ICH Q14 Enhanced Approach

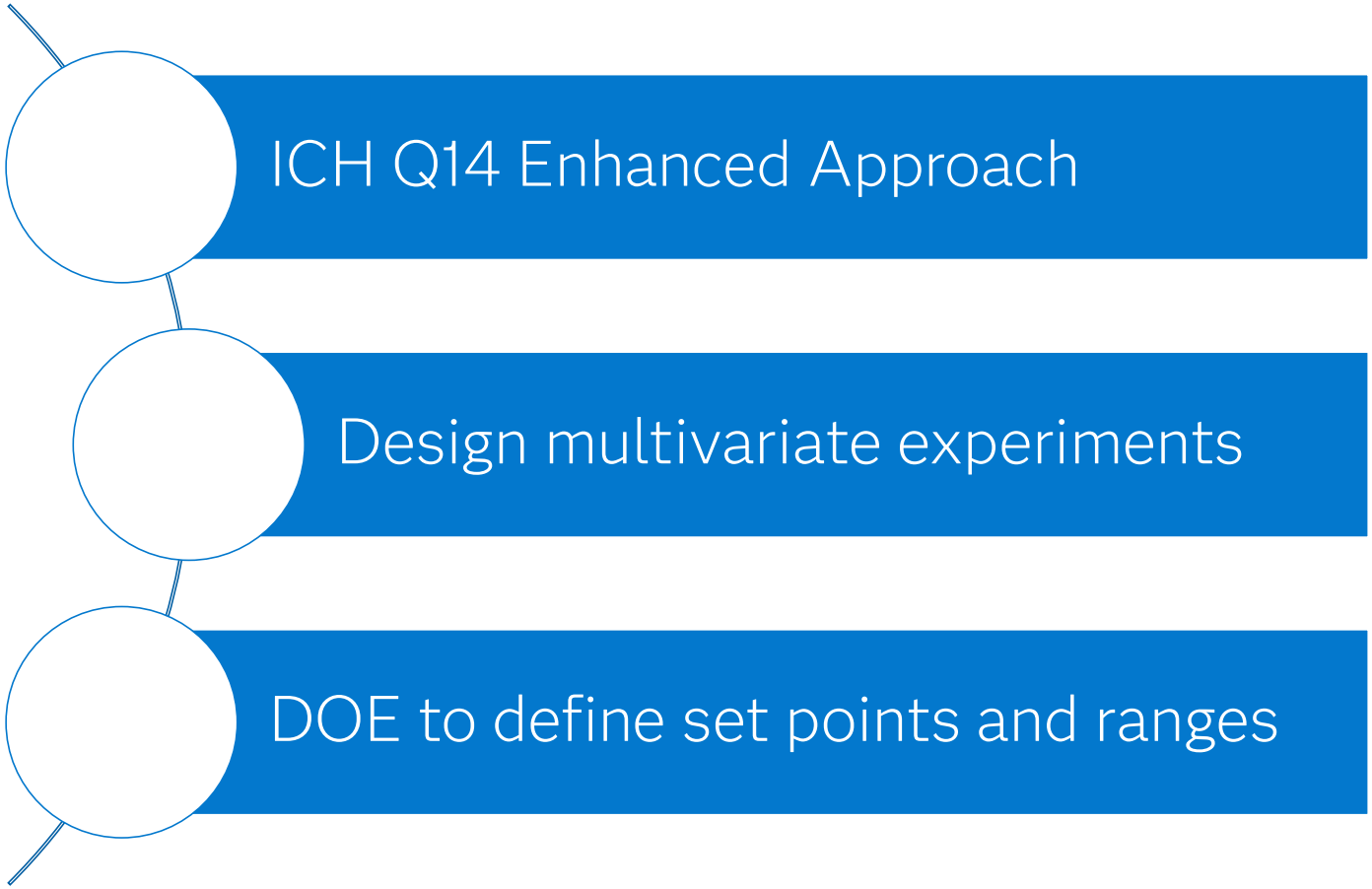
DOE for Analytical Method Development

Brendan Leary, Principal Account Executive, JMP
Byron Wingerd, Principal Systems Engineer, JMP
Andrea Coombs, Principal Systems Engineer, JMP

Andrea Coombs
Principal Systems Engineer

Byron Wingerd
Principal Systems Engineer

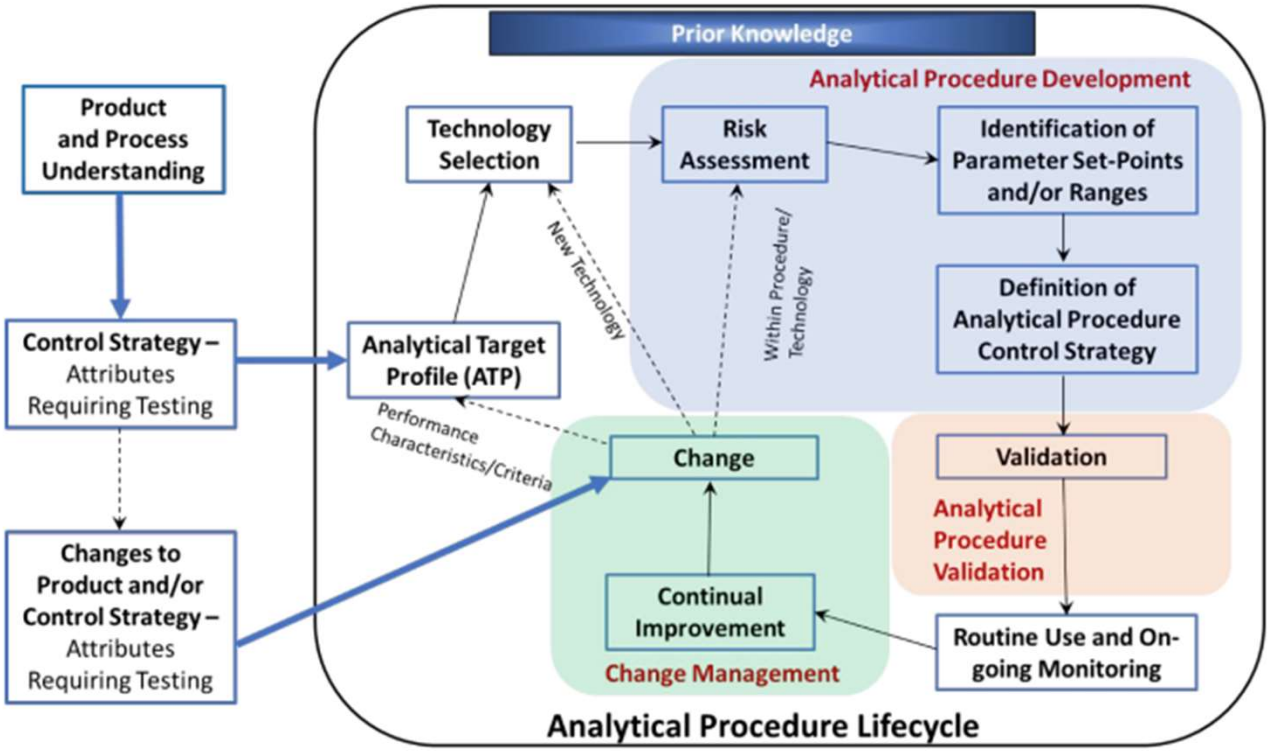
Agenda



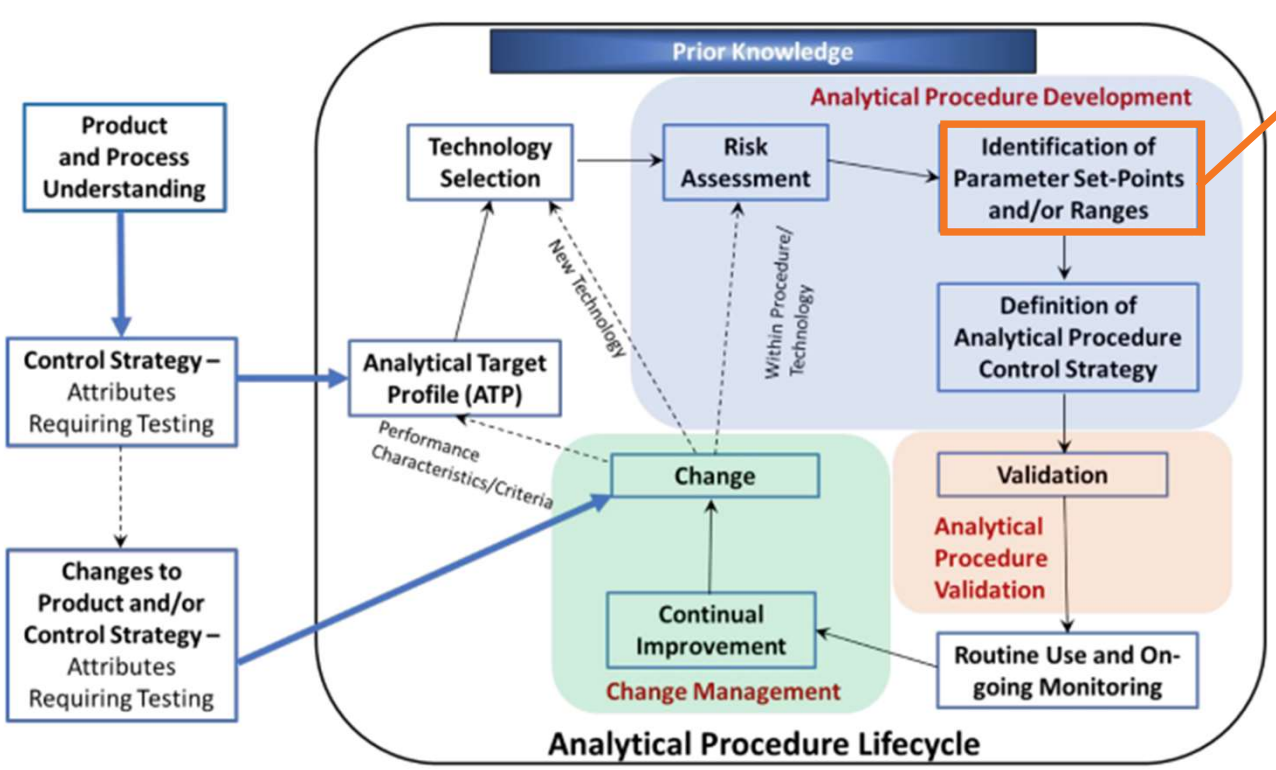
ICH Q14: Analytical Procedure Development

A science and risk-based approach to developing and maintaining the suitability of analytical test methods over their lifecycles.

The Analytical Procedure Life Cycle

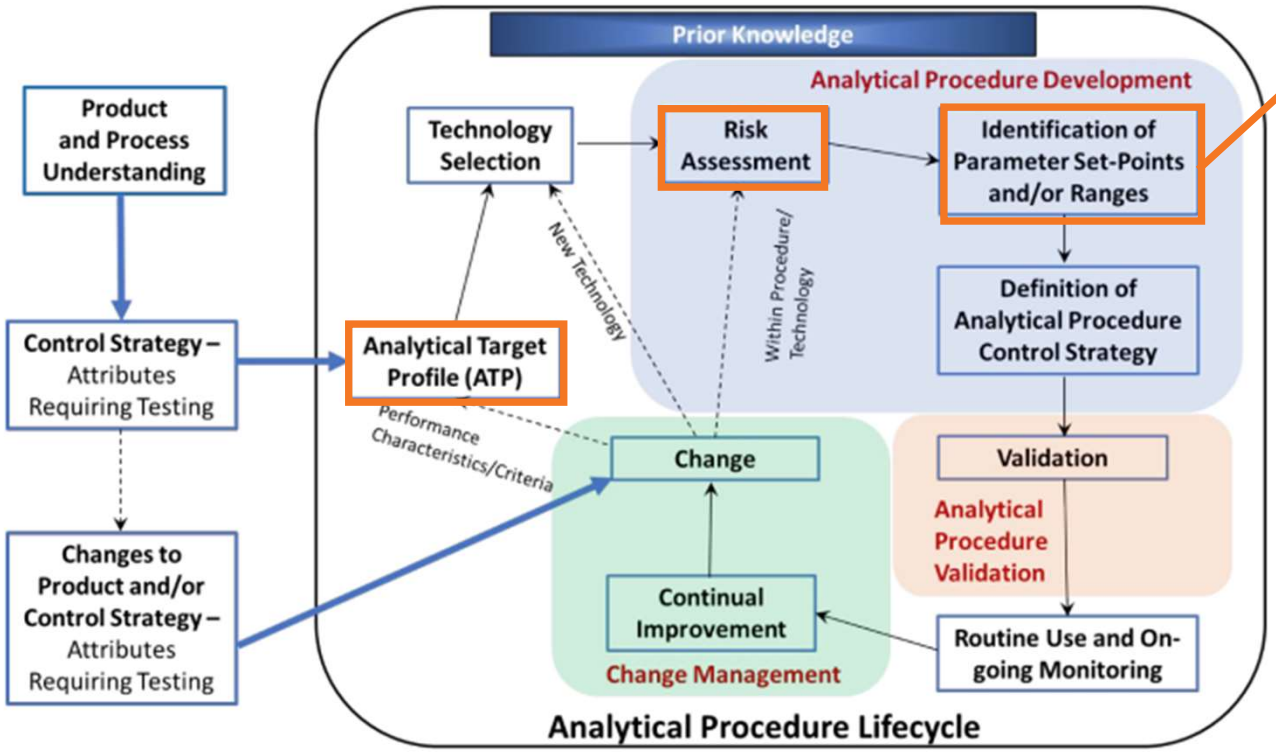


The Analytical Procedure Life Cycle



DOE to identify parameter set-points and ranges

The Analytical Procedure Life Cycle

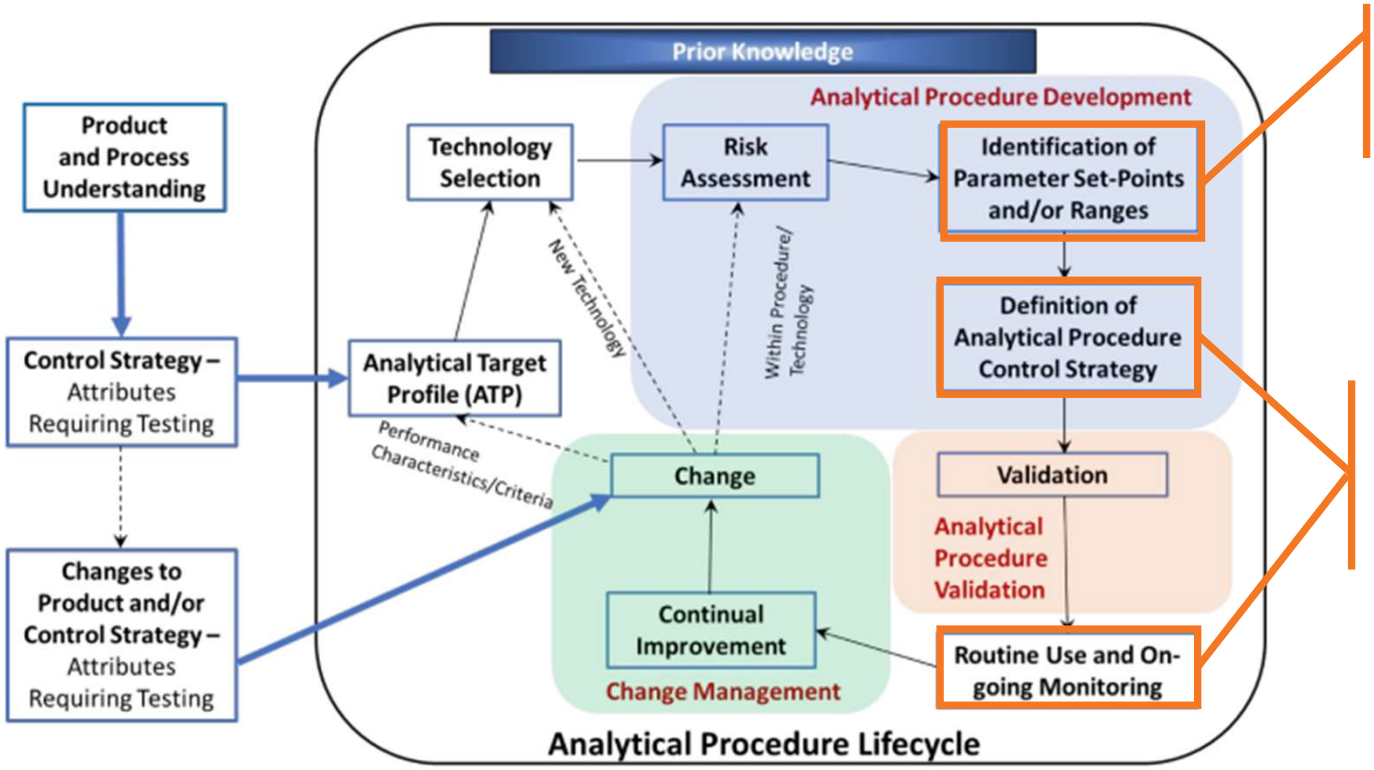


DOE to identify parameter set-points and ranges

Analytical Target Profile
A prospective summary of the performance characteristics describing the intended purpose and the anticipated performance criteria of an analytical measurement

Risk Assessment
Evaluation of prior knowledge to identify the analytical procedure parameters that can impact performance of the procedure

The Analytical Procedure Life Cycle



DOE to identify parameter set-points and ranges

DOE model to support control strategy for routine monitoring

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

Multivariate Experiment (DOE)

Design of experiments (DOE) is a structured set of many tests that systematically changes the way a system works and measure the results to find the relationship between what you changed and what you measured

DOE model is a mathematical equation that describes this relationship.

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

Multivariate Experiment (DOE)

Parameters/ Factors (inputs)

The independent or predictor variables that are a possible source of variation.

Parameters and their ranges are identified in the Risk Assessment.

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

Multivariate Experiment

Parameters/ Factors (inputs)

Responses (outputs)

The dependent or resulting variable that measures the outcome of interest.

Responses defined in the Analytical Target Profile.

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

Multivariate Experiment (DOE)

Parameters/ Factors (inputs)

Responses (outputs)

Interactions

One of many effects that can be included in a DOE model. Others include main effects and higher order terms like quadratic effects.

The relationship of one factor and the response depends on the level of another factor.

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

Multivariate Experiment (DOE)

Parameters/ Factors (inputs)

Responses (outputs)

Interactions

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

Multivariate Experiment (DOE)

Parameters/ Factors (inputs)

Responses (outputs)

Interactions

Set point

The parameter level that optimizes a response.

Determined from a DOE model.

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"… ranges for the relevant parameters and their interactions can be investigated in multivariate experiments … (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose…

… Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

Multivariate Experiment (DOE)

Parameters/ Factors (inputs)

Responses (outputs)

Interactions

Set point

Proven Acceptable Range (PAR)

The range of parameter for which operation within this range, while keeping other parameters constant, will result in an analytical measurement meeting relevant performance criteria.

Defined by the DOE model.

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

Multivariate Experiment (DOE)

Parameters/ Factors (inputs)

Response (outputs)

Interactions

Set point

Proven Acceptable Range (PAR)

Method Operational Design Region (MODR)

A combination of parameter ranges within which the analytical procedure performance criteria are fulfilled and the quality of the measured result is assured.

Defined by the DOE model.

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

Terminology

Multivariate Experiment (DOE)

Parameters/ Factors (inputs)

Response (outputs)

Interactions

Set point

Proven Acceptable Range (PAR)

Method Operational Design Region (MODR)

ICH Q14 Enhanced Approach

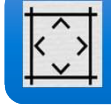
Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments ... (to) provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

The DOE Approach

 Describe	Use responses defined in the Analytical Target Profile Use inputs (factors) defined in the Risk Assessment
 Specify	Define DOE model (main, interaction, quadratic effects)
 Design	Experiment designed using responses, factors, model
 Collect	Run the experiment, collect the results
 Fit	Analyze the results and fit the DOE model
 Predict	Use the DOE model define setpoints, PARs, MODR

DOE Example

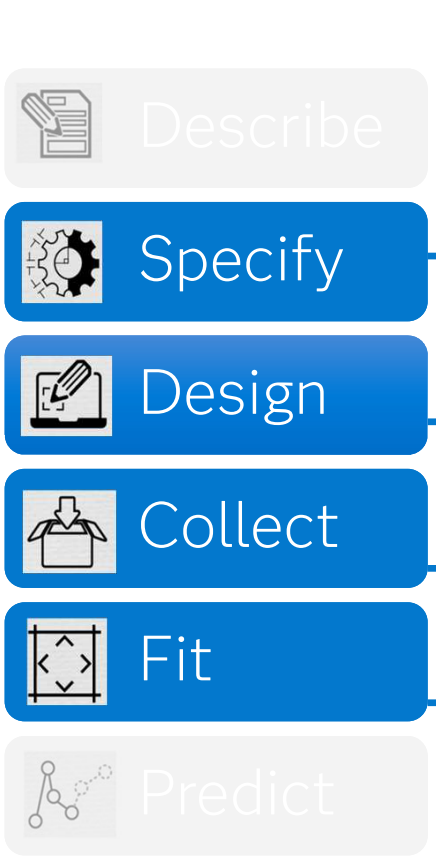
A Basic Example…

- Describe the Responses
  - What do we want to measure?
  - Typically defined in the Analytical Target Profile
  - For example…
    - Signal
    - Background
  - What are the goals for each response?
    - Signal: Lower Specification Limit → Maximize
    - Background: Upper Specification Limit → Minimize
    - If you have Lower and Upper Specification Limit → Target

Response Goals will help to determine optimal setpoints, PARs, and MODR

- Describe Factors
  - What do we want to change?
  - Typically defined by SMEs in Risk Assessment
  - For example…
    - Two Continuous Factors:
      - Time (5, 8)
      - Concentration (15, 45)
    - One Categorical Factor with 3 levels:
      - Vendor (good, fast, cheap)

The DOE Approach



- Specify the Model
  - Main Effects
  - Higher order terms (quadratics)
  - Interactions
- Specify the Number of Runs
- Generate a design using your inputs in previous steps
  - Factors, model, number of runs
- Run the experiment and enter responses
- Analyze the results
- Refine the DOE model

Are you new to DOE?

Using DOE can help you...

- get to market faster
- better understand your analytical procedures
- transfer reliable methods to the QC labs
- quickly respond to invalids and deviations

DOE may be a new approach

- can be costly to learn DOE

Easy DOE

- simplifies and guides you through the DOE process
- reduces the barrier to entry

Demo

The DOE Approach

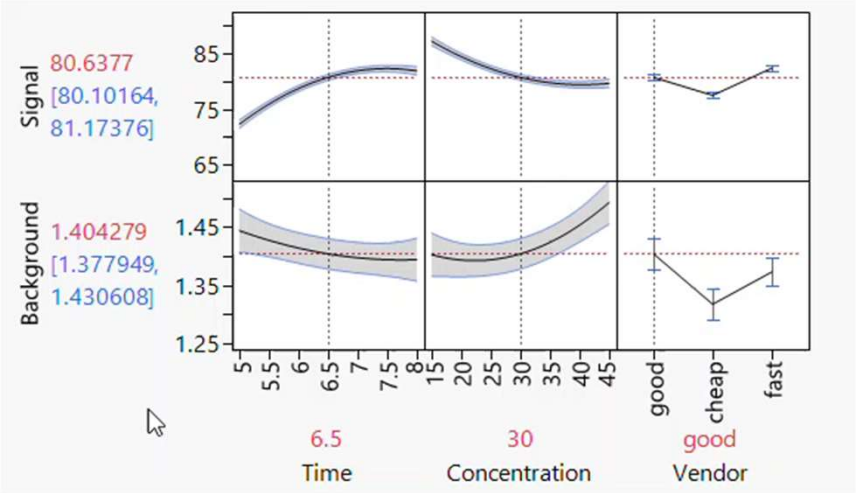
- Use refined DOE model to address the goals
  - Find the Optimal set points and PARs for time and temperature and choose the best vendor that maximizes signal and minimizes background

The DOE Approach

The Prediction Profiler

- Describe
- Specify
- Design
- Collect
- Fit
- **Predict**

- Understand your DOE model



The DOE Approach

The Prediction Profiler

Describe

Specify

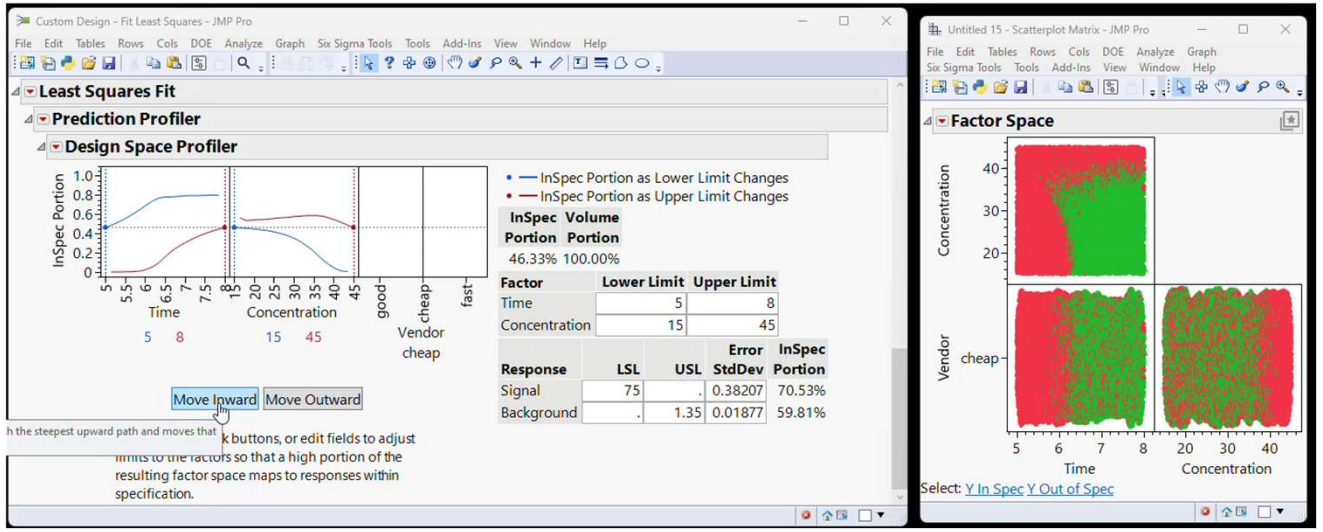
Design

Collect

Fit

Predict

- Define PARs, MODR that maximizes signal and minimized background



The DOE Approach

The Prediction Profiler

Describe

Specify

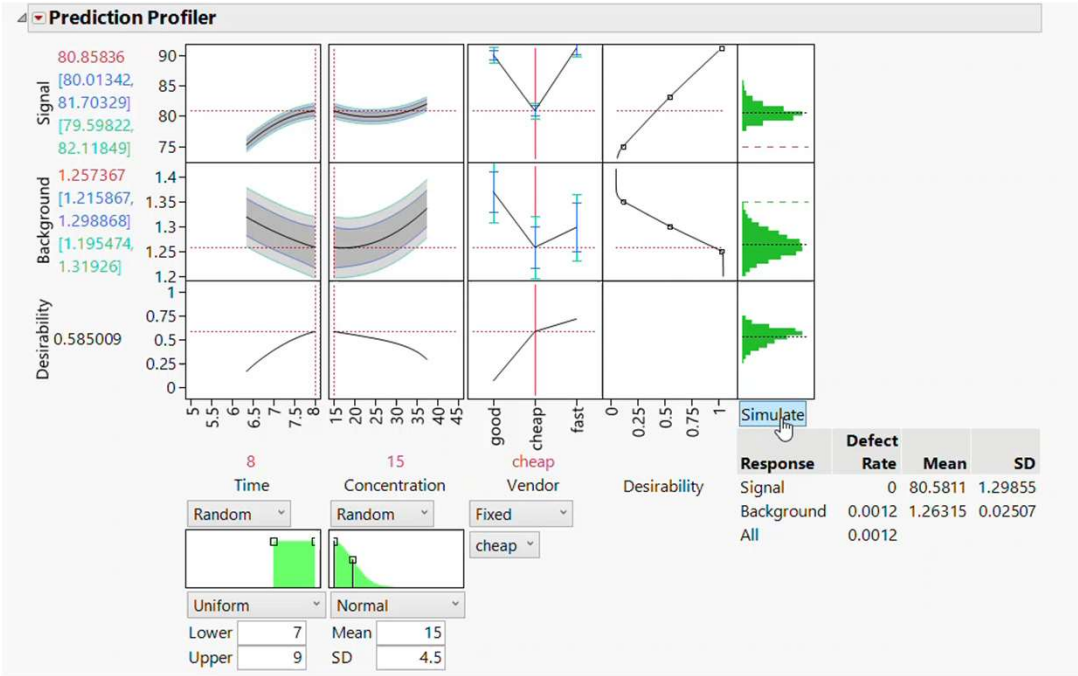
Design

Collect

Fit

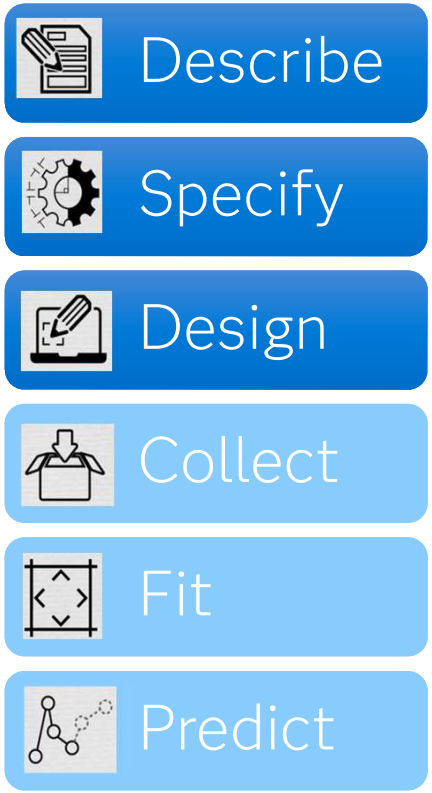
Predict

- Optimize setpoints within PAR



Custom DOE

Construct Designs That Meet Your Needs



- Construct wide variety of designs that are custom built
- Flexibility in the design
  - factors of many types (Continuous, discrete numeric, categorical, blocking, mixture, etc)
  - effects of primary interest (interactions, higher order terms)
  - number of runs

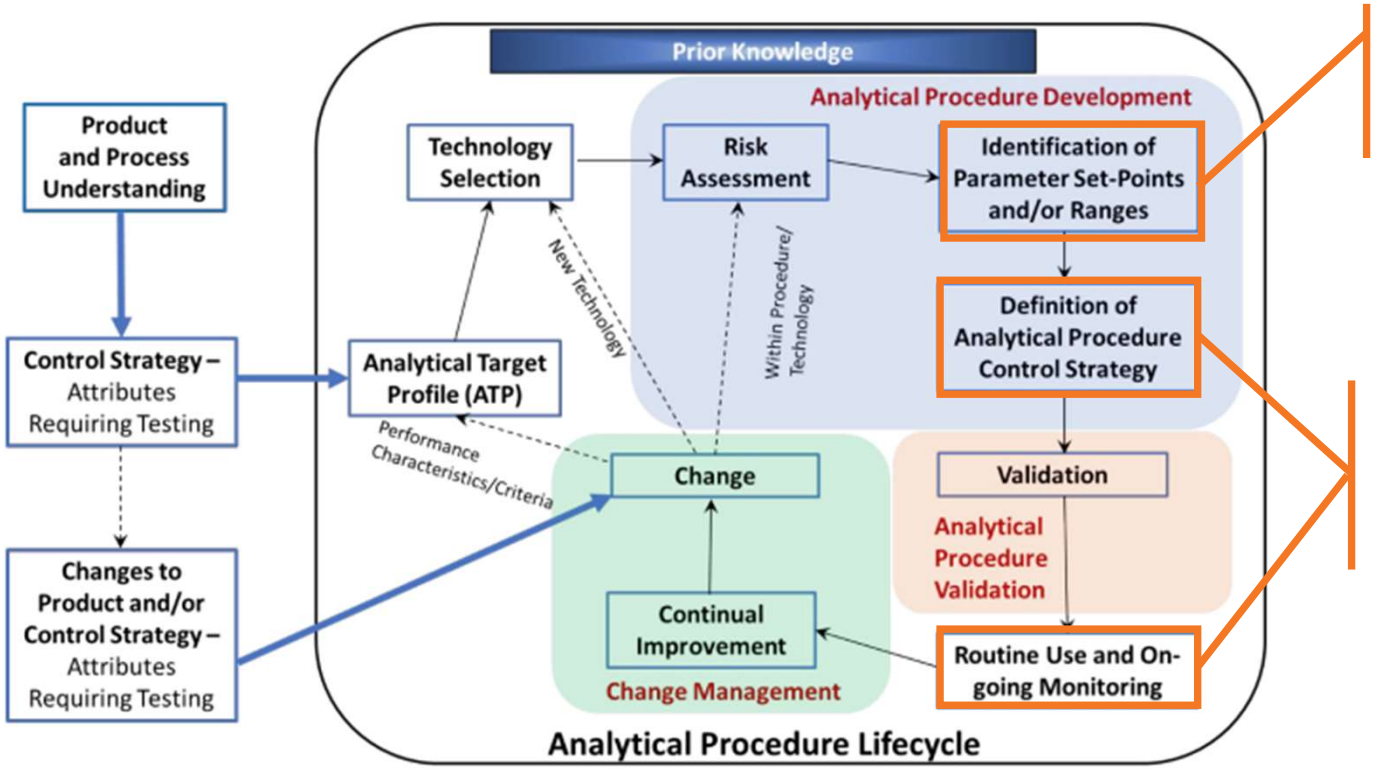
JMP creates the data table

DOE model is included in the data table

Demo

Control Strategy

The Analytical Procedure Life Cycle



DOE to identify parameter set-points and ranges

DOE model to support control strategy for routine monitoring

ICH Q14 Enhanced Approach

Section V. B. (5.2) Analytical Procedure Parameter Ranges

"... ranges for the relevant parameters and their interactions can be investigated in multivariate experiments (DOE)... *(to)* provide an understanding of the relationships between analytical procedure parameters (inputs) and the responses of the analytical procedure (outputs).

Fixed set points may be defined for some parameters. For others, PARs could be defined while still others could be included into a MODR. An MODR consists of combined ranges of two or more analytical procedure parameters within which the analytical procedure is shown to be fit for the intended purpose...

... Moving within an approved PAR or MODR does not require regulatory notification."

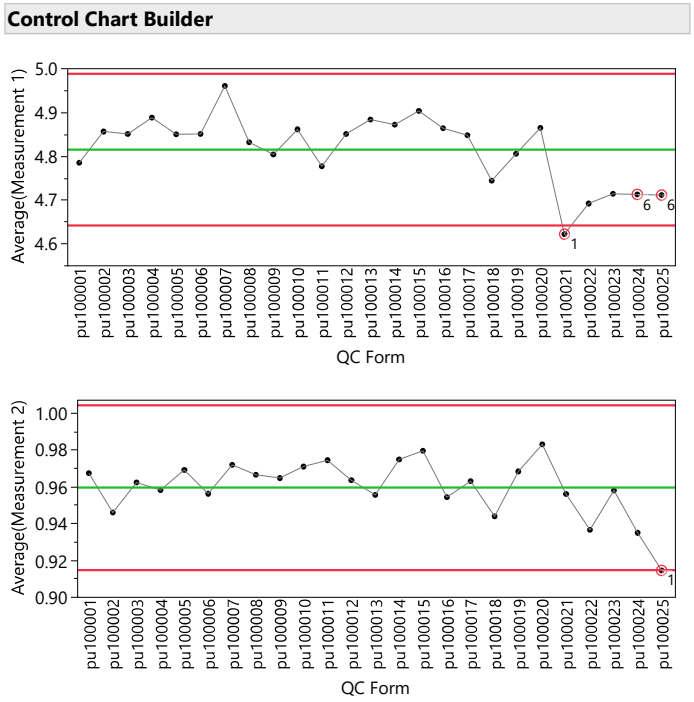
ICH Q14 Enhanced Approach

Section VI. (6) Analytical Procedure Control Strategy

"Ongoing monitoring of selected analytical procedure outputs is recommended to look for any trends, in line with PQS expectations. Review of analytical procedure outputs facilitates the procedure lifecycle management and enables proactive intervention to avoid failures."

Analytical Procedure Control Strategy

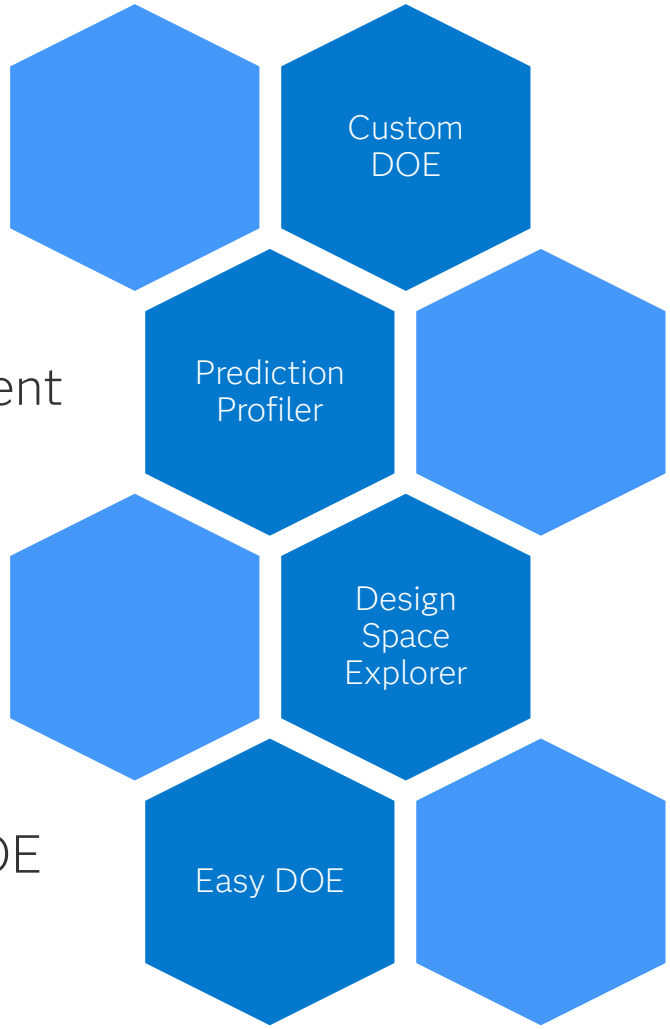
- Routine monitoring to look for trends
- Proactive intervention to avoid failures
- Create an In-Control Action Plan (ICAP) based on DOE Model
- Automated workflow
  - Retrieve data from LIMS
  - Create control charts
  - Alarm if procedure is off target
  - Calculate change within PAR



Summary

Summary

- ICH Q14 enhanced approach
- Design and analyze multivariate experiment (DOE)
  - Define set points, PARs, and MODR
  - Get to market faster
  - Better understanding of your analytical procedure
- Tools to reduce the barrier of entry to DOE



Try JMP for Free

jmp.com/try