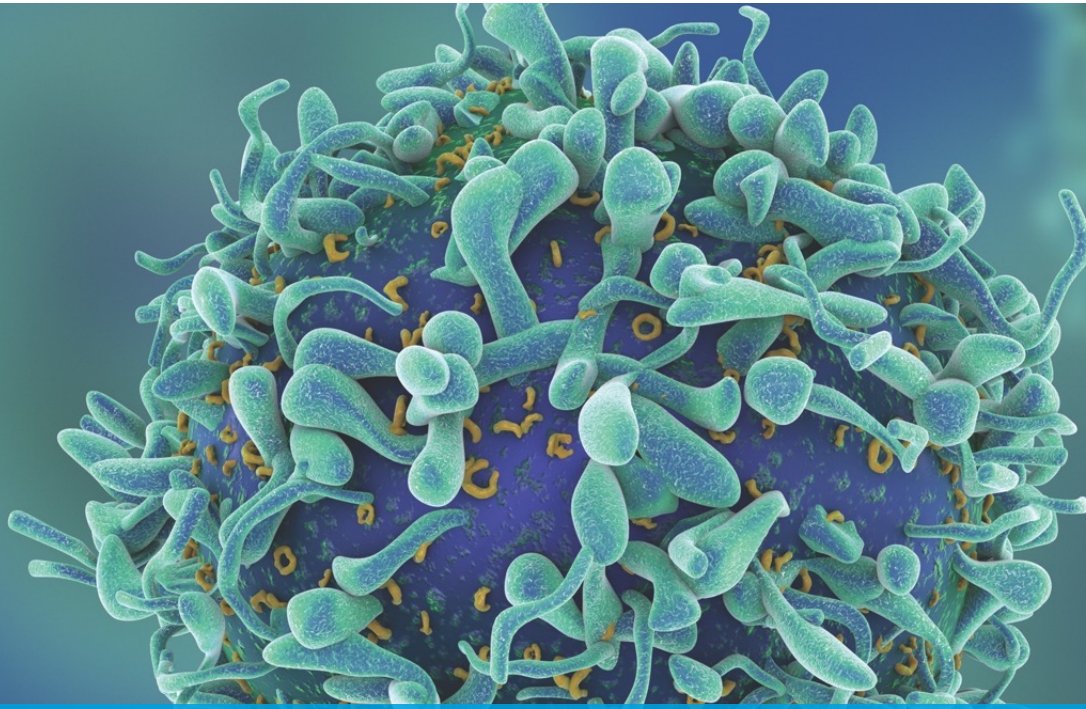




Lessons from QTL process installation in a Big Pharma company

Rohan Shirolkar – Manager, Risk Management - Central Monitoring

Nathalie van Borrendam – Associate Director, Risk management - Central Monitoring

3D illustration of T cells or cancer cells

Janssen R&D

Phuse 1-4 May 2022

Presenters

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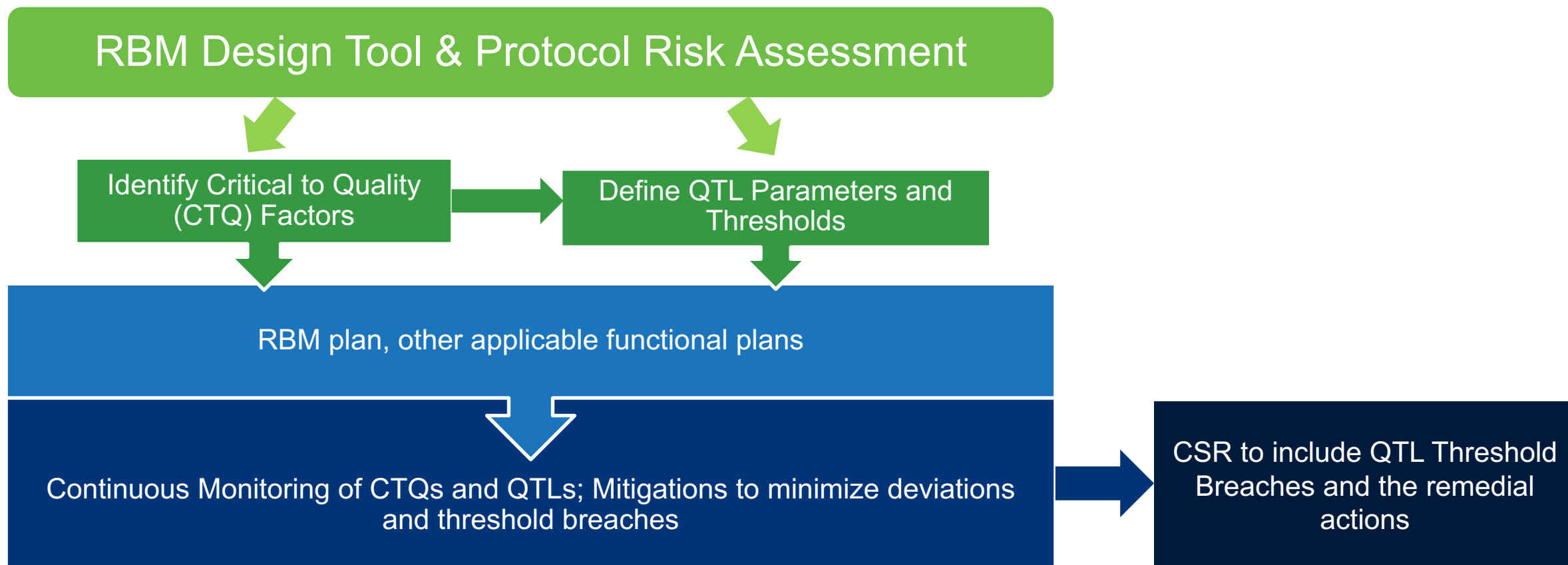
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QTL as a part of ARBM strategy

ICH E6 R2 Require Quality Tolerance Limits to:

- 1) identify systematic issues that can impact subject safety or reliability of trial results and
- 2) ensure that important deviations from the predefined QTLs and associated remedial actions taken are reported in the Clinical Study Report (CSR)



Identifying QTL Threshold by statistician



Protocol

Assess Protocol Assumption



Simulated data

E.g. Use simulations to use effect on power



Reference Studies

Indication, compound, impact of parameter, specifics for parameter



QTL threshold

Determine threshold based on statistical analysis

Agree QTL Threshold with QTL Core Team and develop monitoring strategy

Example of QTL implementation

Critical to Quality Factor	Parameter	Definition and Justification	QTL	Justification for QTL	Secondary Threshold	Justification for Secondary Threshold	Potential Mitigation Actions
Subject retention and subsequent safety/survival follow-up.	10% annual drop out rate	Proportion of subjects that have been randomized and discontinued from the trial. Per SAP the sample size calculation has taken into consideration an estimated annual dropout rate of 10%. To achieve approximately 80% power.	10% subjects discontinued annually	The percentage of 10% was assumed during the sample size calculation in the design stage of the trial. This was based on earlier drop out rate in the anticipated study population.	5 % subjects discontinued annually	Operative threshold allowing enough time to prevent drop out of 5% by implementing corrective action plans.	Create programmed reports for calculation of % annual drop out. Monthly review of reports. Identify issues and trends and follow up with appropriate functions. On reaching a breach study team to perform a root cause analysis on trial, country and/ or site level. Determining based on the root cause, mitigation actions: - Central team to perform more frequent review of the data - Follow up with local team on the root cause. - Re-train sites and subjects - Initiate discussions on potential protocol amendment and/or increase recruitment
Disease Evaluations assessments must be performed per T&E.	2 or more missed consecutive DE assessment	Portion of subjects that have missed 2 or more consecutive DE assessment. For any event identified, if the event date and the latest date of scheduled disease evaluation immediately preceding the event differs more than 2.5 disease evaluation intervals, which indicates that subject missed at least two scheduled disease evaluations, then this event will not be considered as an event in the analysis. Instead, the subject will be censored.	10 % of subjects with 2 or more missing consecutive disease evaluation assessments.	Based on the protocol assumptions, data simulation was performed and verified with historical data. Based on the results the 10% was considered the appropriate limit.	5 % of subjects with 2 missing consecutive disease evaluation visits.	Operative threshold allowing enough time to prevent to reach the 5% by implementing corrective action plans.	Create programmed reports to identify missed assessments. Monthly review of reports. Identify issues and trends and follow up with appropriate functions. On reaching a breach study team to perform a root cause analysis on trial, country and/ or site level or at the vendor. Determining based on the root cause, mitigation actions: - Central team to perform more frequent review of the data - Follow up if vendor process is compliant - Follow up with local team on the root cause. - Re-train sites and subjects - Re-train vendor on assessment handling / evaluation

Lessons Learned





Thank you for your attention

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As a scientist at Janssen, Jeff uses his unique perspective and an array of artistic techniques to express his vision.