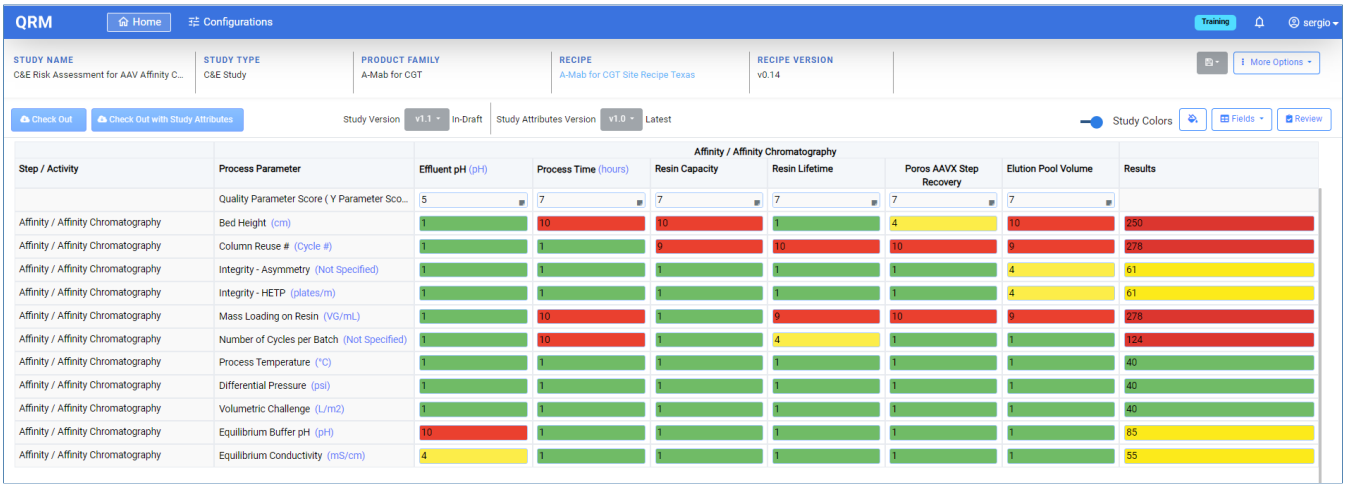
DeltaV™ Process Risk Assessment



		Affinity / Affinity Chromatography						
Step / Activity	Process Parameter	Effluent pH (pH)	Process Time (hours)	Resin Capacity	Resin Lifetime	Poros AAVX Step Recovery	Elution Pool Volume	Results
	Quality Parameter Score (Y Parameter Sco...	5	7	7	7	7	7	
Affinity / Affinity Chromatography	Bed Height (cm)	1	10	10	1	4	10	250
Affinity / Affinity Chromatography	Column Reuse # (Cycle #)	1	1	9	10	10	9	278
Affinity / Affinity Chromatography	Integrity - Asymmetry (Not Specified)	1	1	1	1	1	4	61
Affinity / Affinity Chromatography	Integrity - HETP (plates/m)	1	1	1	1	1	4	61
Affinity / Affinity Chromatography	Mass Loading on Resin (VG/mL)	1	10	1	9	10	9	278
Affinity / Affinity Chromatography	Number of Cycles per Batch (Not Specified)	1	10	1	4	1	1	124
Affinity / Affinity Chromatography	Process Temperature (°C)	1	1	1	1	1	1	40
Affinity / Affinity Chromatography	Differential Pressure (psi)	1	1	1	1	1	1	40
Affinity / Affinity Chromatography	Volumetric Challenge (L/m2)	1	1	1	1	1	1	40
Affinity / Affinity Chromatography	Equilibrium Buffer pH (pH)	10	1	1	1	1	1	85
Affinity / Affinity Chromatography	Equilibrium Conductivity (mS/cm)	4	1	1	1	1	1	55

DeltaV Process Risk Assessment leverages process manufacturing specifications to facilitate risk assessments.

- Easy to manage risk assessments using existing recipe data
- Simple identification of critical process parameters and quality attributes within process specifications
- Risk ranking and filtering functionality
- Multiple quantitative risk studies, such as Cause and Effect (C&E) and Failure Mode Effect Analysis (FMEA)

Introduction

Safety and efficacy of a pharmaceutical product is highly dependent on the understanding of critical quality attributes (CQAs) of the product and the critical process parameters (CPPs) of the manufacturing process.

Different risk assessments are conducted during drug development to evaluate the impact of CPPs on CQAs. Those risk assessments require knowledge of the manufacturing specification, including the process steps and their sequence. Risk assessments are also needed when a product/process is transferred to a different manufacturing site and/or a different scale. Emerson's Process Knowledge Management (PKM™) software suite provides a structured repository and collaboration model for manufacturing specifications that facilitate drug development, risk assessments and technology transfers. PKM suite includes:

- DeltaV Process Specification Management (PSM)
- DeltaV Process Risk Assessment (PRA)
- DeltaV Recipe Transfer Management (RTM)

DeltaV PRA software is a web-based application that seamlessly integrates process manufacturing specifications to facilitate risk assessments during the development and manufacturing of pharmaceuticals.

The process definition is captured in DeltaV PSM. This information typically includes:

- Key process steps and the sequence of those steps
- Critical Quality Attributes
- Process parameters and operating ranges
- Parameter classification (key, critical, non-critical, etc.)
- Required materials
- Equipment properties

DeltaV PRA has full access to the process definition in DeltaV PSM and use that information to help teams perform risk assessments. For example, using a cause-and-effect methodology, users can determine which CPPs affect CQAs the most. All process information, including process steps and process parameters, is available, and there is no need to define those manually, as is typically the case with standalone risk management solutions. In addition, subsequent modifications in the process definition (e.g., change of a range) are automatically updated in risk studies.

Benefits

DeltaV PRA facilitates risk assessments by allowing users to identify CPPs and CQAs within manufacturing specifications and make those parameters and attributes available in templatized risk studies.

Centralized Management of Critical Parameters. DeltaV PRA provides centralized management of CPPs and CQAs to create a single source of reference for risk assessments.

Improved Change Control. DeltaV PRA has embedded change control functionality to maintain the integrity of the study and simplify GxP compliance.

Easy Access of Relevant Data. Information within risk studies can easily filtered based on the step, activity, and parameters.

Enhanced Risk Understanding. Color-coding of risk ranks facilitates the visualization and understanding unlocking faster and better decision-making.

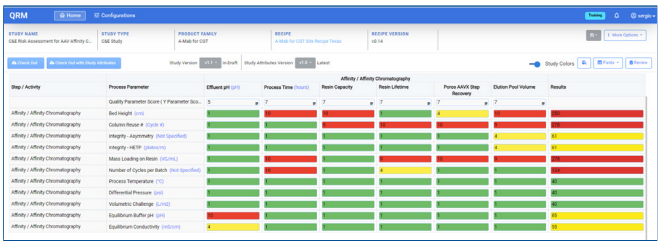
Product Description

Studies in DeltaV PRA facilitate risk assessments across the lifecycle of a product. There are four types of risk studies:

1. Cause and Effect (C&E)
2. Failure Mode Effect Analysis (FMEA)
3. Parameter Study (PS)
4. Functional Relationship Table (FRT)

C&E Studies (Parameter Risk Assessment)

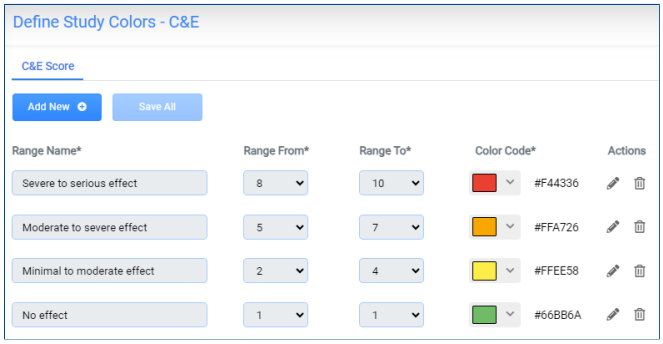
DeltaV PRA includes Cause and Effect Studies to help correlate CPPs and CQAs by ranking the impact of CPPs on CQAs for a specific recipe or portion of the recipe. Users can create C&E studies for individual steps (process operations) or the whole recipe (process specification). Once the C&E studies are created from the process definition information (captured in DeltaV PSM), a team evaluates the relationship between the process parameters and the quality attributes. Typically, the evaluation starts by assigning an attribute score for each quality attribute based on the impact on product safety and/or efficacy. Then, the relationship between process parameters and quality attributes is scored. The attribute score and the relationship score are combined in the Result column. The picture below shows an example of a C&E Study based on the case study described in the Project A-Gene document by the Alliance for Regenerative Medicine and the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIMBL).



Example of Cause and Effect Study.

In addition of the CPPs and CQAs, users can define additional study attributes as supplemental information for risk studies.

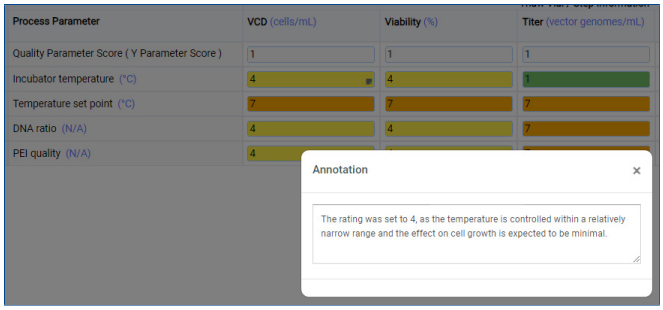
C&E studies can be color-coded based on predefined thresholds.



User-defined thresholds for color-coding.

Changes in the parameters included in the studies, as well as score values, are under change control, and modifications are tracked in the audit trail. Customizable workflows are available for the review and approval of risk studies.

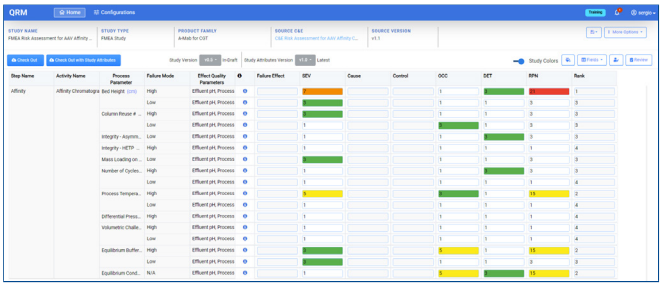
Users can use annotation to document the reason for a given score.



Annotations can be used to document scores or other fields within studies.

FMEA Studies

Failure Mode Effect Analysis Studies are built on top of C&E studies to identify and mitigate the risk for critical process parameters. FMEA studies help identify and describe the potential ways a process might fail and evaluate the impact of each failure mode. Risks are ranked based on a Risk Prioritization Number (RPN) calculated from the severity, occurrence, and detectability assessed for each identified risk. The picture below shows an example of an FMEA Study based on the case study described in the Project A-Gene document by the Alliance for Regenerative Medicine and the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIMBL).



Example of FMEA study.

Users can easily create FMEA studies from C&E studies. When creating an FMEA study, users can select parameters and filter them based on the C&E scores. Users can also select specific failure modes to be included in the FMEA study.

Parameter Studies

Parameter studies combine and summarize information across multiple studies in a single table. This information can be used to prioritize different parameters and the risks they may have on a certain recipe. When creating a Parameter Study, users can run queries to further filter the parameters to be used in the study.

FRT Studies

A Functional Relationship Table (FRT) is used to display the relationship between parameters across multiple C&E Studies.

Change Control

Risk studies must be check out before authorized users can performed modifications such as refreshing parameter information or changing individual rankings within the studies (e.g., severity ranking within a FMEA study). Approval workflows are used to review and approve risk studies. Authorized users can view previous versions of the study. Modifications in process definitions (DeltaV PSM) are controlled by separate user roles. System administrators can assign roles independently to control who can modify either or both the process definition and/or risk studies.

Typical PRA Implementation

DeltaV PRA is typically implemented along DeltaV PSM and starts with a trial period where a few unit operations are configured into DeltaV PSM and DeltaV PRA to ensure alignment to current process.

This pilot period usually lasts 3 months. Once the pilot has ended, DeltaV PSM and DeltaV PRA are implemented at one site, and it might include interfaces to systems like ERP or MES. The final implementation phase built on the success at the first rollout and PKM is deployed at multiple sites.

Licensing Ordering Information

DeltaV PRA is licensed based on the total number of user licenses. Contact your local Emerson sales office or representative for pricing specific to your system.

Related Products

- DeltaV Process Specification Management provides a structured repository for process specifications and a collaboration model that facilitates drug development.
- DeltaV MES improves manufacturing operation to drive production goals and creating an optimized manufacturing environment for Life Sciences organizations.
- DeltaV DCS is an easy-to-use automation system that simplifies operational complexity and lowers project risk.
- DeltaV Real-Time Scheduling allows customer to visualize the facility constraints, accommodate variability, maximize production, and understand the implications of any change in the manufacturing process.

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