GILEAD

E.VIEW

GILEAD EXCELLENCE IN EUROPE

NEWS FROM THE OLD WORLD

❯

2019: Outcomes and metrics from external Gilead audits in Europe

PARTNERSHIPS

❯

Chromicent GmbH:
QbD approach across all stages of analytical method lifecycle

FROM THE BENCH TO THE SHELF

❯

ChIMiC
the new Belgian Scientific Consortium

PILLS OF ...
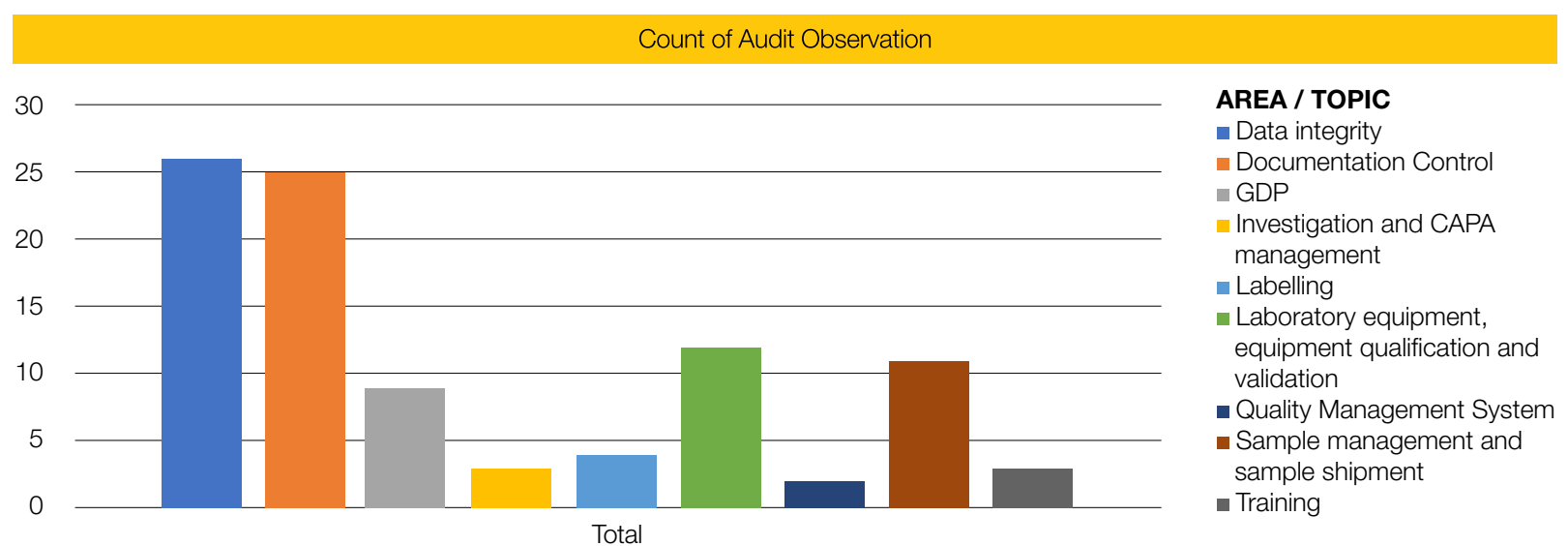
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...Project management

2019: Outcomes and metrics from external Gilead audits in Europe

AO supports Gilead external audits of suppliers as analytical SME's. Here below a picture of Tier 1 supplier outcomes and metrics of recurrent analytical observations related to the twelve months between June 2018 and June 2019 in the EMEA region.

A total of 15 Tier 1 supplier audits have been performed in between June 2018 and June 2019 in the EMEA region, spanning Contract Labs (CTL), packaging sites, API, DP and sterile manufacturers.

Site type	Germany	Ireland	Italy	Spain	Russia	Total
API CMO	1		3	2		6
CTL		1	2			3
DP CMO	3				1	4
Packaging CMO	1					1
Sterile DP CMO			1			1
Grand Total	5	1	6	2	1	15

Count of Audit Observation

AREA / TOPIC
- Data integrity
- Documentation Control
- GDP
- Investigation and CAPA management
- Labelling
- Laboratory equipment, equipment qualification and validation
- Quality Management System
- Sample management and sample shipment
- Training

Analytical observations identified during these audits mostly pertain to the areas of Data Integrity, Quality Compliance and Documentation Control. The most recurring gaps can be summarized as below:

- **Data Integrity:** e.g. gaps in the areas of audit trail, segregation of duties, system user configuration, periodic software review, software no longer supported by the vendors, trial injections, User Requirement Specifications insufficient to describe Functions and Roles.
- **Laboratory equipment, equipment validation and qualification:** e.g. incompleted equipment qualification records, inadequate equipment qualification with respect to the operational range, inadequate calibration acceptance criteria, IPCs lab equipment not fully qualified, Performance Qualification not carried out.
- **Document Control:** e.g. lack of documentation versioning, vendor's methods not aligned with Gilead methods, inappropriate documentation archiving, lack of record inventory, lack of proceduralised processes, loose sheets to be used to record GMP activities, logbook distribution not controlled by the quality unit.
- **GDP:** e.g. ALCOA deficiencies, lack of supervisor signatures, use of pencil, raw data not available in their original format, operations, such as sample aliquoting, not documented.
- **Quality system:** e.g. inadequate investigation and CAPA management, incomplete training records, lack of periodic re-training, lack of organizational definition and segregation of roles for QA/QC.
- **Sample management and sample shipment:** e.g. lack of sample traceability, lack sample reconciliation, spare samples found in the lab.
- **Labelling:** e.g. lack or inadequate labelling for either instruments or sample or sample solutions.

? *Do you have questions? Contact:* **AO-Milan&GSIUC@gilead.com**

Chromicent GmbH: QbD approach across all stages of analytical method lifecycle

Gilead and Chromicent have established collaborations in the field of analytical method development and optimization since April 2018 leveraging Quality by Design (QbD) concepts Design of Experiment (DoE) for early assessment of method robustness. A total of seven projects were successfully completed and one poster was jointly presented at HPLC2019 conference in Milan. Alexander H. Schmidt and Mijo Stanic, both founders, have worked closely with our SEL, FIL, Vesatolimod, GS-6207 teams to help build a solid knowledge around our analytical methods.
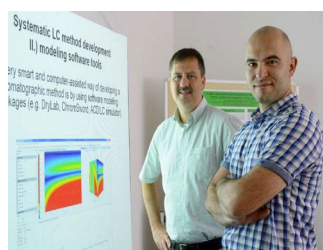
Company profile

Chromicent is a Pharmaceutical Service Provider founded in 2013, based in Berlin Adlershof (Germany), with 550 mq lab Space and 15 staff, half of them PhD.
The company main areas of expertise are software-aided method development, statistical assessment of method robustness, non-linear modelling tools and method lifecycle management (MLCM).

A variety of state-of-the-art instrumentation is available, with a wide range of chromatography and detectors combinations (see Table 1).
The firm also has a key expertise in Supercritical Fluid Chromatography (SFC) field in which they are leading a number of co-funded R&D projects:
- Modeling tools for SFC based methods ("DryLab SFC")
- Genotoxic impurity separation and identification by SFC
- Extractables and Leachables determination by SFC-MS/MS
- Two-dimensional chromatography LC x SFC or SFE x SFC

Chromicent capabilities

CHROMATOGRAPHY	DETECTORS	OTHER CAPABILITIES
UPLCs (5) › 4 x HClass › 1 x UPLC	5 x PDA 3 x MS, QDa), TQD, Xevo TQS micro 1 x ELSD , FLR, RI	1 x Sub visible particle measurement system 1 x Lyophilisator 1 x ASE (Accelerated Solvent Extractor)
HPLCs (7) › 5 x Alliance 2695 › 1 x Alliance 717 › 1 x Prep HPLC	6 x PDA, 3 x UV 2 x CAD 3 x RI 2 x CAD 1 x FLR, ELSD, Conductivity Electrochemical, Chiral, CLND	1 x Photo stability chamber for ICH Q1b 4 x Climate chambers 2 x Dissolution testers 1 x Spectral photometer
Bio-UHPLC, Arc (1)	PDA (E)	**SOFTWARE CAPABILITIES**
Ion-Chromatography (1)	1 x Conductivity	Empower 3 DryLab Fusion Design Expert (8.0)
GC (1)	1 x FID, TCD	

Service portfolio

- **Method Development**
  › Systematic method development strategies through modelling software (DryLab), or statistical software (Fusion)
  › Quality by Design in analytical method development and sample preparation
- **Consulting**
  › Analytical Instrument Qualification (AIQ)
  › Advanced preparation for GMP inspection/audits
  › Risk assessment
  › Laboratory instruments sales/purchase
- **Training**
  › Training for HPLC, UPLC, and UPC technologies (theory and praxis)
 › LC Troubleshooting
- **Auditing**

? *Do you have questions on Chromicent? Contact:* **AO-Milan&GSIUC@gilead.com**

ChIMiC – the new Belgian Scientific Consortium aimed at delivering hardware and software solutions to enlarge the analytical separation space

The ChIMiC project brings together engineering, life science and chemistry competences from 5 top universities in Belgium, with the mission of promoting scientific excellence in fundamental research to help solve complex separation problems in all academic and industrial labs mining the content of (bio-) chemical mixtures. Gilead had the chance to meet some of the founders of ChIMiC at the HPLC2019 conference in Milan, last June.

Prof Gert Desmet, Prof Deirdre Cabooter and Prof Ken Broeckhoven shared with us the goals and the specific tools that ChiMiC will leverage bringing the academic and pharma industry world closer with their applied research.
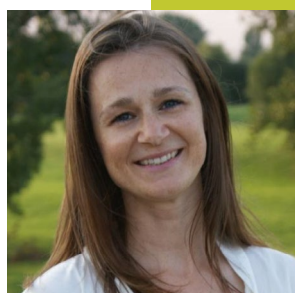
Prof Deirdre Cabooter
(University of Leuven)

"Artificial intelligence and self-learning algorithms are therefore needed to generate a self-learning expert system that can help the analyst in method design and selection. The outcome of this research will be a powerful decision-supporting software tool combined with new or existing hardware solutions to harness the potential of multi-dimensional separations".

Prof Gert Desmet
Vrije University of Brussels

"The overall project goal is to build a system that can guide analysts towards optimal combinations of separation and detection modes based on "some" preliminary information of sample composition".
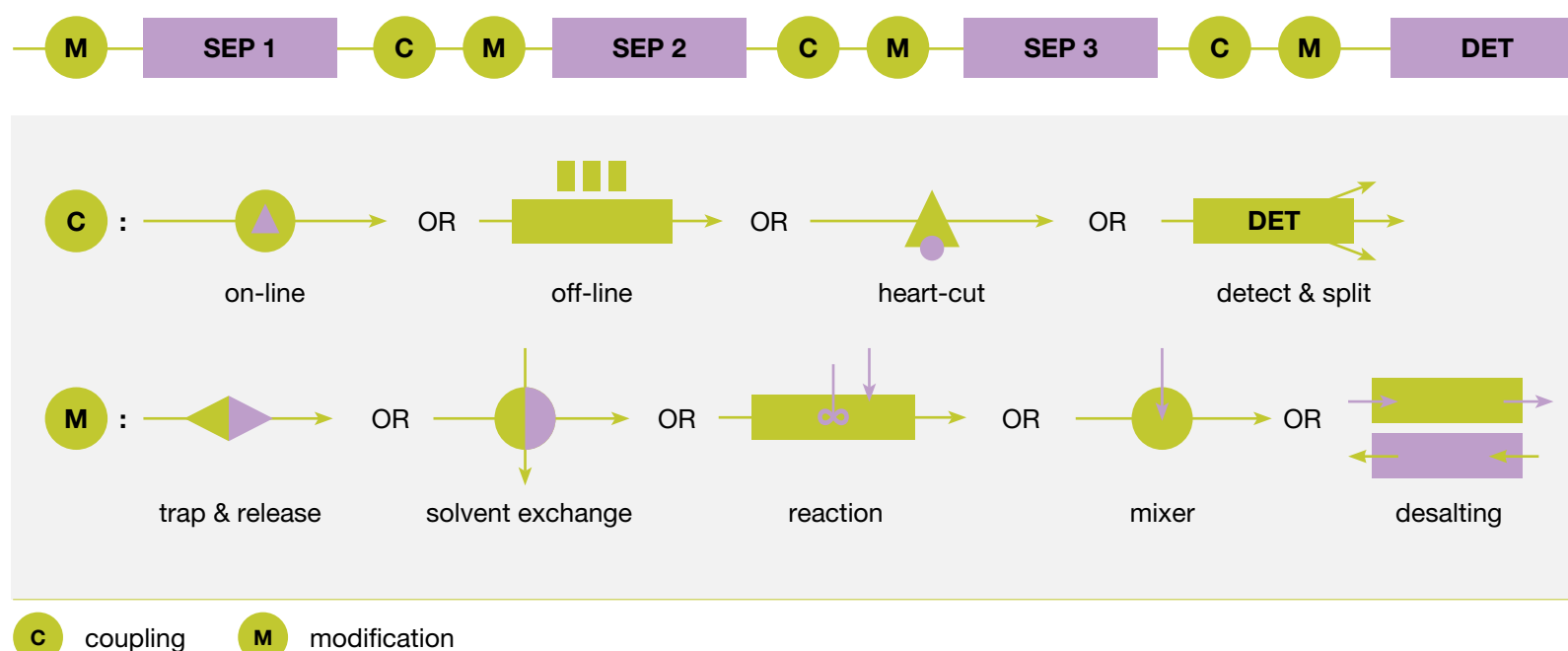
Prof Ken Broeckhoven
Vrije University of Brussels

"Multi-dimensional separations and their incalculable number of possible combinations can access increased separation capacity and selectivity. These hardware solutions are currently barely exploited due to the high amount of information that needs to be processed to optimize separations".

Read more: chimic.be

M — SEP 1 — C — M — SEP 2 — C — M — SEP 3 — C — M — DET

C : on-line OR off-line OR heart-cut OR DET detect & split

M : trap & release OR solvent exchange OR reaction OR mixer OR desalting

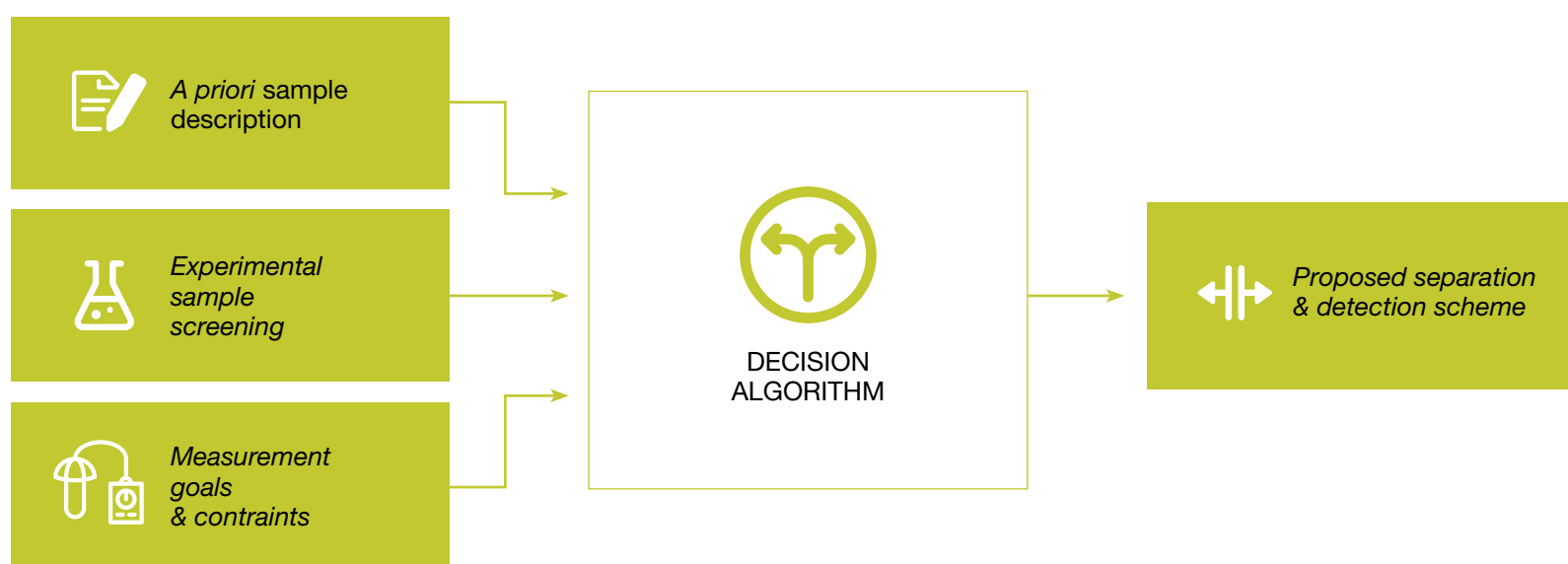C coupling   M modification

Separation Modes

GC (polar), GC (non-polar), SFC (RP), SFC (NF), LC (RP), LC (IEX), LC (chiral), LC (HILIC), LC (SEC), CEC and CE

Sample descriptors

Polarity, solubility, lipophilicity, molecular weight, structural details

Self-learning expert system

Optimisation of separation through the management of a huge amount of information, combination of separation and detection techniques and experimental verification.

A priori sample description

Experimental sample screening

Measurement goals & contraints

DECISION ALGORITHM

Proposed separation & detection scheme

? *Do you have questions on ChIMiC? Contact:* **AO-Milan&GSIUC@gilead.com**

… Project management

PROJECT

A process in which human, materials and financial resources are organized in a new way to achieve a defined output, within defined constraints of time and cost.

Keywords

⊕ **NEW**   🕐 **TEMPORARY**

↕ **FLEXIBLE**

PROJECT VS PROCESS

The discriminants are the output (one-off vs repetitive), the type of achievements (unique vs standard), the duration (time limited vs permanent), the competence (new vs consolidated).

Development of NEW product → **PROJECT**

Routine Manufacture → **PROCESS**

PROJECT MANAGMENT

The sum of principles and methods for managing projects.

| PROJECT PHASES | INITIATING | PLANNING | EXECUTNG & CONTROLLING | CLOSING |

1. Initiating:
› definition of project team, stakeholders and establishment of project charter
› feasibility assessment ► outcome of this phase is: **GO/NO GO**.

2. Planning:
› determination of scope/budget, meant to define a structure that addresses the following questions: **WHAT? WHO? WHEN? At WHAT COST?**
› project structure definition: the most commonly used is the Work Breakdown Structure (WBS).
› selection of a progress monitoring tool (Milestone, units complete, % complete etc.) and risk evaluation.

3. Executing and controlling:
› tracking of status
› project performance
› cost monitoring

4. Closing:
› output assessment (Earned Value)
› financial assessment (ROI)
› closing communication to the stakeholder
› lessons learnt
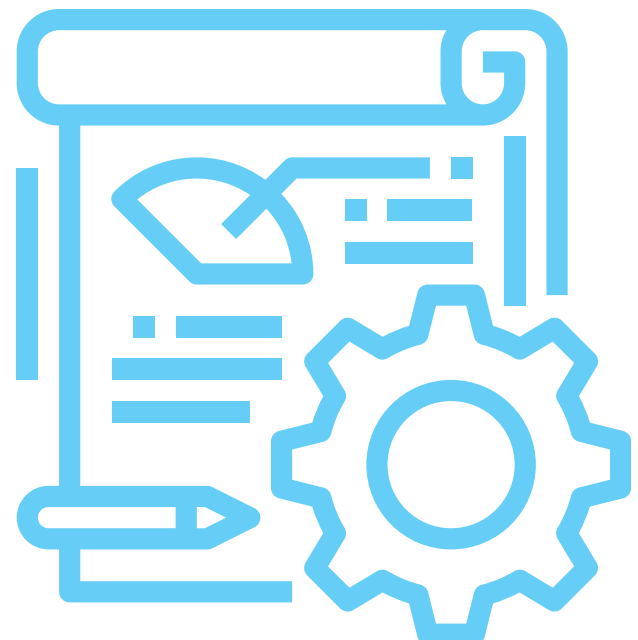
Uncertainty

Each modification leads to an increase of project duration and costs. The later in the project phase the modification is implemented, the higher the impact on the project
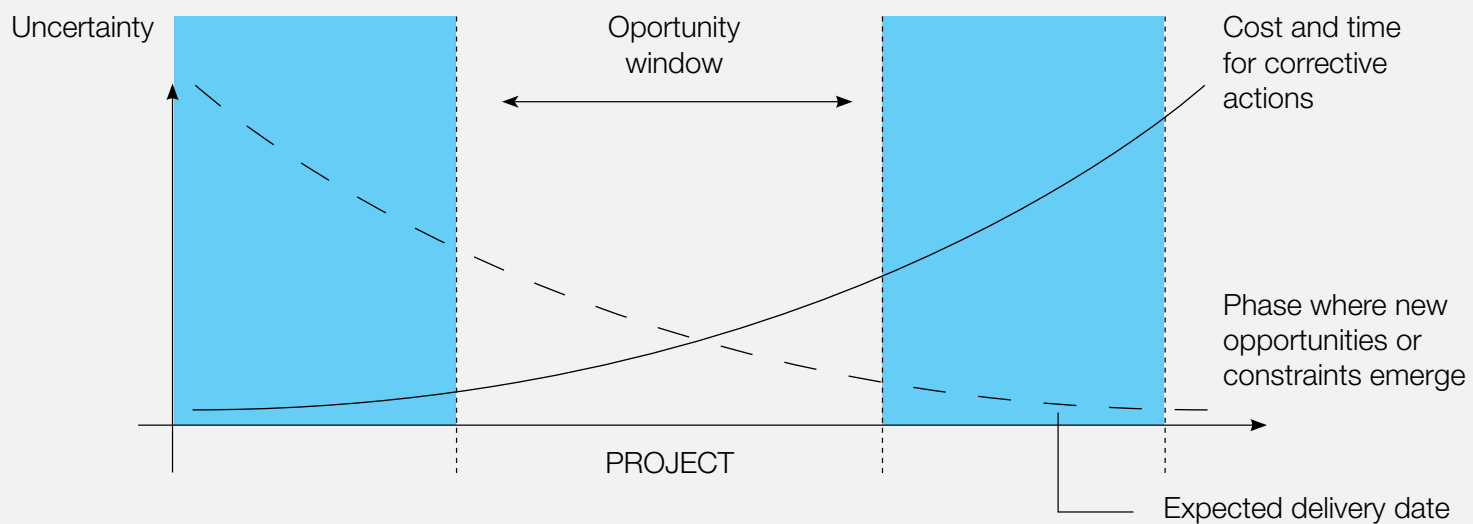
How uncertainty can be decreased at early stage?
› Get all the stakeholder involved since the beginning to have an effective project team
› Share knowledge on similar projects.
› Anticipate the constrains.
  Execute project plan

Uncertainty should be decreased and kept under control but at the same time also flexibility is essential...the trade-off between these two antagonistic characteristics should be established based on the kind of context/company.
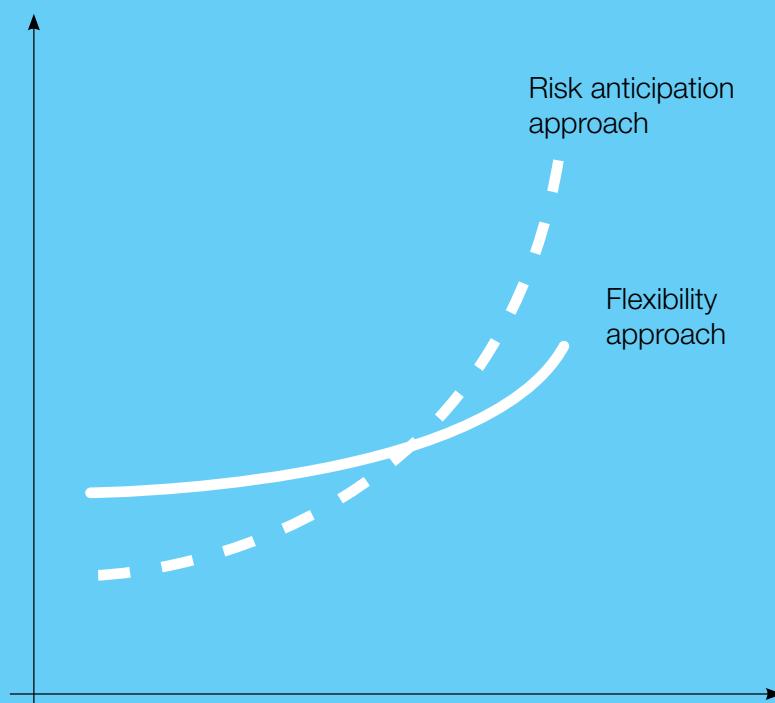
International standards

PMI Project Management Institute   IPMA® international project management association

? *Do you have questions or want to give your feedback?*
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