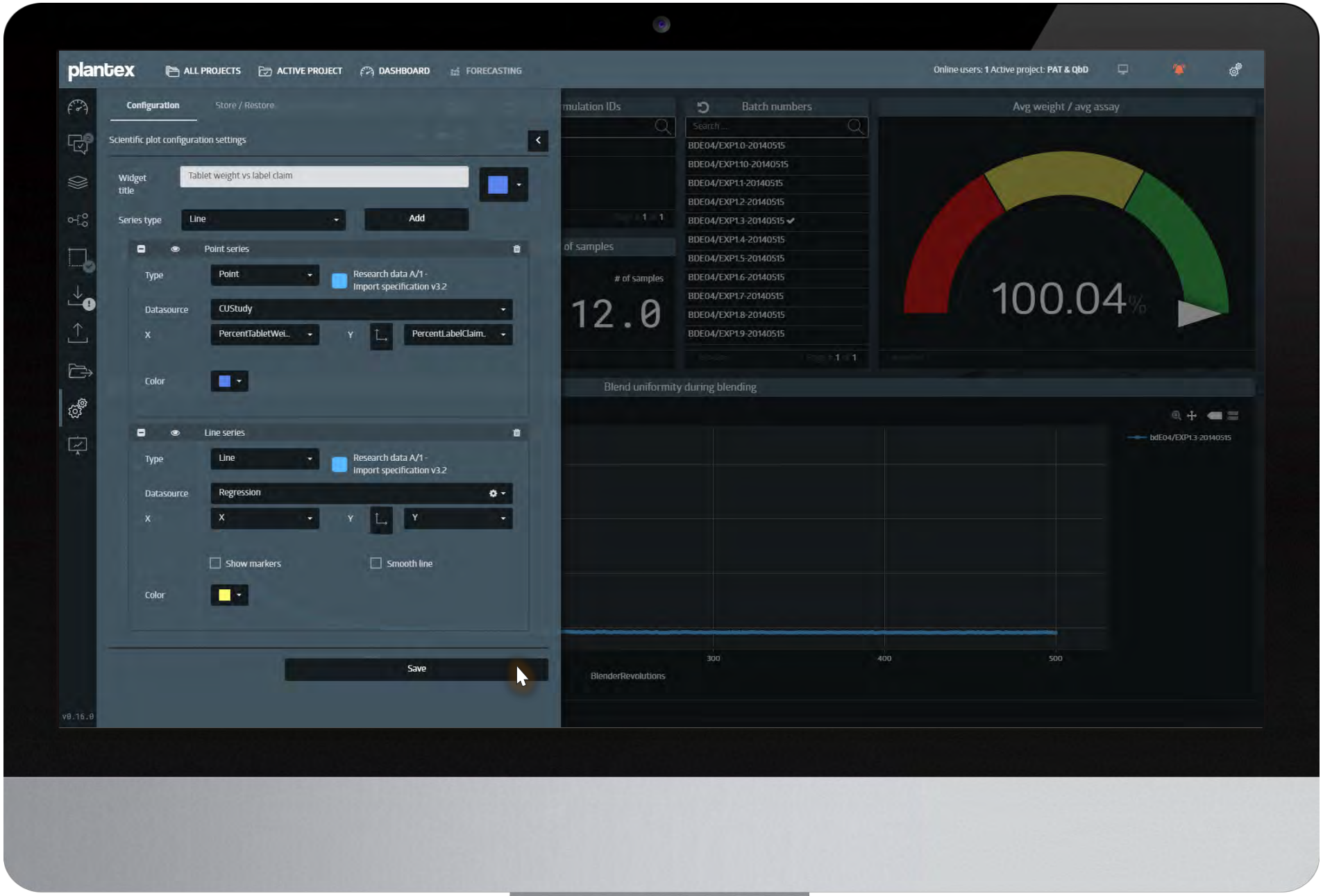



plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Configuration
Store / Restore
Scientific plot configuration settings
Widget title
Tablet weight vs label claim
Series type
Line
Add
Point series
Type
Point
Research data A/1 - Import specification v3.2
Datasource
CUStudy
X
PercentTabletWei..
Y
PercentLabelClaim..
Color
Save
v0.16.0
mulation IDs
of samples
# of samples
12.0
Batch numbers
Search ...
BDE04/EXP1.0-20140515
BDE04/EXP1.10-20140515
BDE04/EXP1.1-20140515
BDE04/EXP1.2-20140515
BDE04/EXP1.3-20140515
BDE04/EXP1.4-20140515
BDE04/EXP1.5-20140515
BDE04/EXP1.6-20140515
BDE04/EXP1.7-20140515
BDE04/EXP1.8-20140515
BDE04/EXP1.9-20140515
Avg weight / avg assay
100.04%
Blend uniformity during blending
bdE04/EXP1.3-20140515
300
400
500
BlenderRevolutions


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Configuration
Store / Restore
Scientific plot configuration settings
Widget title
Tablet weight vs label claim
Series type
Line
Add
Point series
Type
Point
Research data A/1 - Import specification v3.2
Datasource
CUStudy
X
PercentTabletWei..
Y
PercentLabelClaim..
Color
Line series
Type
Line
Research data A/1 - Import specification v3.2
Datasource
ProductionData
X
EnvHumidity
Y
EnvTemperature
Show markers
Smooth line
Color
Save
v0.16.0
mulation IDs
of samples
# of samples
12.0
Batch numbers
Search ...
BDE04/EXP1.0-20140515
BDE04/EXP1.10-20140515
BDE04/EXP1.1-20140515
BDE04/EXP1.2-20140515
BDE04/EXP1.3-20140515
BDE04/EXP1.4-20140515
BDE04/EXP1.5-20140515
BDE04/EXP1.6-20140515
BDE04/EXP1.7-20140515
BDE04/EXP1.8-20140515
BDE04/EXP1.9-20140515
Avg weight / avg assay
100.04%
Blend uniformity during blending
bdE04/EXP1.3-20140515
300
400
500
BlenderRevolutions


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Configuration
Store / Restore
Scientific plot configuration settings
Widget title
Tablet weight vs label claim
Series type
Line
Add
Point series
Type
Point
Research data A/1 - Import specification v3.2
Datasource
CUStudy
X
PercentTabletWei..
Y
PercentLabelClaim..
Color
Line series
Type
Line
Research data A/1 - Import specification v3.2
Datasource
Select the datasource...
X
Formulations
Computed
Computed source
Sequence
Regression
Color
Save
v0.16.0
mulation IDs
of samples
# of samples
12.0
Batch numbers
Search ...
BDE04/EXP1.0-20140515
BDE04/EXP1.10-20140515
BDE04/EXP1.1-20140515
BDE04/EXP1.2-20140515
BDE04/EXP1.3-20140515
BDE04/EXP1.4-20140515
BDE04/EXP1.5-20140515
BDE04/EXP1.6-20140515
BDE04/EXP1.7-20140515
BDE04/EXP1.8-20140515
BDE04/EXP1.9-20140515
Avg weight / avg assay
100.04%
Blend uniformity during blending
bdE04/EXP1.3-20140515
300
400
500
BlenderRevolutions


plantex
PQL
Sequence
Regression
Source
CUStudy
Predictor
PercentTabletWeightMean
Response
PercentLabelClaimMean
Cancel
Save
Add
esearch data A/1 -
nport specification v3.2
PercentLabelClaim


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Configuration
Store / Restore
Scientific plot configuration settings
Widget title
Tablet weight vs label claim
Series type
Line
Add
Point series
Type
Point
Research data A/1 - Import specification v3.2
Datasource
CUStudy
X
PercentTabletWei..
Y
PercentLabelClaim..
Color
Line series
Type
Line
Research data A/1 - Import specification v3.2
Datasource
Regression
X
X
Y
Y
Show markers
Smooth line
Color
Save
v0.16.0
mulation IDs
of samples
# of samples
12.0
Batch numbers
Search ...
BDE04/EXP1.0-20140515
BDE04/EXP1.10-20140515
BDE04/EXP1.1-20140515
BDE04/EXP1.2-20140515
BDE04/EXP1.3-20140515
BDE04/EXP1.4-20140515
BDE04/EXP1.5-20140515
BDE04/EXP1.6-20140515
BDE04/EXP1.7-20140515
BDE04/EXP1.8-20140515
BDE04/EXP1.9-20140515
Avg weight / avg assay
100.04%
Blend uniformity during blending
bdE04/EXP1.3-20140515
300
400
500
BlenderRevolutions


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Tablet weight vs label claim
PercentLabelClaimMean, Y
PercentTabletWeightMean, X
Point series
Regression line
Formulation IDs
Search ...
D84634-EXP1
Batch numbers
Search ...
BDE04/EXP1.0-20140515
BDE04/EXP1.10-20140515
BDE04/EXP1.1-20140515
BDE04/EXP1.2-20140515
BDE04/EXP1.3-20140515
BDE04/EXP1.4-20140515
BDE04/EXP1.5-20140515
BDE04/EXP1.6-20140515
BDE04/EXP1.7-20140515
BDE04/EXP1.8-20140515
BDE04/EXP1.9-20140515
Page # 1 of 1
# of samples
# of samples
12.0
Avg weight / avg assay
100.04%
Blend uniformity during blending
BlendUniformity [% RSD]
BlenderRevolutions
bdE04/EXP1.3-20140515
v8.16.0


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Tablet weight vs label claim
Point series
Regression line
PercentLabelClaimMean, Y
PercentTabletWeightMean, X
Formulation IDs
Search ...
D84634-EXP1
Batch numbers
Search ...
BDE04/EXP1.0-20140515
BDE04/EXP1.10-20140515
BDE04/EXP1.1-20140515
BDE04/EXP1.2-20140515
BDE04/EXP1.3-20140515
BDE04/EXP1.4-20140515
BDE04/EXP1.5-20140515
BDE04/EXP1.6-20140515
BDE04/EXP1.7-20140515
BDE04/EXP1.8-20140515
BDE04/EXP1.9-20140515
# of samples
# of samples
36.0
Avg weight / avg assay
100.02%
Blend uniformity during blending
bdE04/EXP1.3-20140515
bdE04/EXP1.4-20140515
bdE04/EXP1.8-20140515
BlendUniformity [% RSD]
BlenderRevolutions
v8.16.0

SPREITZENBARTH CONSULTANTS

Regression

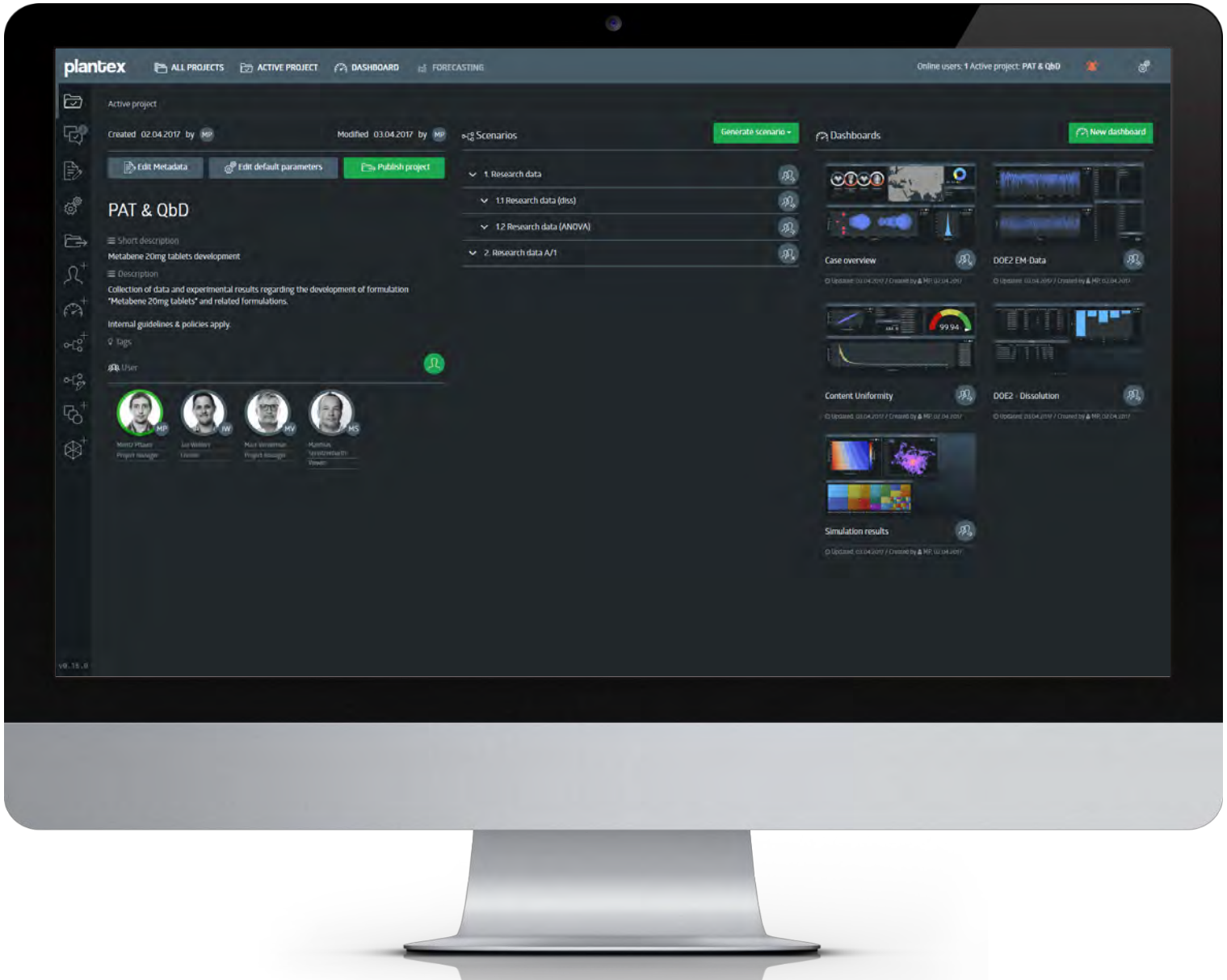
As we saw in the last screen, the yellow regression line is there and updates according to the data, when we add more batches back by un-filtering them.

When we control the blend uniformity with the NIRS probe to make sure it is in an acceptable range, the tablet weight can be used to **predict** the **critical quality parameter assay.**

Dissolution

Going back to the project view, we now want to look at the experimental design and results regarding tablet dissolution (another CQA).

We will open the “DOE2 – Dissolution” dashboard and take a look at the parameters used in the design and how the experiment was carried out.



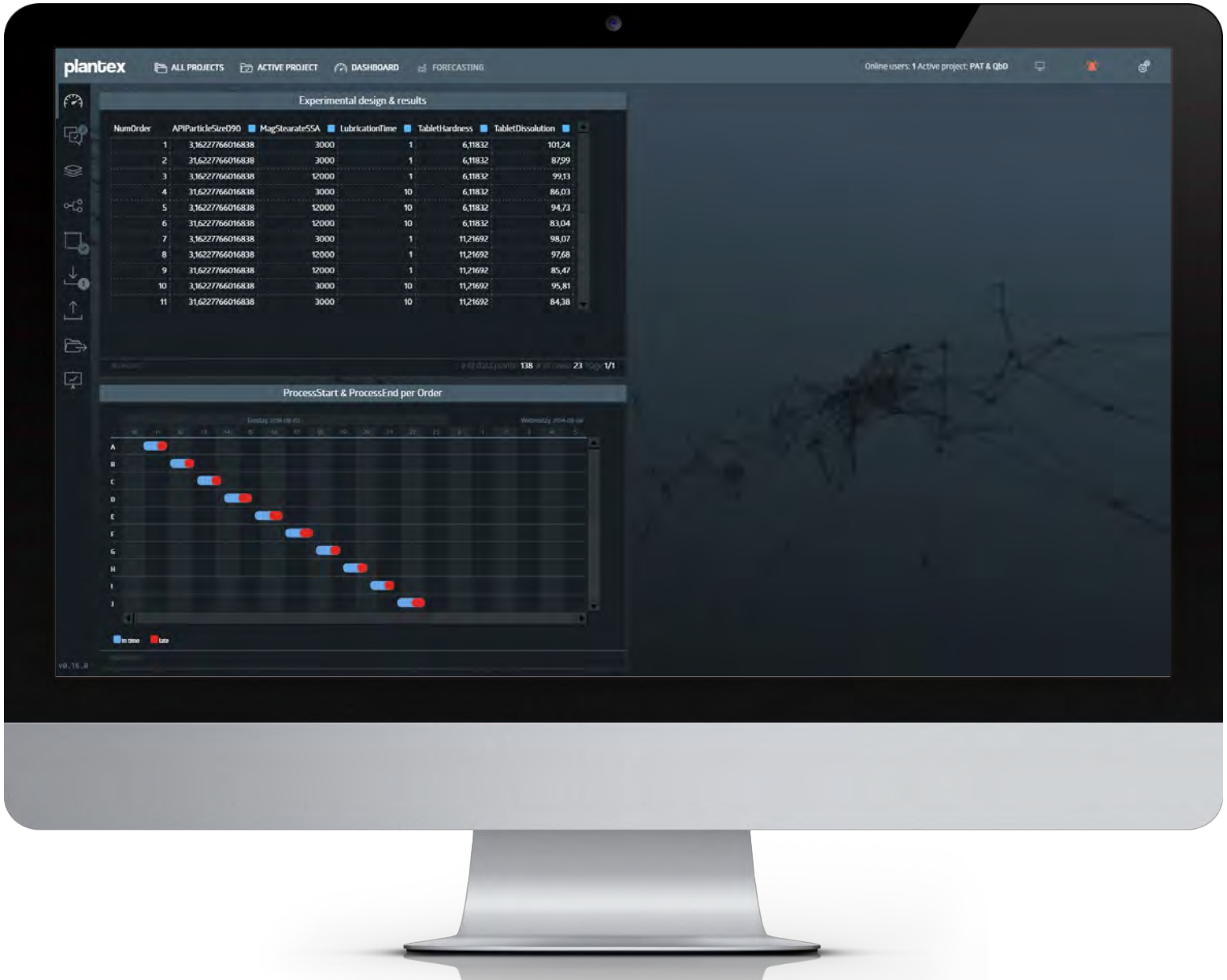
Dissolution DoE

Design of Experiment (DoE) was used to choose the different parameters for the experimental batches.

Predictor values were:

1. API particle size
2. Magnesium stearate surface area
3. Lubrication time
4. Tablet hardness

The measured results was Dissolution (% after 20 mins)

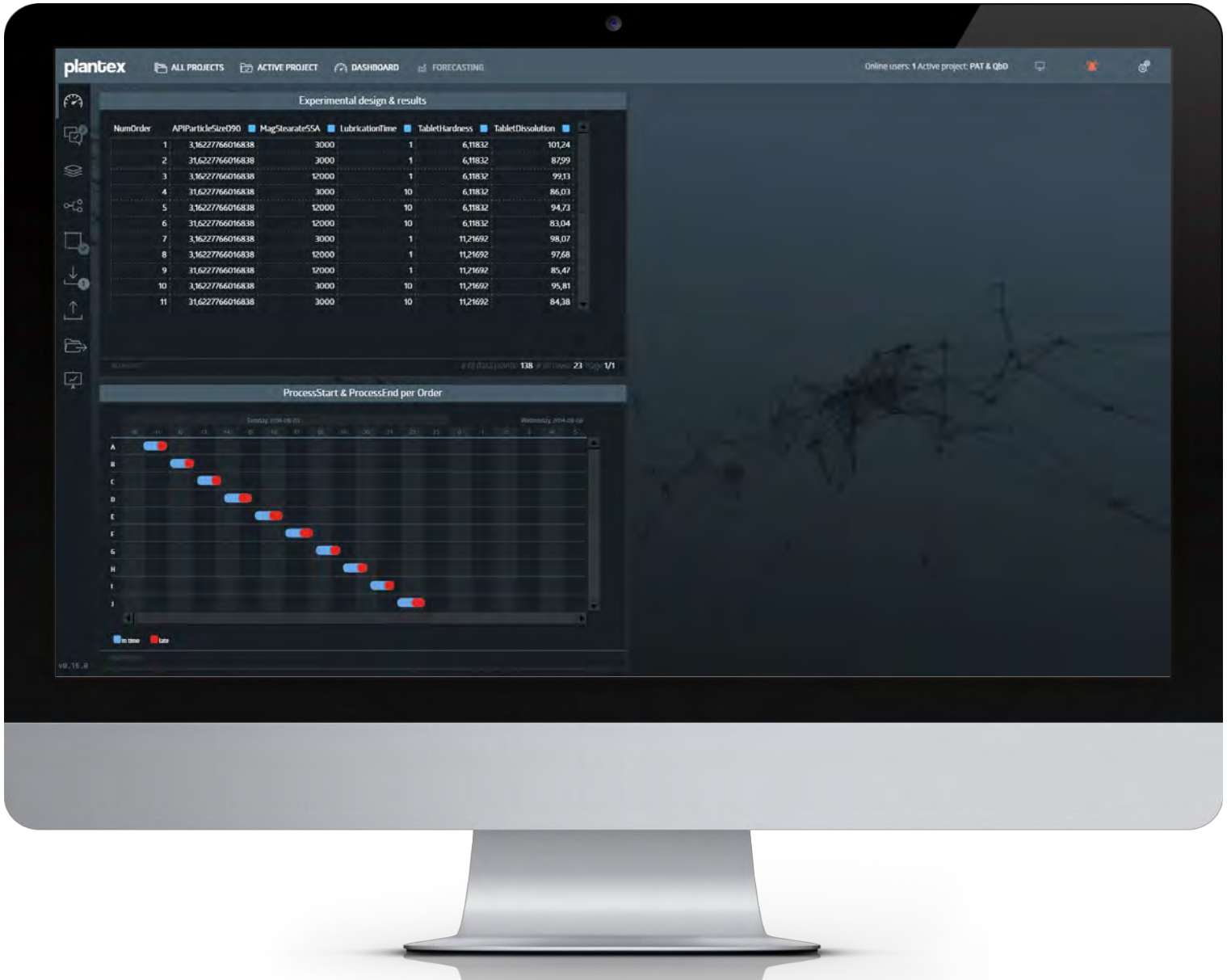


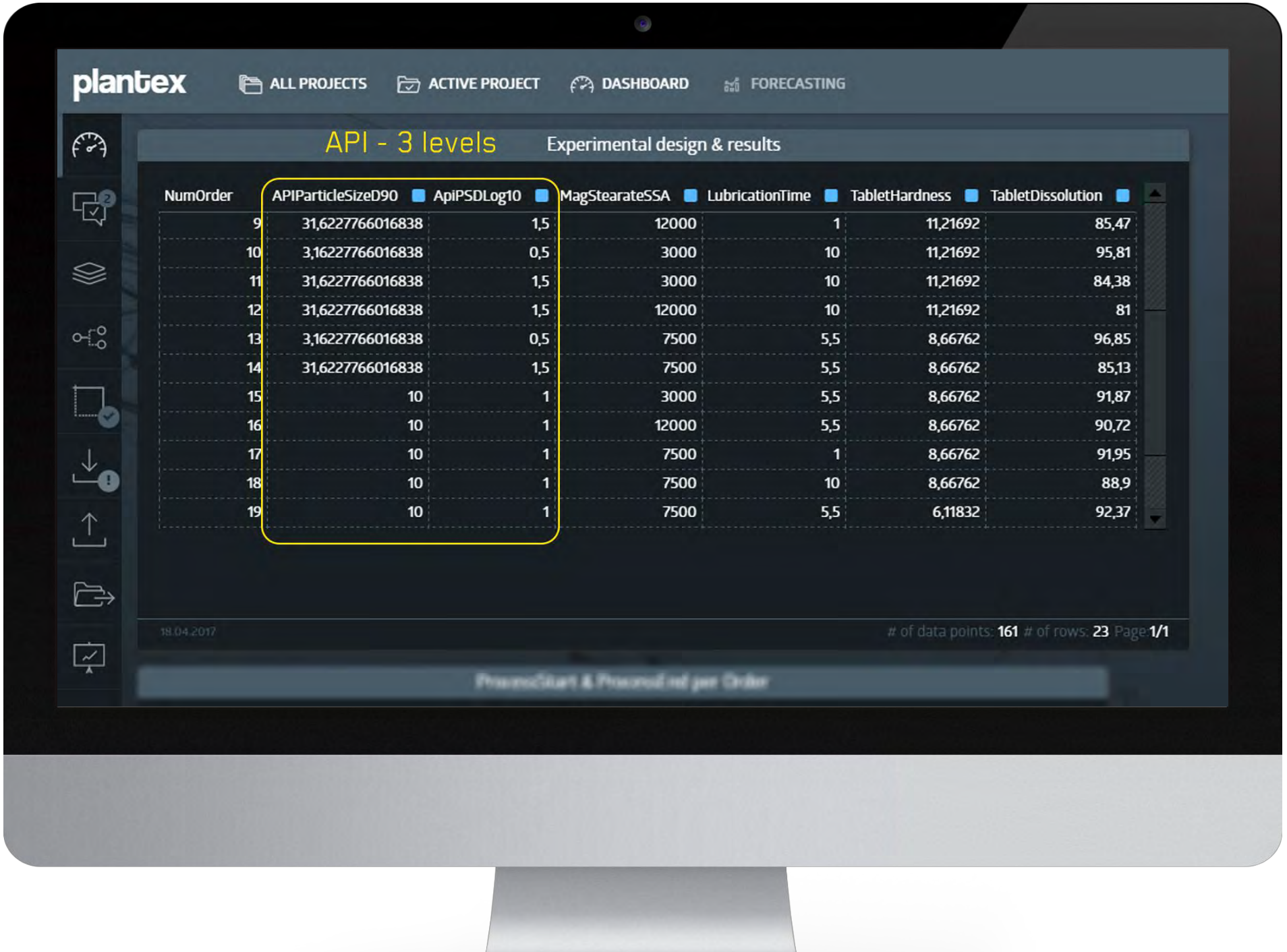
Dissolution DoE

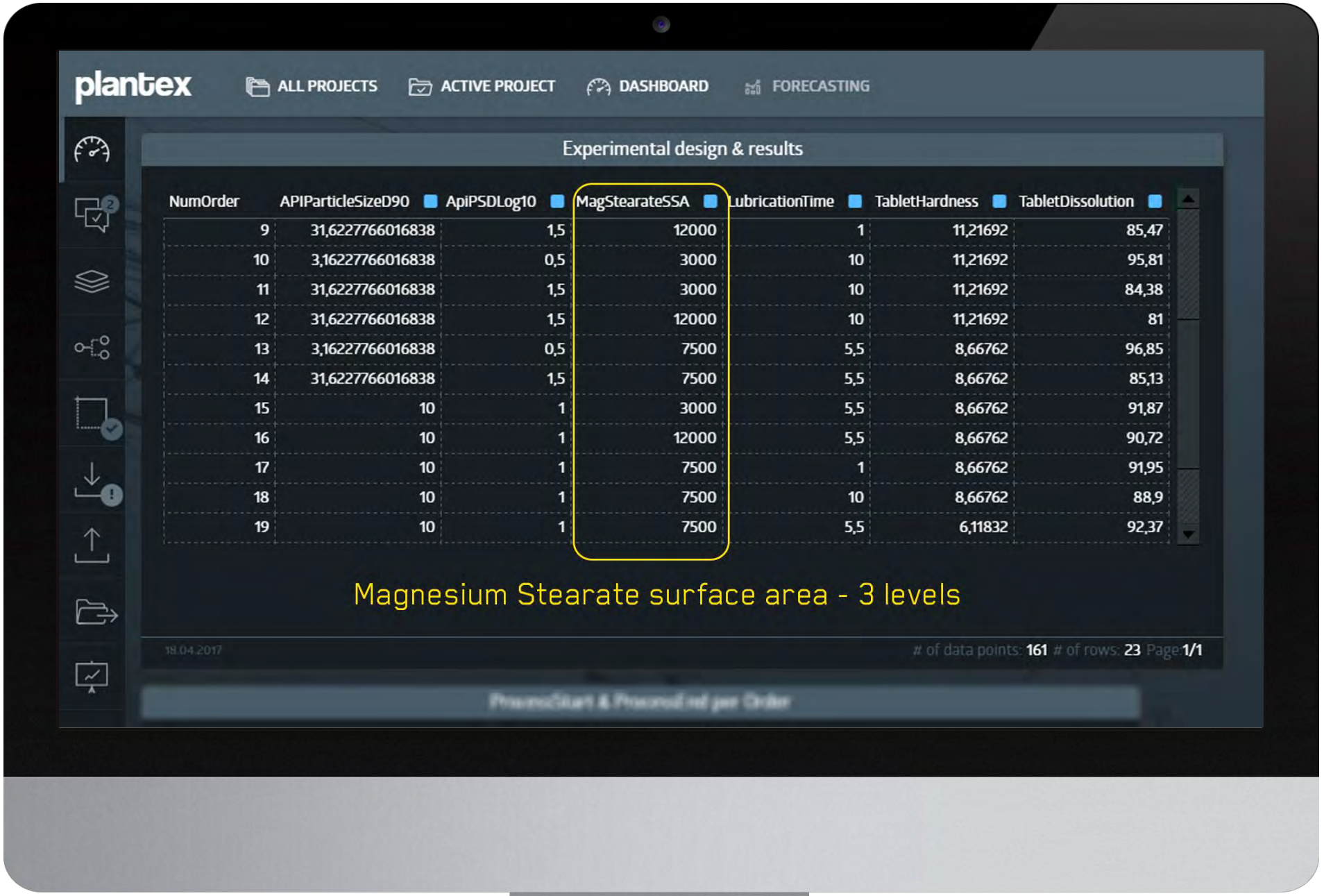
The goal of the experiment was to determine which of the parameters affect the CQA dissolution.

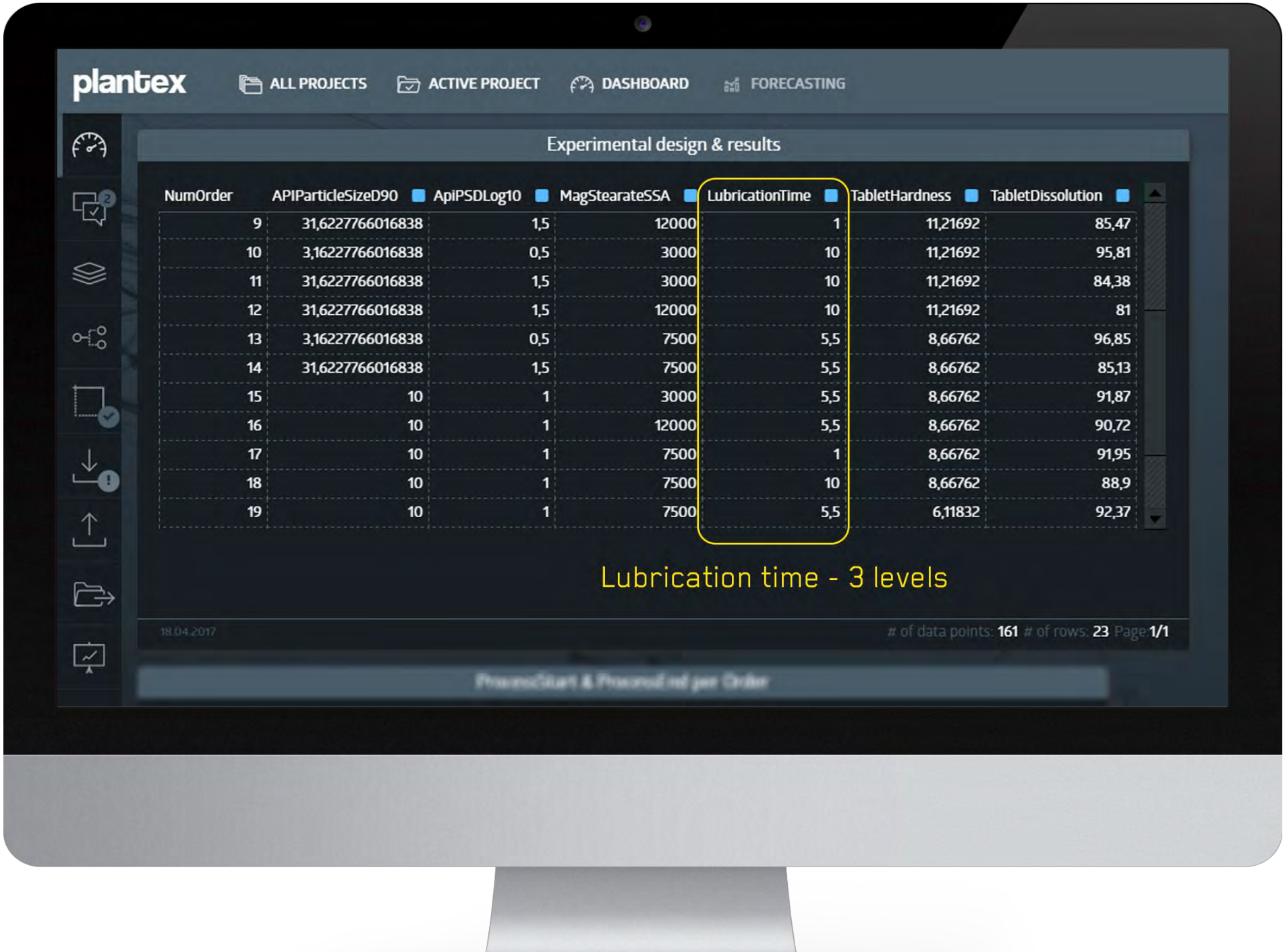
Furthermore the results will be used to model the relationship mathematically.

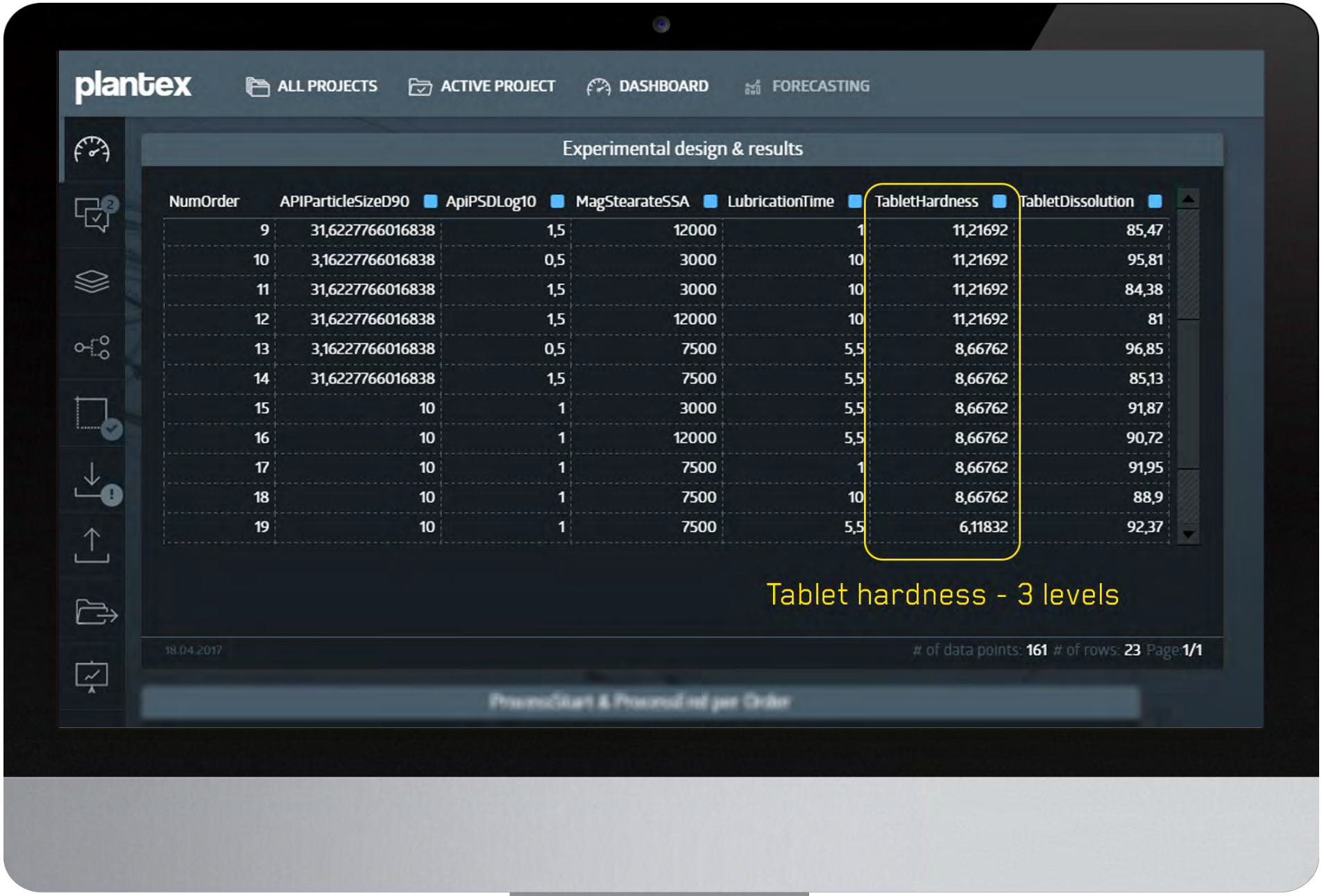
The next slides detail the experimental design.

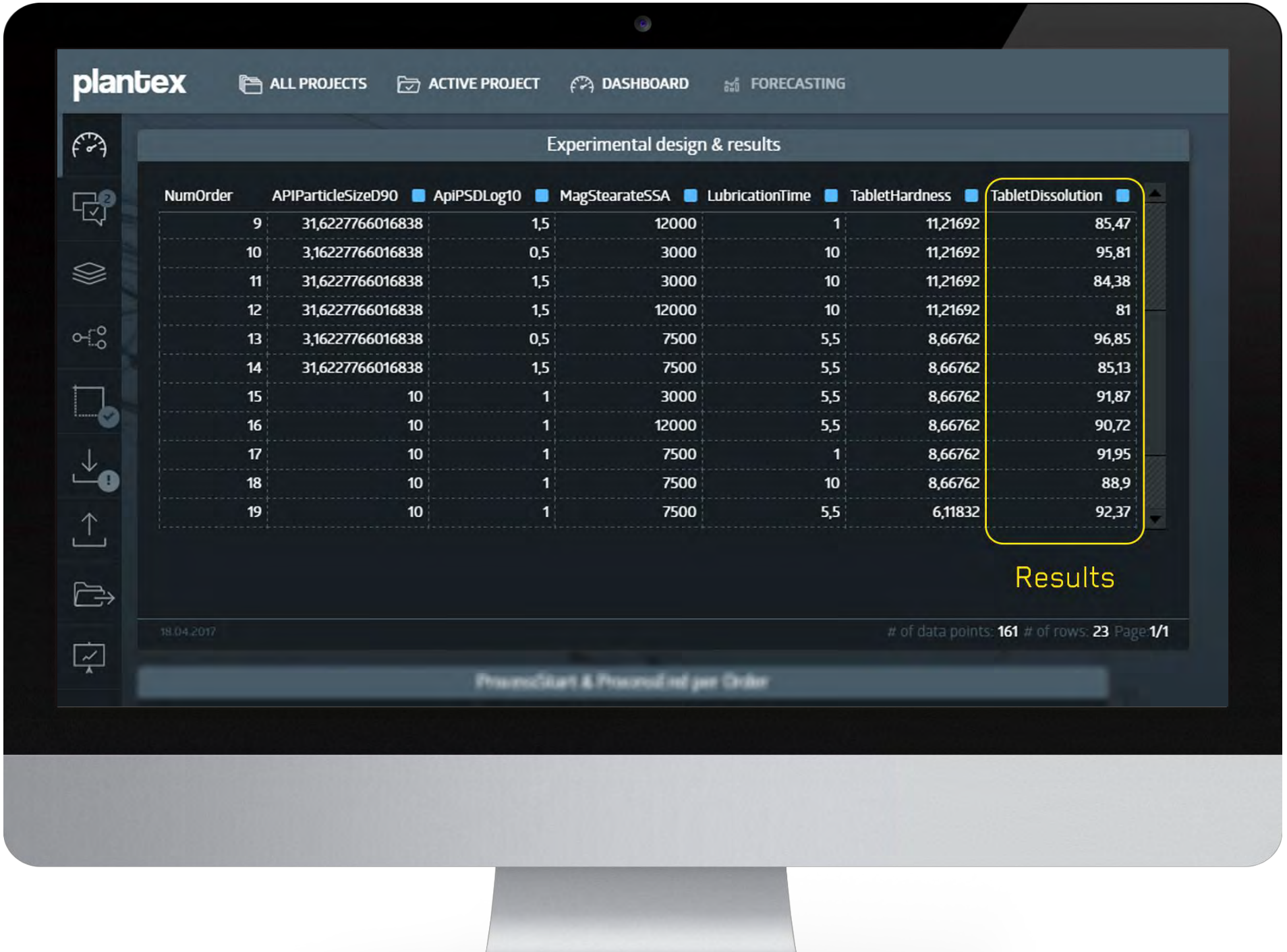


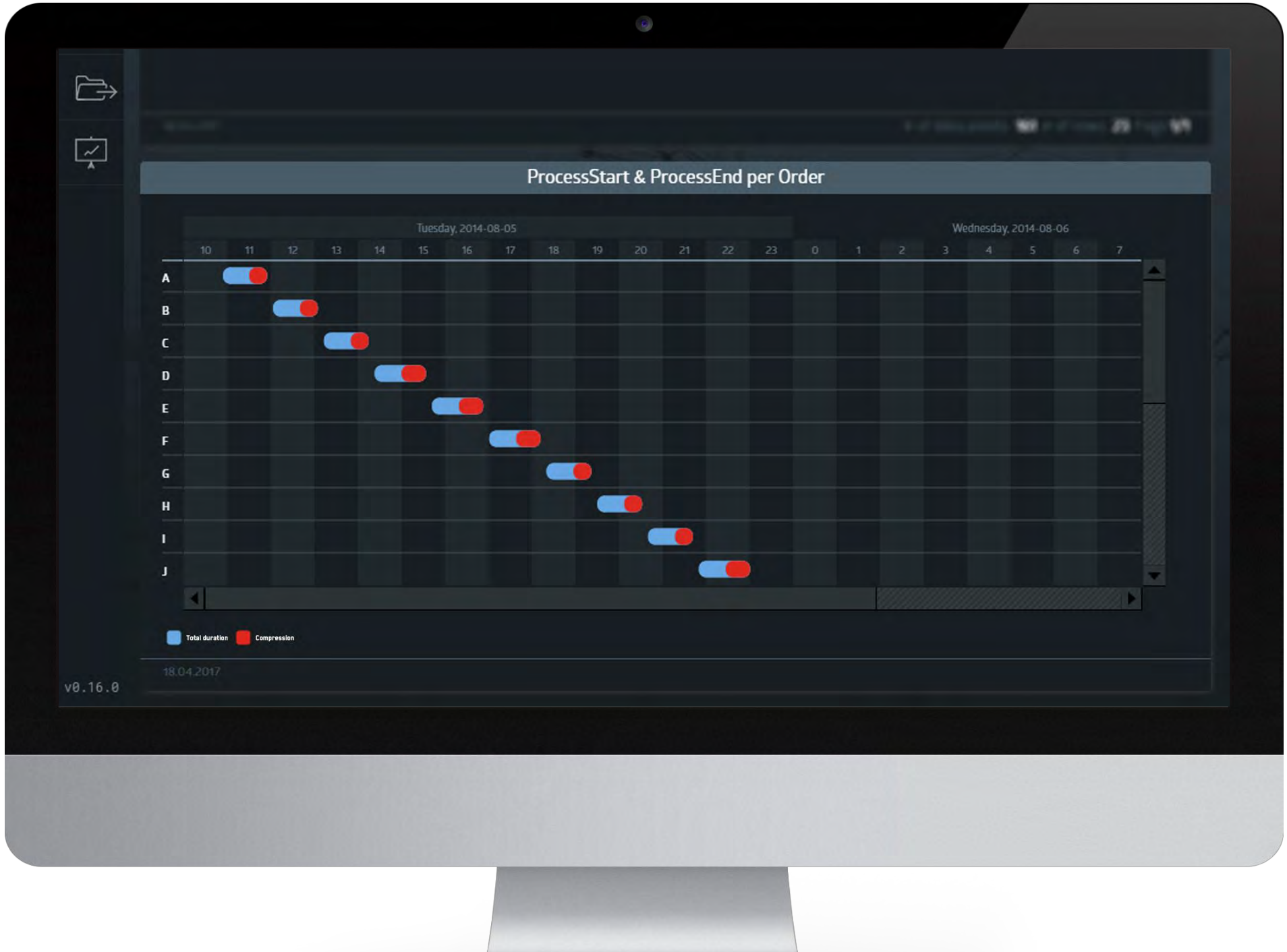

plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
API - 3 levels
Experimental design & results
NumOrder
APIParticleSizeD90
ApiPSDLog10
MagStearateSSA
LubricationTime
TabletHardness
TabletDissolution
9 31,6227766016838 1,5 12000 1 11,21692 85,47
10 3,16227766016838 0,5 3000 10 11,21692 95,81
11 31,6227766016838 1,5 3000 10 11,21692 84,38
12 31,6227766016838 1,5 12000 10 11,21692 81
13 3,16227766016838 0,5 7500 5,5 8,66762 96,85
14 31,6227766016838 1,5 7500 5,5 8,66762 85,13
15 10 1 3000 5,5 8,66762 91,87
16 10 1 12000 5,5 8,66762 90,72
17 10 1 7500 1 8,66762 91,95
18 10 1 7500 10 8,66762 88,9
19 10 1 7500 5,5 6,11832 92,37
18.04.2017
# of data points: 161 # of rows: 23 Page: 1/1


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Experimental design & results
NumOrder | APIParticleSizeD90 | ApiPSDLog10 | MagStearateSSA | LubricationTime | TabletHardness | TabletDissolution
9 | 31,6227766016838 | 1,5 | 12000 | 1 | 11,21692 | 85,47
10 | 3,16227766016838 | 0,5 | 3000 | 10 | 11,21692 | 95,81
11 | 31,6227766016838 | 1,5 | 3000 | 10 | 11,21692 | 84,38
12 | 31,6227766016838 | 1,5 | 12000 | 10 | 11,21692 | 81
13 | 3,16227766016838 | 0,5 | 7500 | 5,5 | 8,66762 | 96,85
14 | 31,6227766016838 | 1,5 | 7500 | 5,5 | 8,66762 | 85,13
15 | 10 | 1 | 3000 | 5,5 | 8,66762 | 91,87
16 | 10 | 1 | 12000 | 5,5 | 8,66762 | 90,72
17 | 10 | 1 | 7500 | 1 | 8,66762 | 91,95
18 | 10 | 1 | 7500 | 10 | 8,66762 | 88,9
19 | 10 | 1 | 7500 | 5,5 | 6,11832 | 92,37
Magnesium Stearate surface area - 3 levels
18.04.2017
# of data points: 161 # of rows: 23 Page: 1/1


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Experimental design & results
NumOrder
APIParticleSizeD90
ApiPSDLog10
MagStearateSSA
LubricationTime
TabletHardness
TabletDissolution
9 31,6227766016838 1,5 12000 1 11,21692 85,47
10 3,16227766016838 0,5 3000 10 11,21692 95,81
11 31,6227766016838 1,5 3000 10 11,21692 84,38
12 31,6227766016838 1,5 12000 10 11,21692 81
13 3,16227766016838 0,5 7500 5,5 8,66762 96,85
14 31,6227766016838 1,5 7500 5,5 8,66762 85,13
15 10 1 3000 5,5 8,66762 91,87
16 10 1 12000 5,5 8,66762 90,72
17 10 1 7500 1 8,66762 91,95
18 10 1 7500 10 8,66762 88,9
19 10 1 7500 5,5 6,11832 92,37
Lubrication time - 3 levels
18.04.2017
# of data points: 161 # of rows: 23 Page: 1/1


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Experimental design & results
NumOrder
APIParticleSizeD90
ApiPSDLog10
MagStearateSSA
LubricationTime
TabletHardness
TabletDissolution
9 31,6227766016838 1,5 12000 1 11,21692 85,47
10 3,16227766016838 0,5 3000 10 11,21692 95,81
11 31,6227766016838 1,5 3000 10 11,21692 84,38
12 31,6227766016838 1,5 12000 10 11,21692 81
13 3,16227766016838 0,5 7500 5,5 8,66762 96,85
14 31,6227766016838 1,5 7500 5,5 8,66762 85,13
15 10 1 3000 5,5 8,66762 91,87
16 10 1 12000 5,5 8,66762 90,72
17 10 1 7500 1 8,66762 91,95
18 10 1 7500 10 8,66762 88,9
19 10 1 7500 5,5 6,11832 92,37
Tablet hardness - 3 levels
18.04.2017
# of data points: 161 # of rows: 23 Page: 1/1


plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Experimental design & results
NumOrder
APIParticleSizeD90
ApiPSDLog10
MagStearateSSA
LubricationTime
TabletHardness
TabletDissolution
9 31,6227766016838 1,5 12000 1 11,21692 85,47
10 3,16227766016838 0,5 3000 10 11,21692 95,81
11 31,6227766016838 1,5 3000 10 11,21692 84,38
12 31,6227766016838 1,5 12000 10 11,21692 81
13 3,16227766016838 0,5 7500 5,5 8,66762 96,85
14 31,6227766016838 1,5 7500 5,5 8,66762 85,13
15 10 1 3000 5,5 8,66762 91,87
16 10 1 12000 5,5 8,66762 90,72
17 10 1 7500 1 8,66762 91,95
18 10 1 7500 10 8,66762 88,9
19 10 1 7500 5,5 6,11832 92,37
Results
18.04.2017
# of data points: 161 # of rows: 23 Page: 1/1

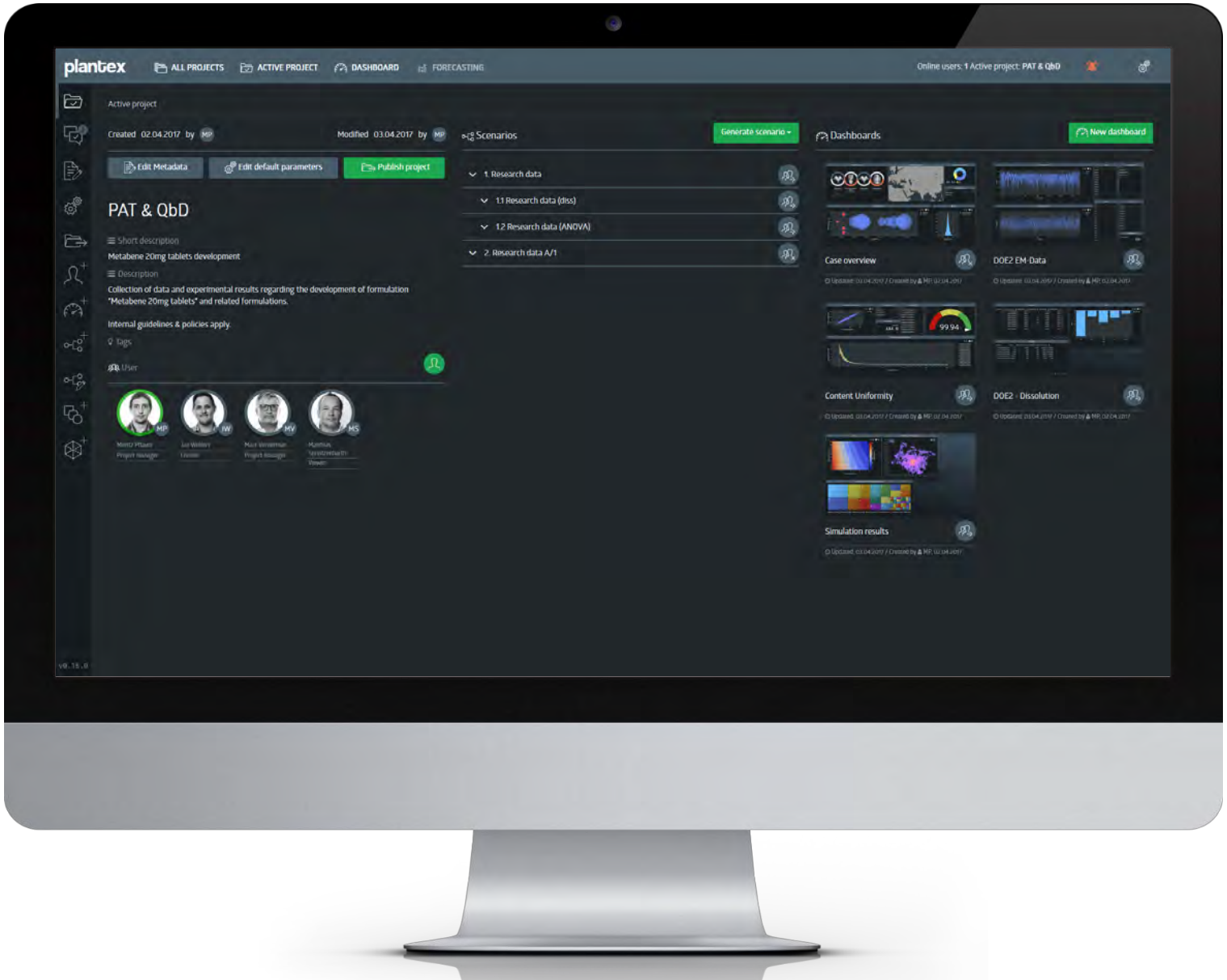

ProcessStart & ProcessEnd per Order
Tuesday, 2014-08-05
Wednesday, 2014-08-06
10 11 12 13 14 15 16 17 18 19 20 21 22 23 0 1 2 3 4 5 6 7
A
B
C
D
E
F
G
H
I
J
Total duration
Compression
18.04.2017
v0.16.0

ANOVA

Next, we want to find out, which factors affect the outcome.

To do this, we can run a **analysis of variance (ANOVA)** on the experimental results.

To do so, we must create a new scenario using a *simulation method.*



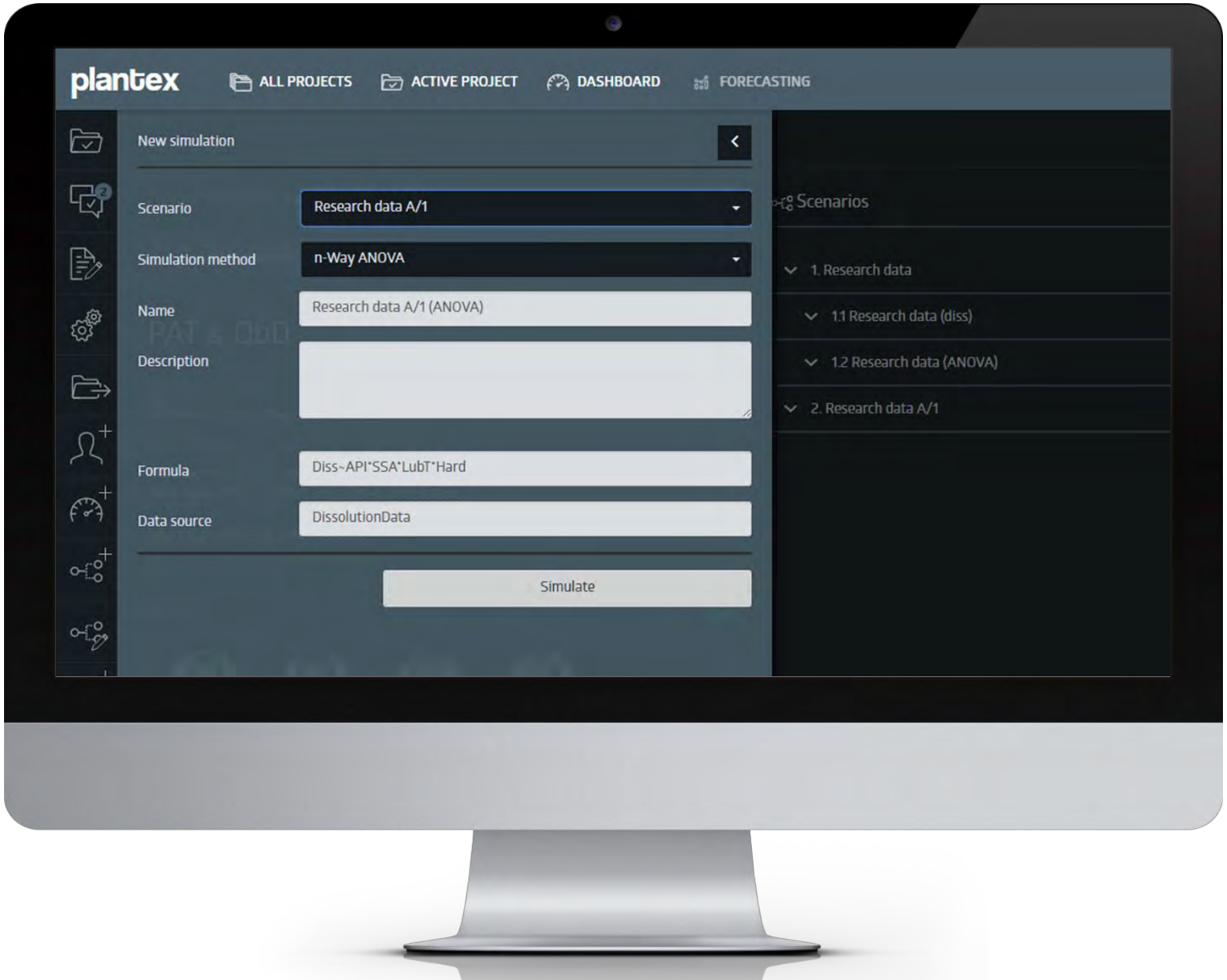
SPREITZENBARTH CONSULTANTS

ANOVA

The base scenario containing the experimental data is chosen, the ANOVA simulation method is selected from the available methods.

The formula means:

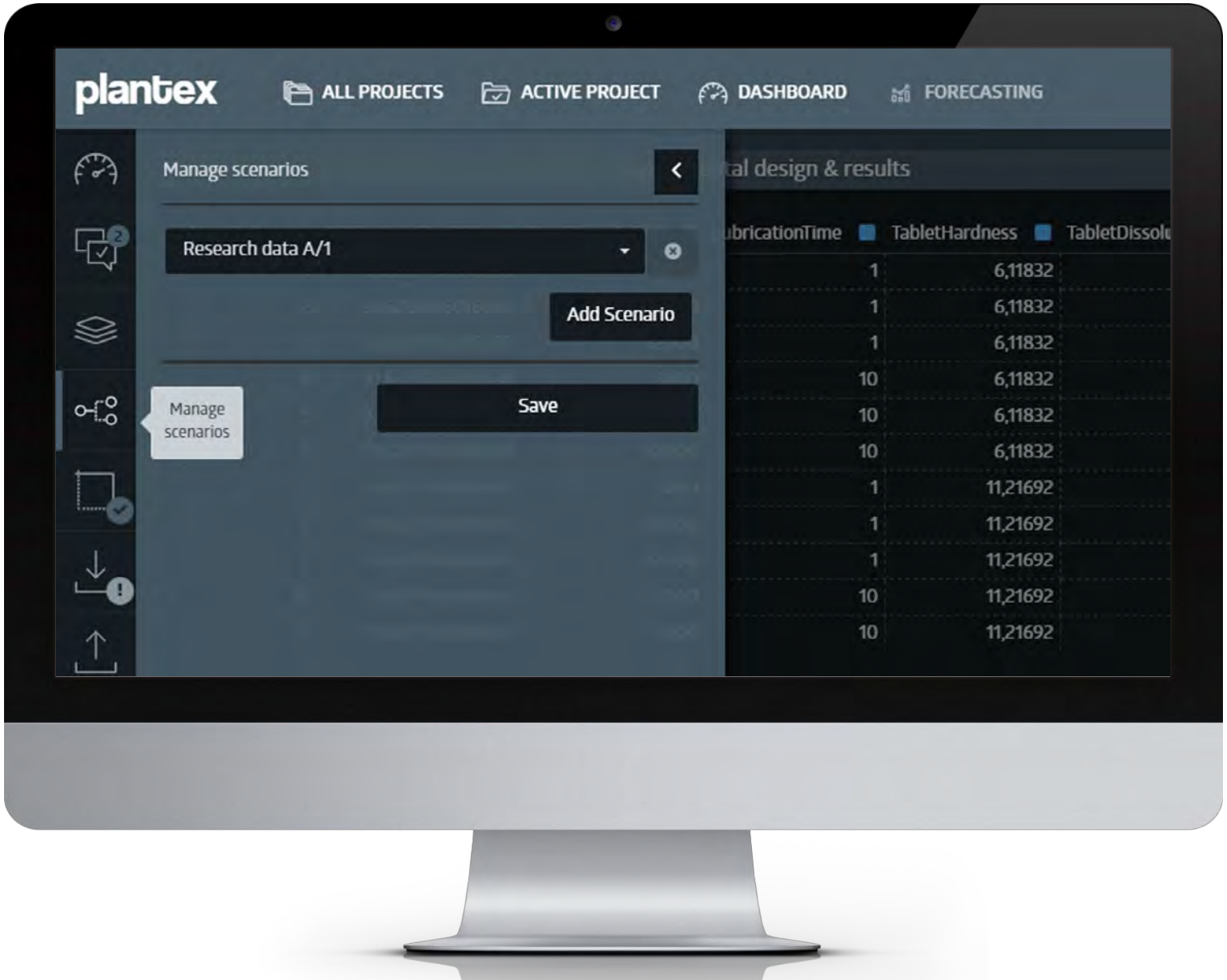
“Look at how **API** (particle size), **SSA** (magnesium stearate surface area), **LubT** (lubrication time) and **Hard** (tablet hardness) affect **Diss** (tablet dissolution)



SPREITZENBARTH CONSULTANTS

ANOVA

After the simulation finished and the new scenario is available, we want to switch it with the old scenario in our existing dashboard.

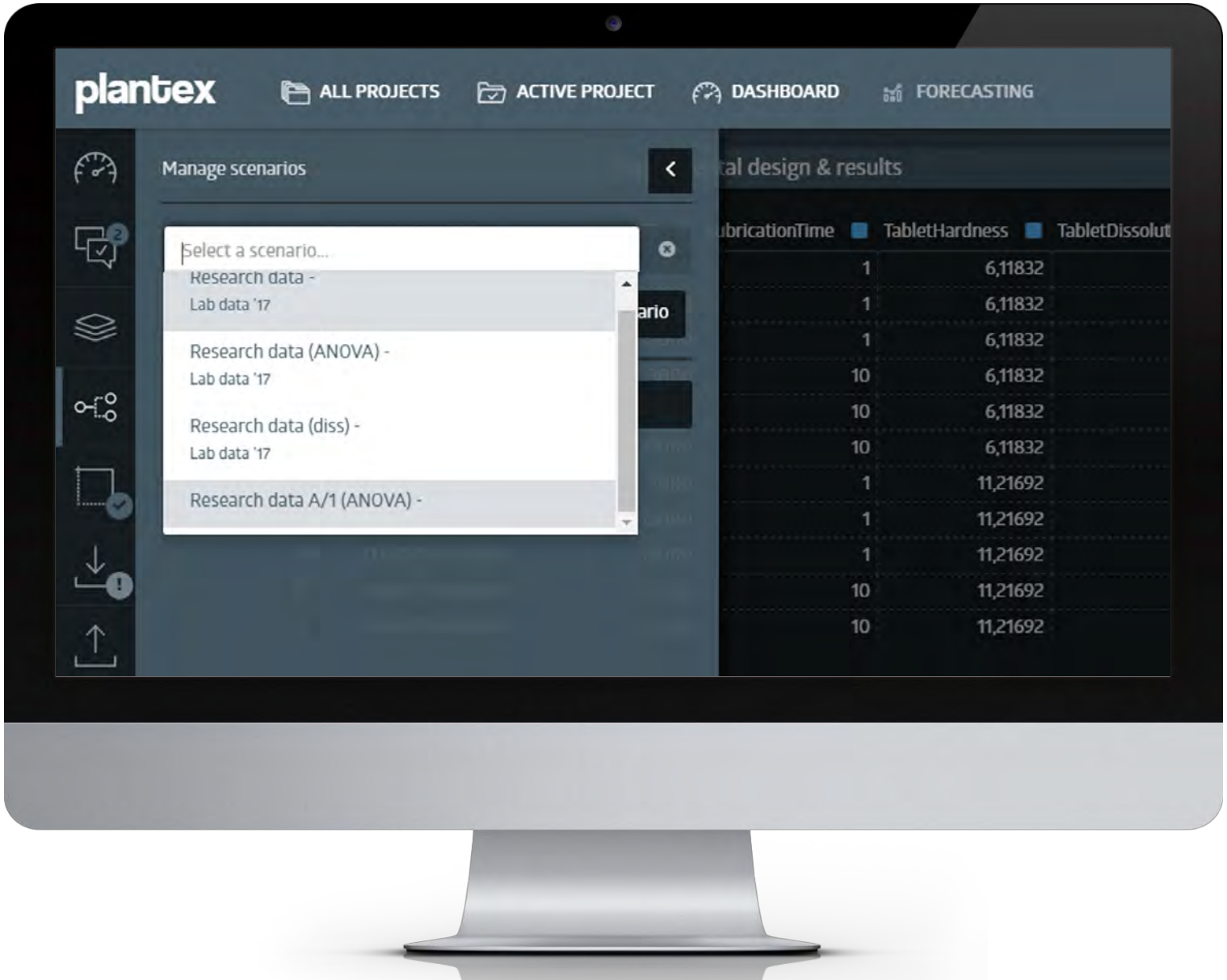


ANOVA

The data a dashboard visualizes depends on the connected scenario(s).

Scenarios are dynamically linked to the dashboards and the user can control which data they want to visualize.

Dashboards in plantex are always just “templates” for the visualization. The data context (scenarios) backing them can change and it will automatically update.

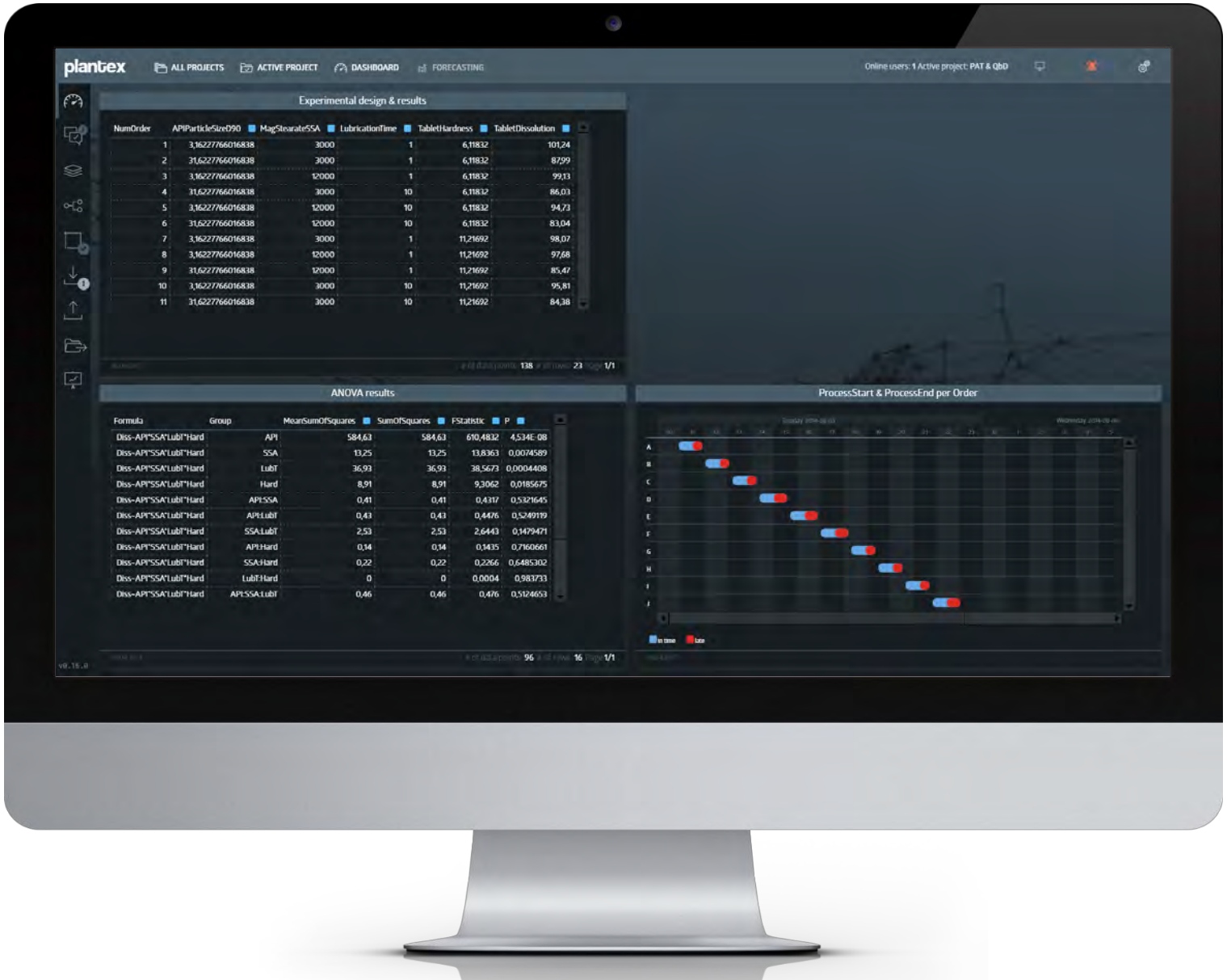


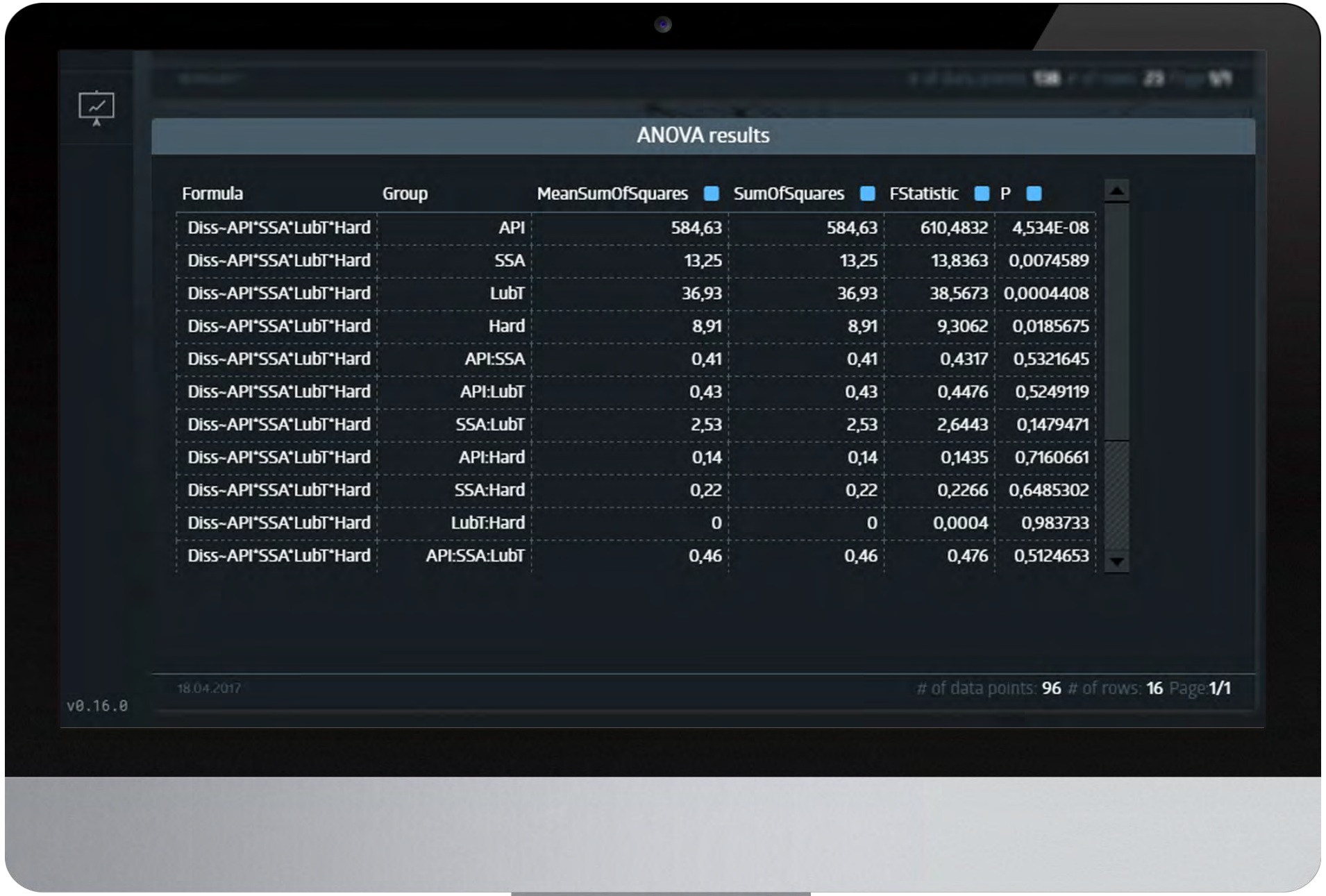
SPREITZENBARTH CONSULTANTS

Results

With the new scenario in the dashboard, we can take a look at the results in tabular form.

The next slide will zoom in on the table showing the raw results.




ANOVA results
Formula
Group
MeanSumOfSquares
SumOfSquares
FStatistic
P
Diss~API*SSA*LubT*Hard API 584,63 584,63 610,4832 4,534E-08
Diss~API*SSA*LubT*Hard SSA 13,25 13,25 13,8363 0,0074589
Diss~API*SSA*LubT*Hard LubT 36,93 36,93 38,5673 0,0004408
Diss~API*SSA*LubT*Hard Hard 8,91 8,91 9,3062 0,0185675
Diss~API*SSA*LubT*Hard API:SSA 0,41 0,41 0,4317 0,5321645
Diss~API*SSA*LubT*Hard API:LubT 0,43 0,43 0,4476 0,5249119
Diss~API*SSA*LubT*Hard SSA:LubT 2,53 2,53 2,6443 0,1479471
Diss~API*SSA*LubT*Hard API:Hard 0,14 0,14 0,1435 0,7160661
Diss~API*SSA*LubT*Hard SSA:Hard 0,22 0,22 0,2266 0,6485302
Diss~API*SSA*LubT*Hard LubT:Hard 0 0 0,0004 0,983733
Diss~API*SSA*LubT*Hard API:SSA:LubT 0,46 0,46 0,476 0,5124653
18.04.2017
# of data points: 96 # of rows: 16 Page: 1/1
v0.16.0

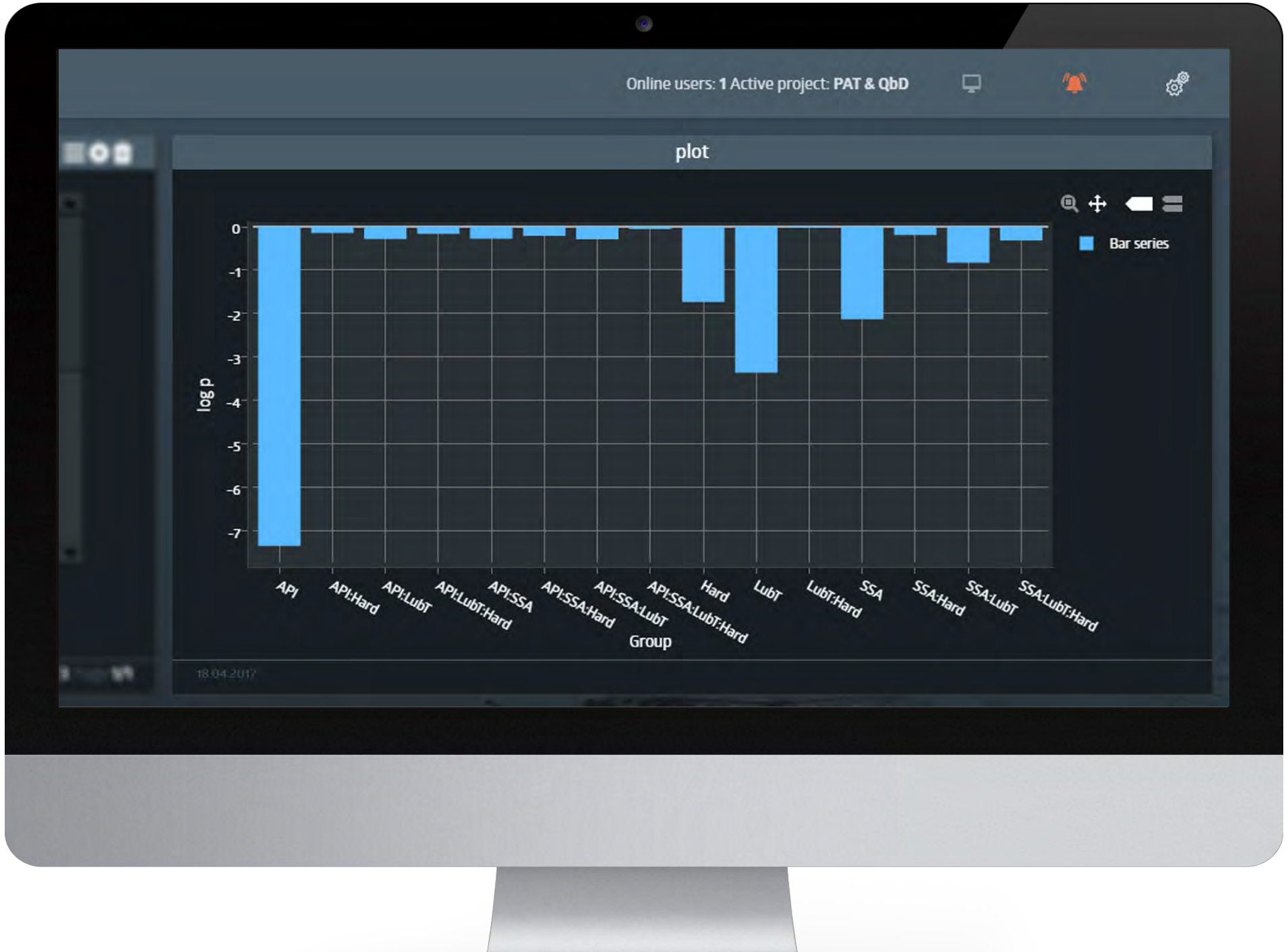
SPREITZENBARTH CONSULTANTS

Visualization

A table is a good tool for a deep dive into the data, but for now we need a straightforward visual representation of which factors are significant.

The new chart on the upper right show the logarithm of the p-value.

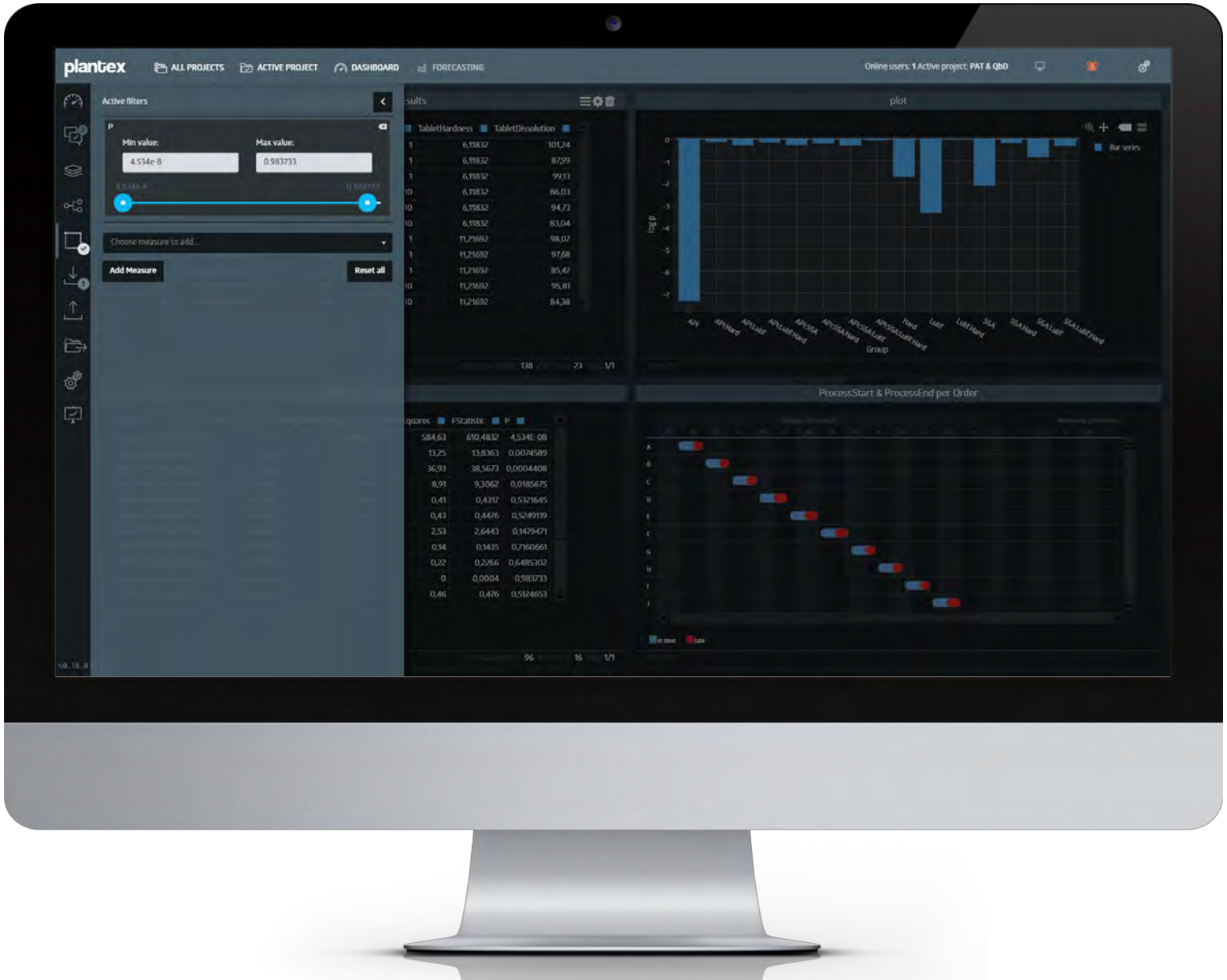
A large bar indicates a low p-value which means the factor is **more significant**.


Online users: 1 Active project: PAT & QbD
plot
Bar series
log p
0
-1
-2
-3
-4
-5
-6
-7
API
API:Hard
API:LubT
API:LubT:Hard
API:SSA
API:SSA:Hard
API:SSA:LubT
API:SSA:LubT:Hard
Hard
LubT
LubT:Hard
SSA
SSA:Hard
SSA:LubT
SSA:LubT:Hard
Group
18.04.2017

SPREITZENBARTH CONSULTANTS

Significance

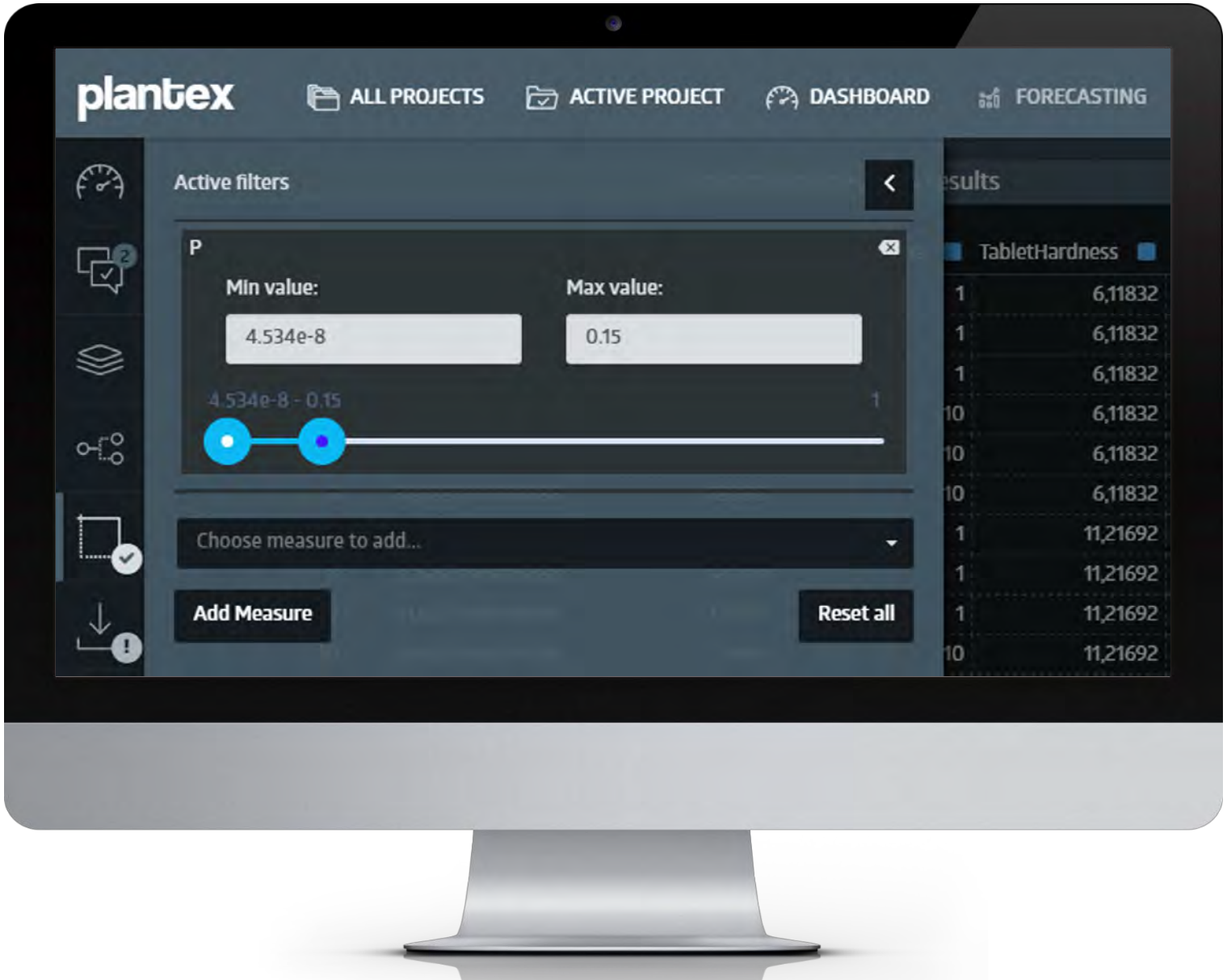
To filter out the values that are not significant, we can use a measure filter on the p-value.

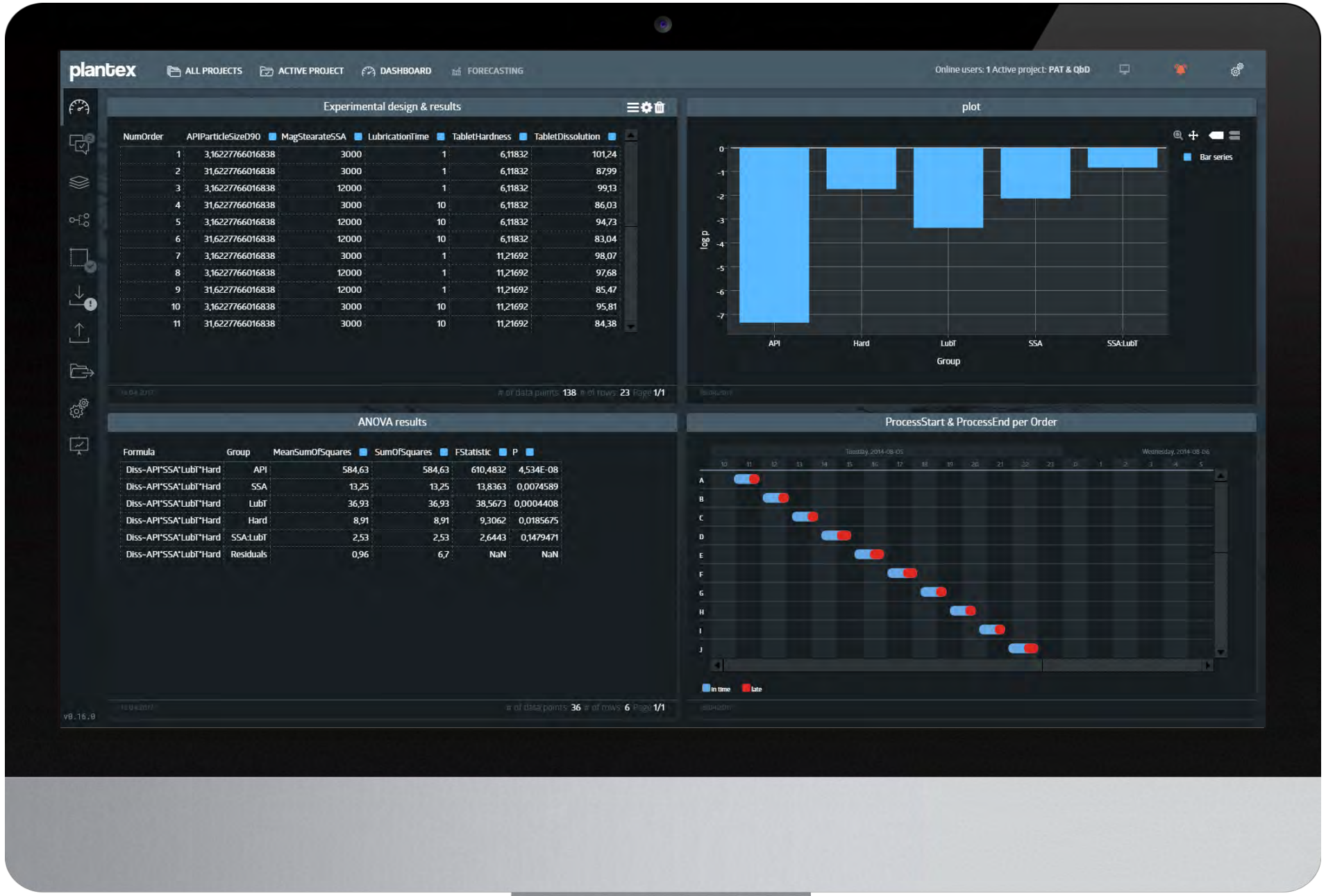


SPREITZENBARTH CONSULTANTS

Significance

Setting the maximum p-value to 0.15 (15%), only the significant factors should remain.



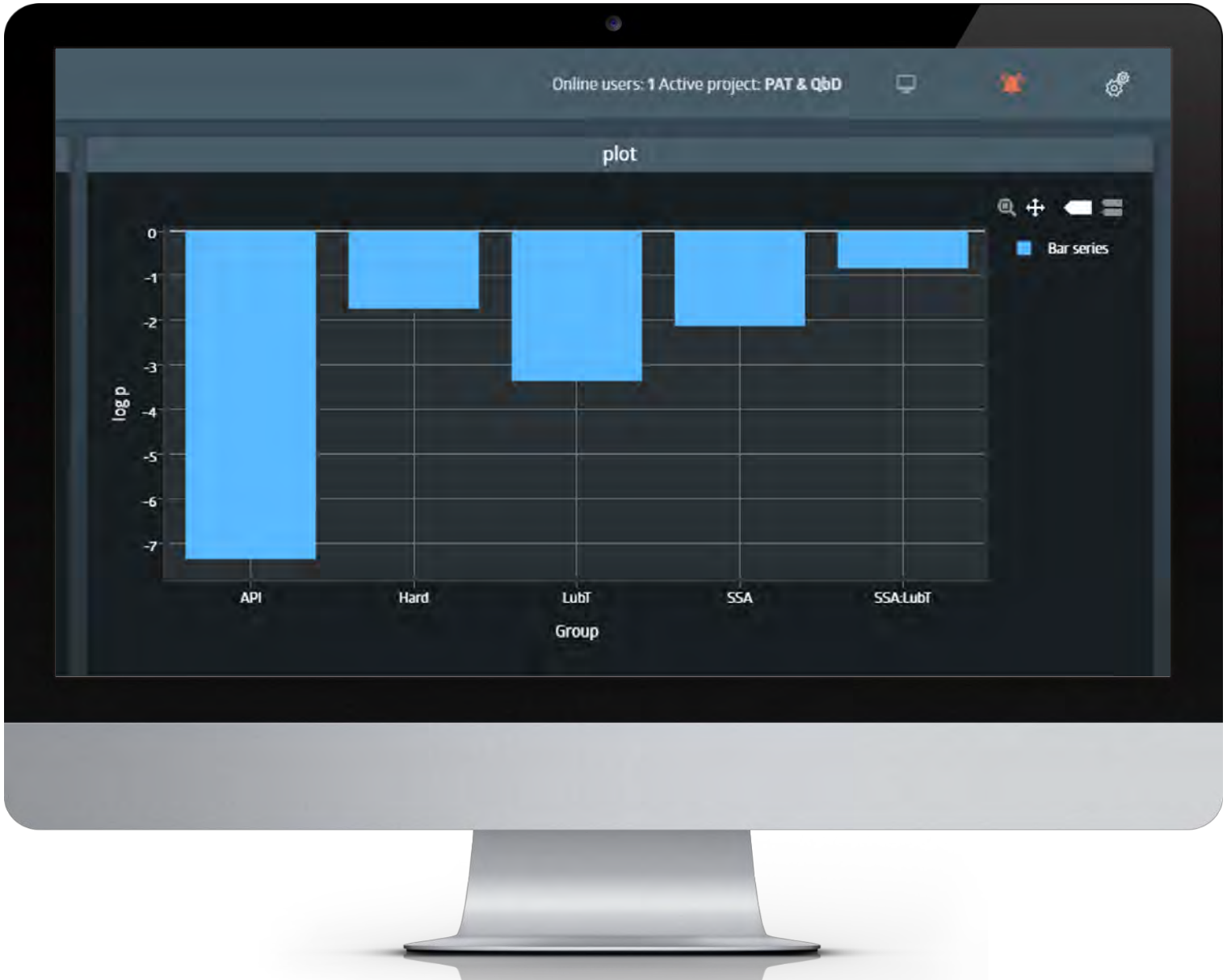

plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Experimental design & results
NumOrder APIParticleSizeD90 MagStearateSSA LubricationTime TabletHardness TabletDissolution
1 3,16227766016838 3000 1 6,11832 101,24
2 31,6227766016838 3000 1 6,11832 87,99
3 3,16227766016838 12000 1 6,11832 99,13
4 31,6227766016838 3000 10 6,11832 86,03
5 3,16227766016838 12000 10 6,11832 94,73
6 31,6227766016838 12000 10 6,11832 83,04
7 3,16227766016838 3000 1 11,21692 98,07
8 3,16227766016838 12000 1 11,21692 97,68
9 31,6227766016838 12000 1 11,21692 85,47
10 3,16227766016838 3000 10 11,21692 95,81
11 31,6227766016838 3000 10 11,21692 84,38
# of data points: 138 # of rows: 23 Page: 1/1
plot
Bar series
log p
0
-1
-2
-3
-4
-5
-6
-7
API
Hard
LubT
SSA
SSA:LubT
Group
ANOVA results
Formula Group MeanSumOfSquares SumOfSquares FStatistic P
Diss~API*SSA*LubT*Hard API 584,63 584,63 610,4832 4,534E-08
Diss~API*SSA*LubT*Hard SSA 13,25 13,25 13,8363 0,0074589
Diss~API*SSA*LubT*Hard LubT 36,93 36,93 38,5673 0,0004408
Diss~API*SSA*LubT*Hard Hard 8,91 8,91 9,3062 0,0185675
Diss~API*SSA*LubT*Hard SSA:LubT 2,53 2,53 2,6443 0,1479471
Diss~API*SSA*LubT*Hard Residuals 0,96 6,7 NaN NaN
# of data points: 36 # of rows: 6 Page: 1/1
ProcessStart & ProcessEnd per Order
Tuesday, 2014-08-05
Wednesday, 2014-08-06
A
B
C
D
E
F
G
H
I
J
in time
late
v8.16.0

SPREITZENBARTH CONSULTANTS

Significance

As we can see, the remaining factors are:

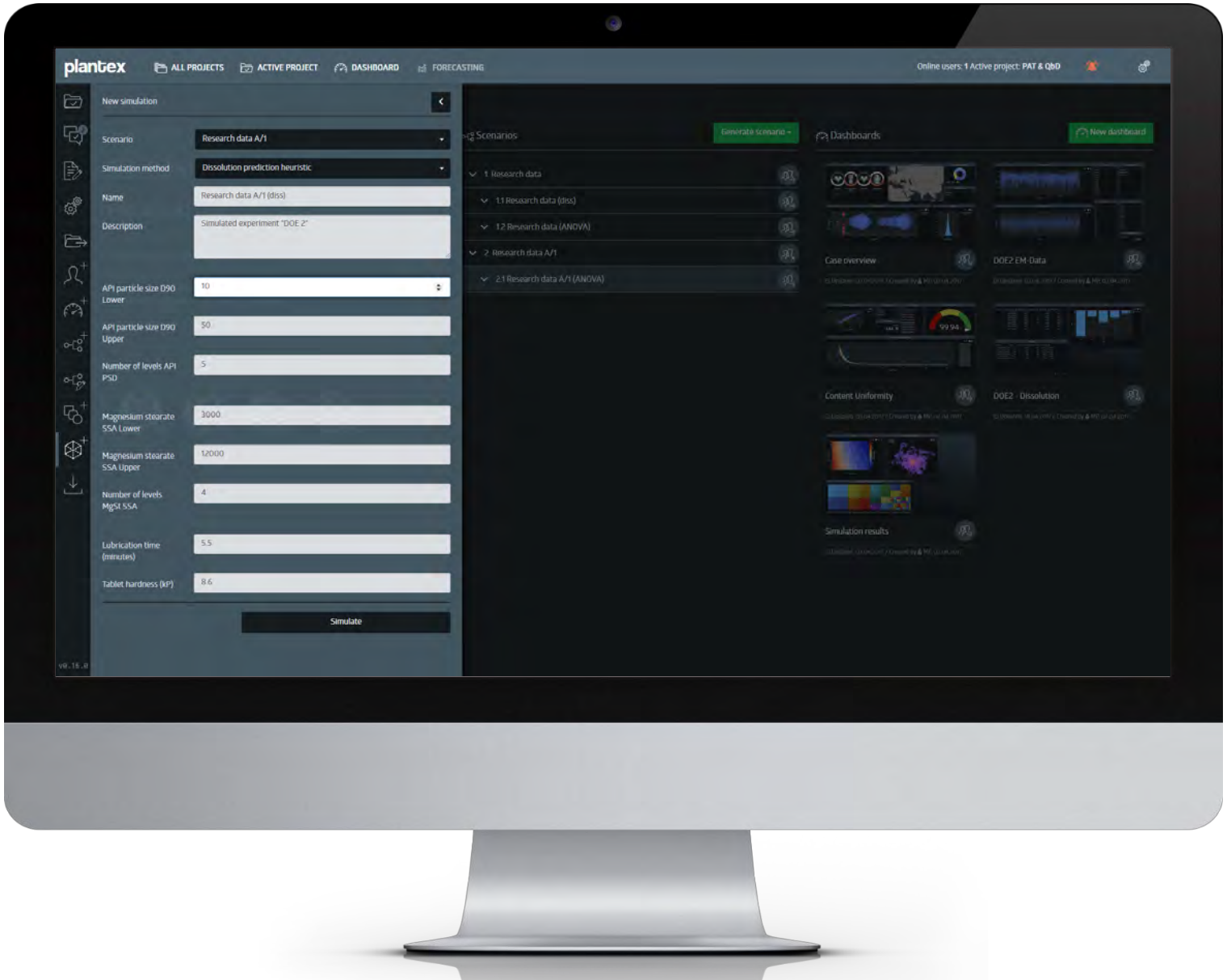
- API particle size
- Lubrication time
- Tablet hardness
- MagSt surface area
- (MagSt surface area) x (lubrication time)



Simulation method

Using the insights we gained from the experiment and the analysis of the results, a simulation method was developed.

It features a mathematical model for **calculating** the dissolution using the significant factors we determined earlier.



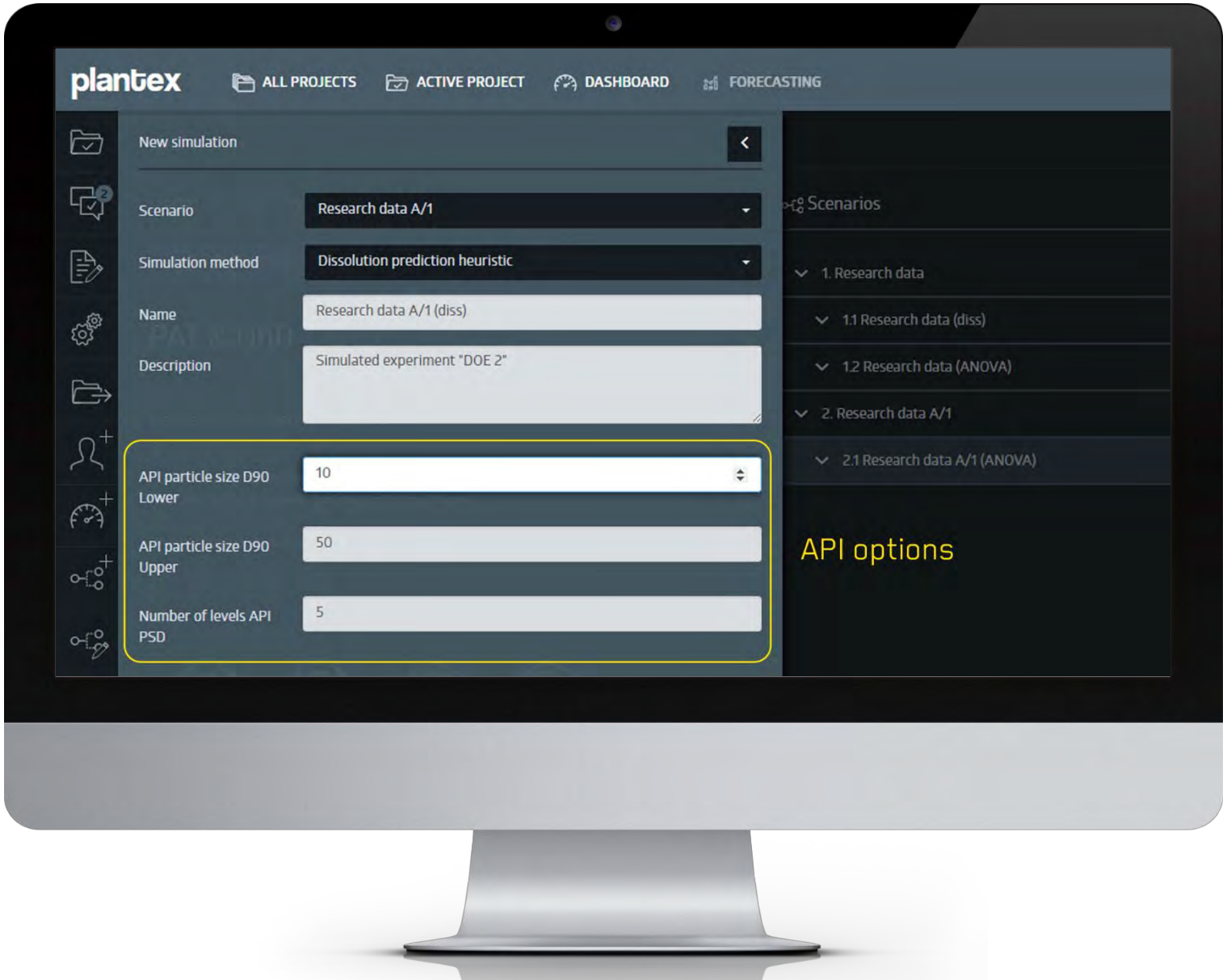
SPREITZENBARTH CONSULTANTS

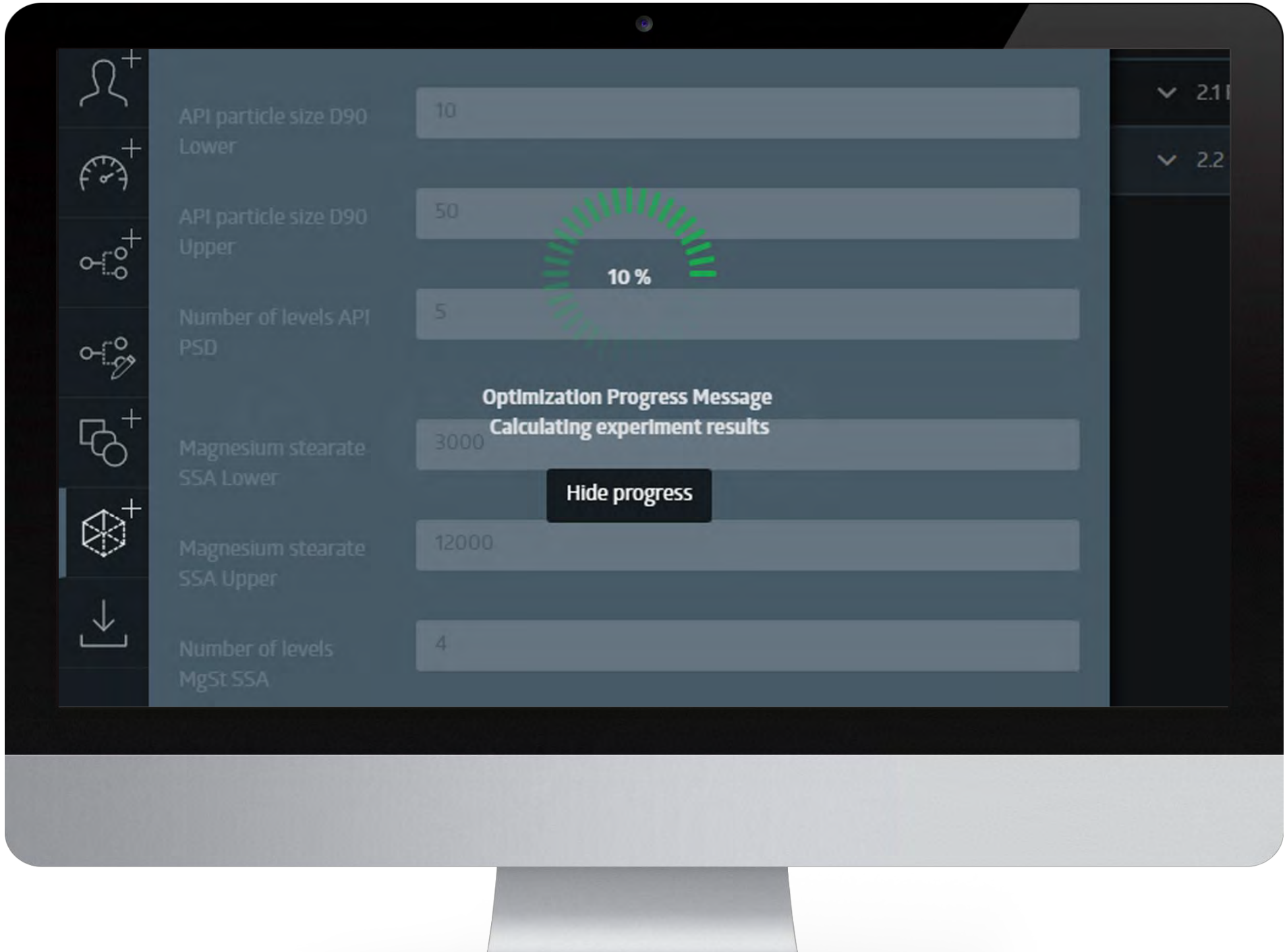
Simulation method

Here we can pick a range of values for which the experiment should be simulated.

We set the lower level of the API particle size to 10 µm and the upper level to 50 µm to see what effect it will have on dissolution.

The result is a new scenario we can compare to the experimental data.

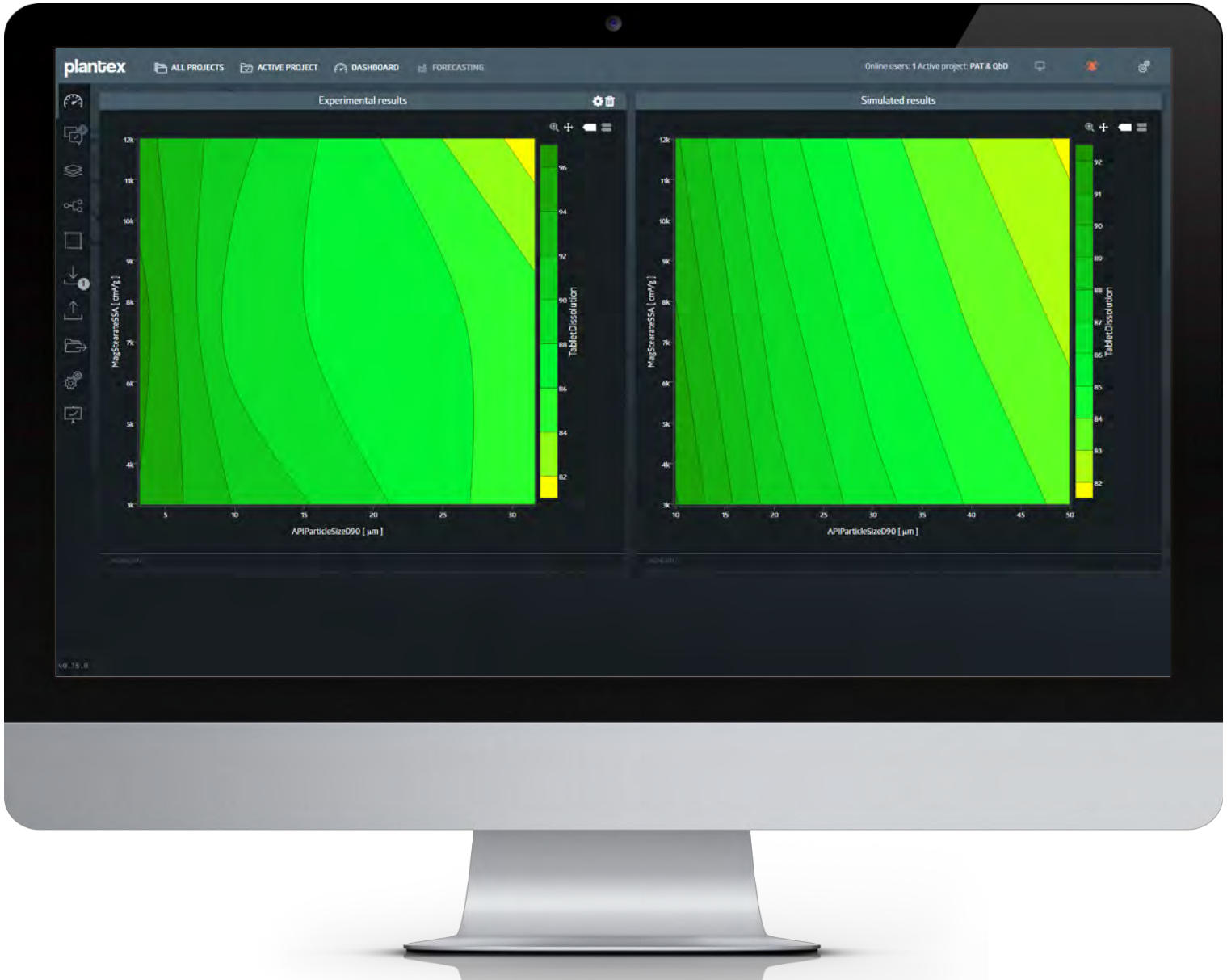


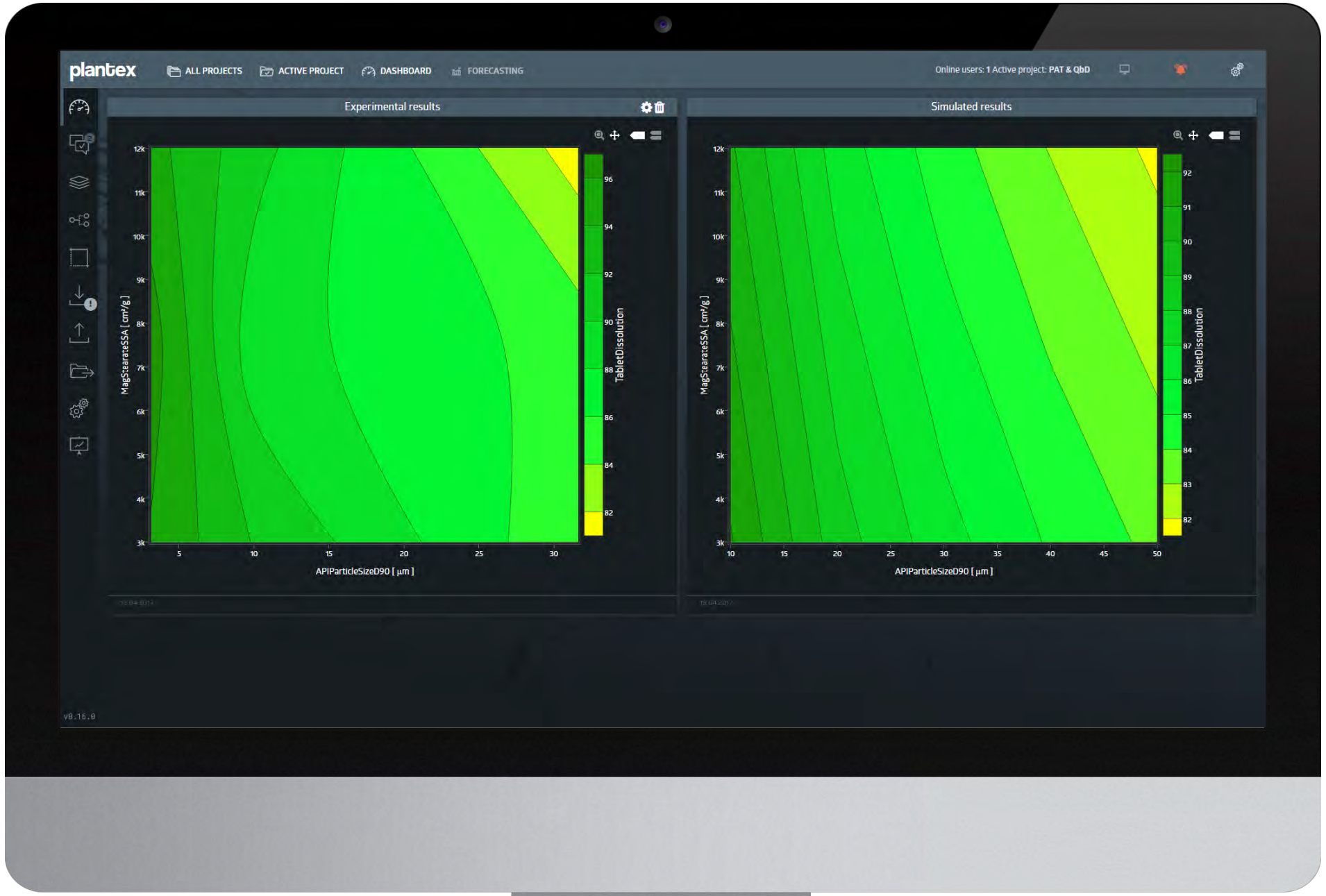

API particle size D90 Lower
10
API particle size D90 Upper
50
10 %
Number of levels API PSD
5
Optimization Progress Message
Calculating experiment results
Magnesium stearate SSA Lower
3000
Hide progress
Magnesium stearate SSA Upper
12000
Number of levels MgSt SSA
4
2.1
2.2

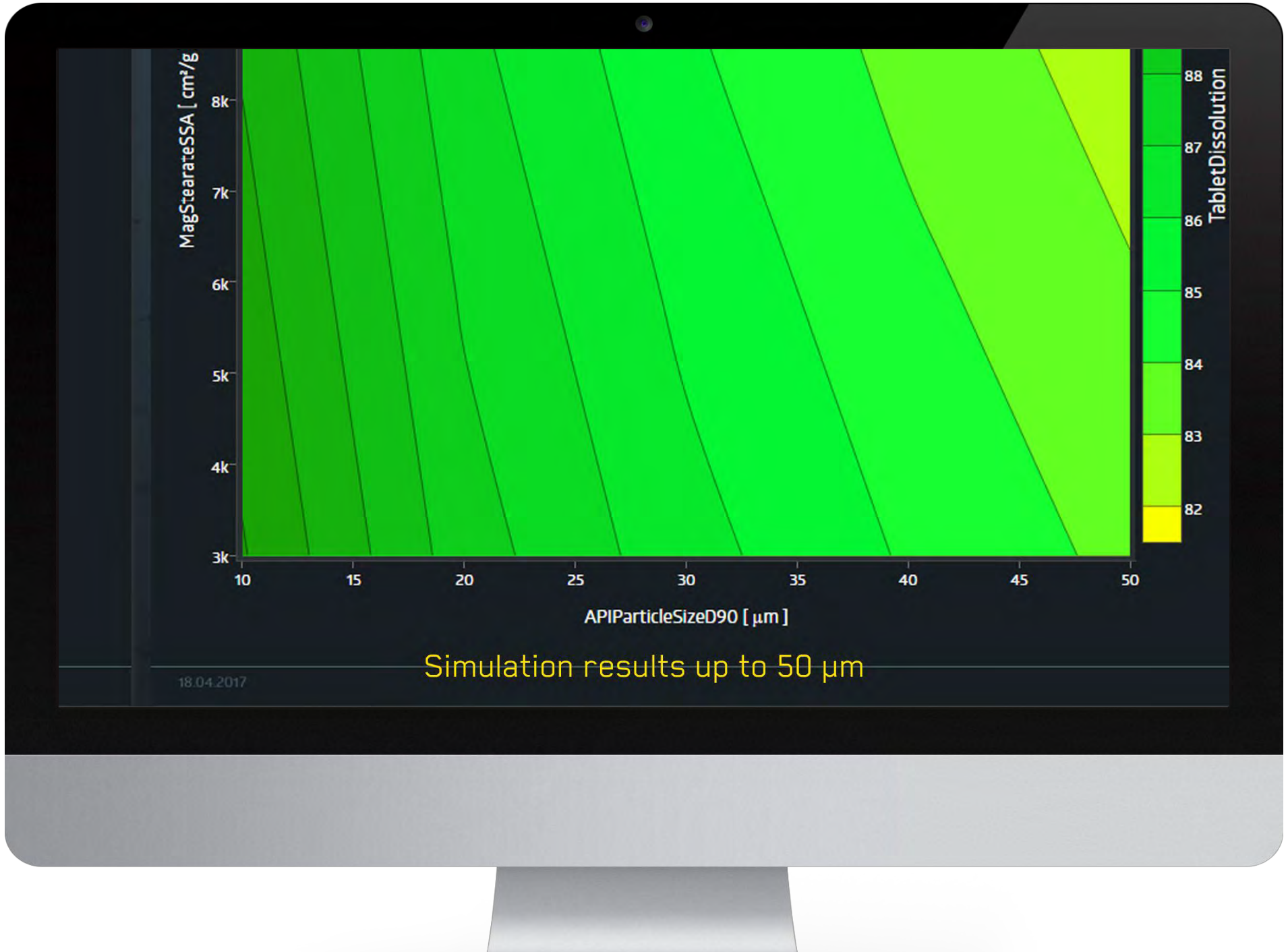
SPREITZENBARTH CONSULTANTS

Simulation results

If we compare the original experimental results to the new scenario containing the simulated results, we can see the extended range of values.




plantex
ALL PROJECTS
ACTIVE PROJECT
DASHBOARD
FORECASTING
Online users: 1 Active project: PAT & QbD
Experimental results
Simulated results
MagS:searaseSSA [cm²/g]
APIParticleSizeD90 [µm]
TabletDissolution
v8.16.0


MagStearateSSA [cm²/g]
8k
7k
6k
5k
4k
3k
10
15
20
25
30
35
40
45
50
APIParticleSizeD90 [µm]
TabletDissolution
88
87
86
85
84
83
82
18.04.2017
Simulation results up to 50 µm

SPREITZENBARTH CONSULTANTS

Conclusion

Using the mathematical model, it is possible to extrapolate the findings of the experiment to ranges that were not tested.

This is only a small fraction of what can (and should) be done in a project like this, but we hope it gave you a glimpse into what plantex can do.

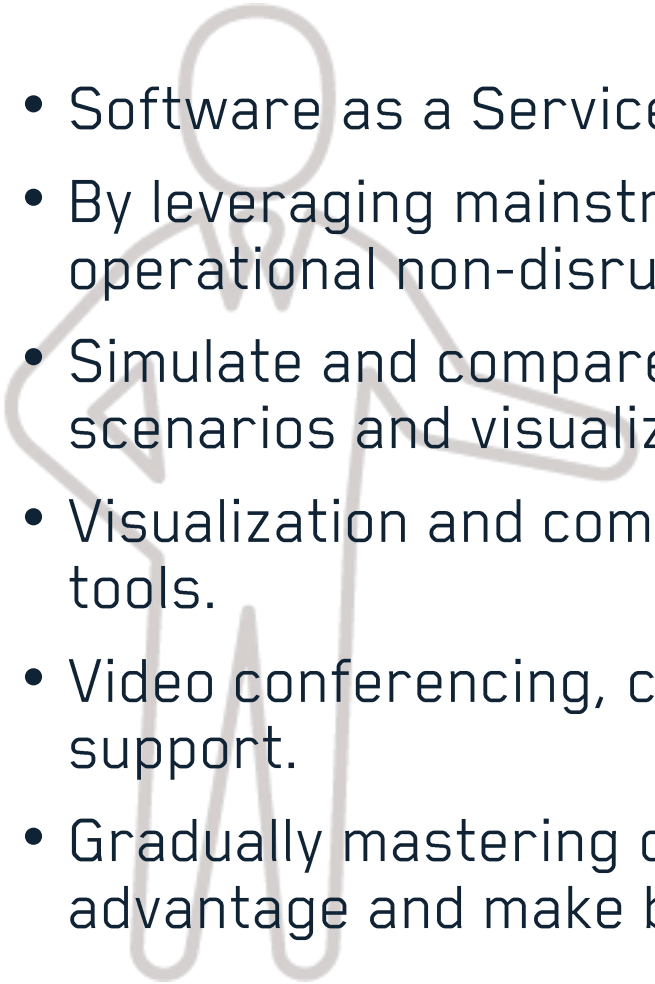
SPREITZENBARTH CONSULTANTS

Discovering Actionable Insights

The complexity of discovering actionable knowledge grows in lock-step with the volume of data!

SPREITZENBARTH CONSULTANTS

plantex



- Software as a Service business application (SaaS)
- By leveraging mainstream technology, we are able to achieve an easy and operational non-disruptive implementation.
- Simulate and compare business situations using self-configurable business scenarios and visualizations.
- Visualization and communication with state-of-the art real-time collaboration tools.
- Video conferencing, chat-, discussion- boards and decision management support.
- Gradually mastering data science and start using your existing data to your advantage and make better well-informed and more objective decisions.

Plantex component

PLANTEX **COLLABORATION LAYER**

(DISCUSSION, CHAT, VIDEO)

OTHER DATA SCIENCE

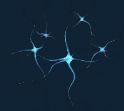
PROJECT TEAMS

BUSINESS SCENARIO

- TRANSFORMATION
- SIMULATION
- OPTIMIZATION

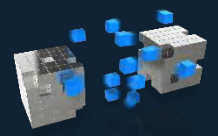
VISUALIZATION

Other Mathematics

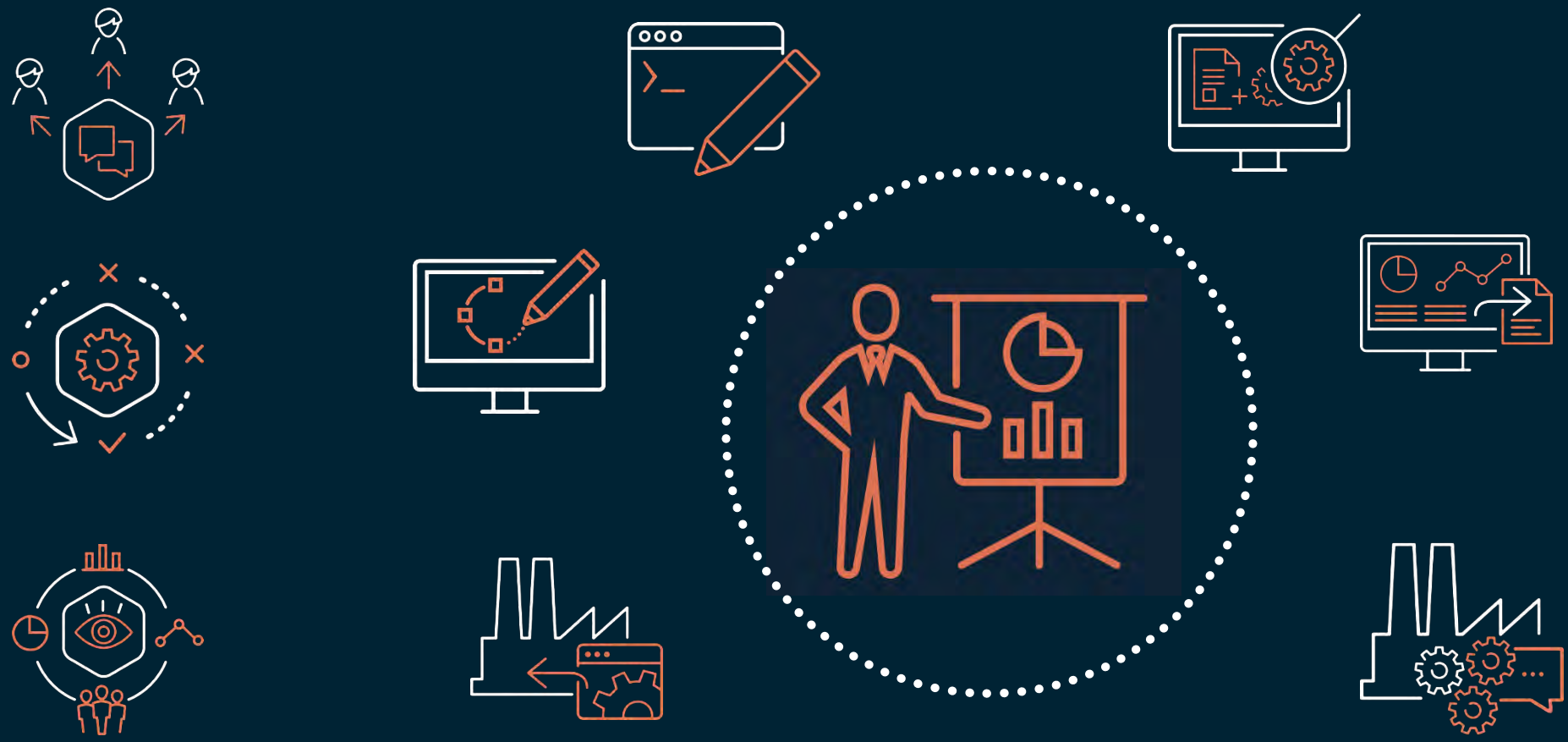


PLANTEX **DATA LAYER**

(Business theme, model, description)



SPREITZENBARTH CONSULTANTS



THANK YOU FOR ATTENDING!