

# Risk Based Approach Applied to the Validation of Report Objects

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*Christoph Ziegler, F. Hoffmann – La Roche AG, Basel, Switzerland*



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# Introduction

- Regulatory authorities recommend a risk based approach when it comes to the validation of report objects.
- E.g. documents published by the FDA recommend that “... *the approach to validation be based on a justified and documented risk assessment and the potential of the system to affect product quality and safety as well as record integrity*” [1].
- In order to apply a risk based approach to the validation of report objects, the following needs to be in place within the statistical reporting department:
  - the detailed processes needs to be reflected within local SOPs
  - the technical background (programming environment / tools / systems) has to allow the implementation of such a concept
  - supportive documents / instruments

# Definition of Risk

- **Risk** = combination of the probability of an error occurring and the severity of that error.
  - Transfer to our daily work
  - Needs to be reflected within the risk management in our reporting process
- **Risk Management** = continuous process of analyzing, evaluating, controlling and monitoring risks that exist within our business processes
- Important: Risk can change over time and might be perceived differently by others

# Report Objects and Reporting Event

- **Report Object** = any object which is sent outside the Biostatistics department, e.g. to regulatory agencies or to other departments within the company.
  - any type of data display or other output produced for delivery such as a summary output, a subject data listing, a dataset, a graph or any other file including clinical trial data in raw form or in a summarized way.
- **Reporting Event** = consists of one or more report objects and is defined as the delivery of report objects at a certain time.
  - A clinical trial usually has more than one reporting event with different objectives, intended audiences and conclusions drawn thereof.
  - Examples: interim analysis, final analysis, deliverables to safety monitoring boards, a submission or deliverables for medical review.

# Risk Assessments – Levels and Contributing Factors

- When applying risk assessments to the statistical reporting of clinical trials, we can differ between
  - the risk of the overall reporting event,
  - the risk of the individual report objects (outputs) and
  - the risk of the individual programs.
- There are lot of different factors that contribute to risk assessments
- It is a challenging team effort between programmers, statisticians and clinical science
- The dependency between reporting event, report objects and programs also needs to be considered in the risk assessment.

# Risk Assessments – Levels and Contributing Factors

- The categories of risk are: LOW, MEDIUM and HIGH
- The risk assessment is done for all three levels (reporting event / report objects / programs).
- Due to the dependency between report object and underlying program(s), the risk of the program is of course at least as high as the highest risk level of the report object it produces
- The level of risk assigned should then determine the method of validation (e.g. code review, double programming, unit testing etc), the method of the final check before the deliverables are sent out and the level of documentation.

# Risk Assessments – Levels and Contributing Factors

Report Objects Risk	LOW	MEDIUM	HIGH
Program Risk	LOW / MEDIUM / HIGH	MEDIUM / HIGH	HIGH
Reporting Event Risk	Based on this matrix, the method of validation, the method of the final check before delivery and the level of documentation can be determined.		
LOW			
MEDIUM			
HIGH			

- Challenge: level and the timing of the validation documentation.
- The level of detail should possibly go hand in hand with the assigned risk

# Risk Assessment of Reporting Events – Contributing Factors

- Type of Reporting Event
  - Interim Analysis, Final Analysis, DSMB, Ad-Hoc Request,...
- Audience of Reporting Event deliverables
  - Company internal (study team / upper management), company external, ...
- Intended Use of Reporting Event deliverables
  - Filing (NDA), Data Review, Efficacy Purposes,...
- Criticality of Data used for Reporting Event / Administrative Issues
  - Importance of trial, early vs repetitive reporting, complexity of data/CRF, data quality aspects, experience of staff, timelines, standardization of environment,...

# Risk Assessment of Report Objects – Contributing Factors

- Type of Report Object
  - Summary, Listing, Graph,...
- Importance of Report Object
  - Key Report Object, Non-Key Report Object,...
- Data dependency
  - Run run on sub-populations / on a subset of the data (e.g. cutoff-date),...
- Program in the background (validation level / complexity)
  - Report Object produced with standard macros / standard reporting system / with “normal” code / with non-standard statistical software,...

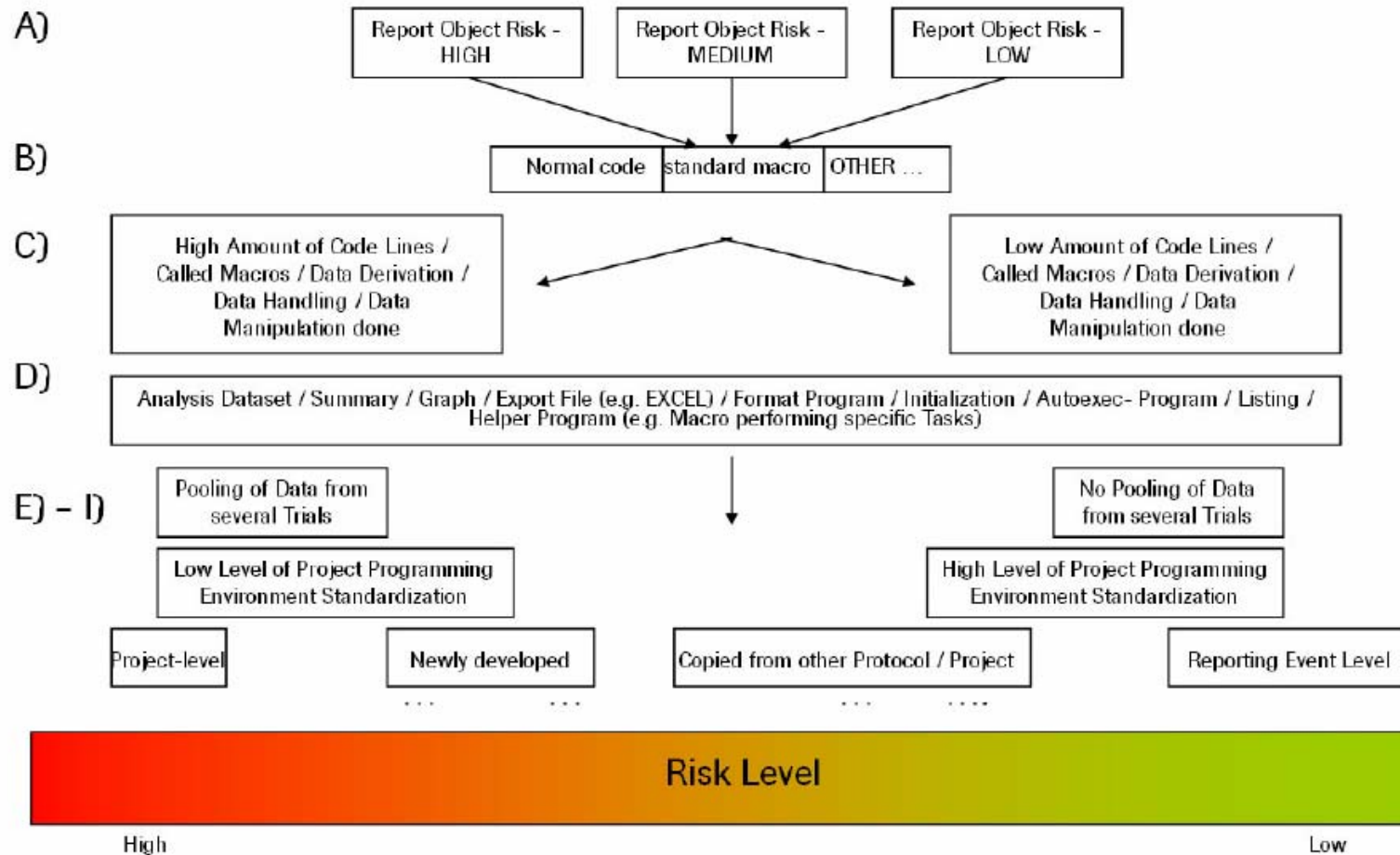
# Risk Assessment of Programs – Contributing Factors

- Risk of corresponding Report Object(s)
- Type of Program Code
- Program Characteristics
- Type of corresponding Report Object(s) / Functionality
- Criticality of underlying Data
- Project Standards / Project Programming Environment
- Level of Program in Change Control System
- Origin of Program
- Level of underlying Specifications
- Management Decisions
- ...

# Decision Tree (Example)

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## Risk Assessment of Programs— Possible Scenarios



# Processes / Technical Background Reporting Environment

- In order to implement the risk assessments the necessary processes and technical background (reporting environment) should be available.
- If possible, the reporting environment should be set up in a way that the risk assessment of programs / report objects / the reporting event can be done directly within the system.
- Ideally, the risk assessment of programs should directly be done in the program change control system.
- For report objects where the targeted audience has been defined as internal in a company or for exploratory use, the risk assessment of report objects should be well visible on the report object itself.
- For report objects where the ultimate audience is company external, it should also be possible to hide the risk assessments to the audience (e.g. to health authorities), because it is an internal process.

# Processes / Technical Background Communication Plan

- The intended use of report object deliverables is an important factor when it comes to risk assessment.
- Each reporting event has an intended use which is used to determine the risk.
- When delivering the report object(s) of a reporting event, it is important to communicate the intended use.
- If e.g. Clinical Science request a report object for unofficial internal review (medium or low risk), they are not allowed to use this report object for e.g. a publication or as a basis for important decisions (high risk).
- The communication plan is an important aspect to emphasize the intended use and to make customers aware that risk assessment related decisions were also based on the intended use.

# Processes / Technical Background

## Plan to document all quality related aspects

- It is recommended to have a central document where all quality related aspects of a reporting event are gathered. Important QA-related aspects are e.g.:
- The location of programs used for a reporting event within the company specific reporting environment
- All risk assessments including justifications (if not done within the reporting environment)
- Data related information
- Location of formal validation and change control (if no appropriate change control system is used)
  - The goal is to have all information concerning a reporting event at one central place.
  - The challenge is how to deal with repetitive reporting events and so-called ad-hoc requests.

# Conclusions / Benefits of a Risk Based Approach

- The risk based approach applied to the validation of report objects is an effective way of validating report objects and underlying analysis programs.
- The approach reduces efforts in low risk areas and focuses the validation activities on high risk areas.
- The approach reduces efforts in low risk areas and focuses the validation activities on high risk areas.
- However, in order to implement a risk based approach the necessary technical background should be in place.
- It has been shown that a lot of different risk factors are contributing to the risk of reporting event, report objects and programs.
- The risk based approach adds a lot of value to the validation process within Biometrics departments and allows dispatching resources where they matter most.

# Thank You



Contact the author at:

Christoph Ziegler

F. Hoffmann – La Roche AG

Malzgasse 30, Bldg. 670/506

4070 Basel

+41 61 68 89200

[christoph.ziegler@roche.com](mailto:christoph.ziegler@roche.com)

[www.roche.com](http://www.roche.com)

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