Opportunities and challenges from ICH Q2 (R2) and Q14 for the analytical lifecycle.

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GSK

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Disclosure statement

Jean-Francois DIERICK is an employee of the GSK group of companies.

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Content of the presentation

- ICH Q2 (R2) and Q14, what's new?
- ICH Q2 (R2) and Q14, what's ready now, ready soon or may be for later?
- ICH Q2 (R2) and Q14, where may it lead us?

ICHQ2 (R2) and ICHQ14

What's new?

Quality by Design principles

- "This guideline describes **science** and **risk-based** approaches for **developing** and **maintaining** analytical procedures suitable for the assessment of the quality of drug substances and drug products. The systematic approach suggested in ICH Q8 Pharmaceutical Development together with principles of ICH Q9 Quality Risk Management can also be applied to the development and lifecycle management of analytical procedures. When developing an analytical procedure, a minimal (also known as traditional) approach or **elements of an enhanced approach can be applied**."
- "The guideline describes considerations for the development of **multivariate analytical procedures** and for **real time release testing** (RTRT)."
- "Using the tools described in ICH Q12… the guideline describes **principles to support change management**… opportunity for **more efficient regulatory approaches** to related post approval changes."

- *Extracted from ICH Q14 draft guidance*

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ICHQ2 (R2) and ICHQ14

What's new?

Less of a
systematic « check the boxes » approach
More of a
systematic « understand and manage your risks » approach

Systematic

Science-driven

Identify the risks (risk=knowledge)
Score the risks (this is also knowledge)

Identify what knowledge is needed
to score / manage the risk
(do DoE when it helps)

- Analytical Quality by Design principles (AQbD) and Risk-based approaches throughout the entire analytical lifecycle

Integrated approach
from development
to routine use
and subsequent changes

Development is important to generate knowledge
that can be used in validation and routine stages

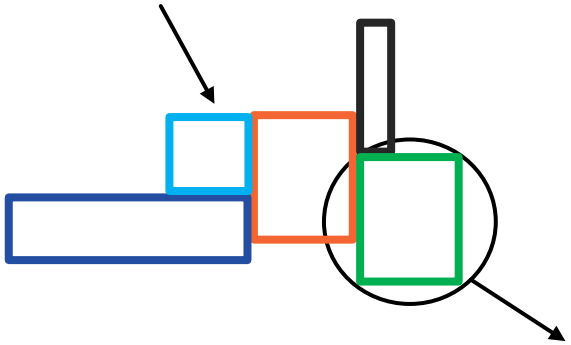
Routine stage is also generating knowledge

ICHQ2 (R2) and ICHQ14, what's new?

A schematic vision of the operating principles

A product

and its different attributes



Some of these attributes

will require control

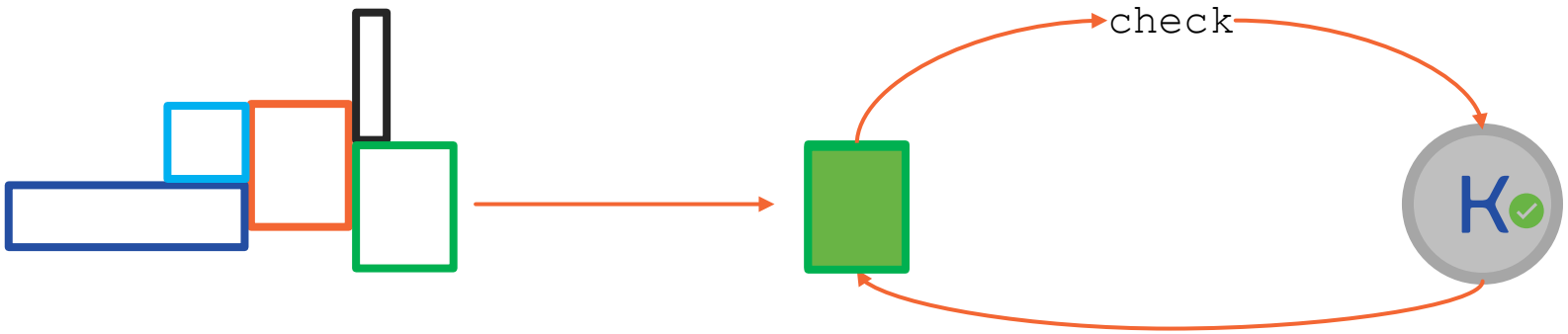
through measurement with an Analytical Procedure

This is the start of the Analytical Lifecycle … and AQbD

ICHQ2 (R2) and ICHQ14, what's new?

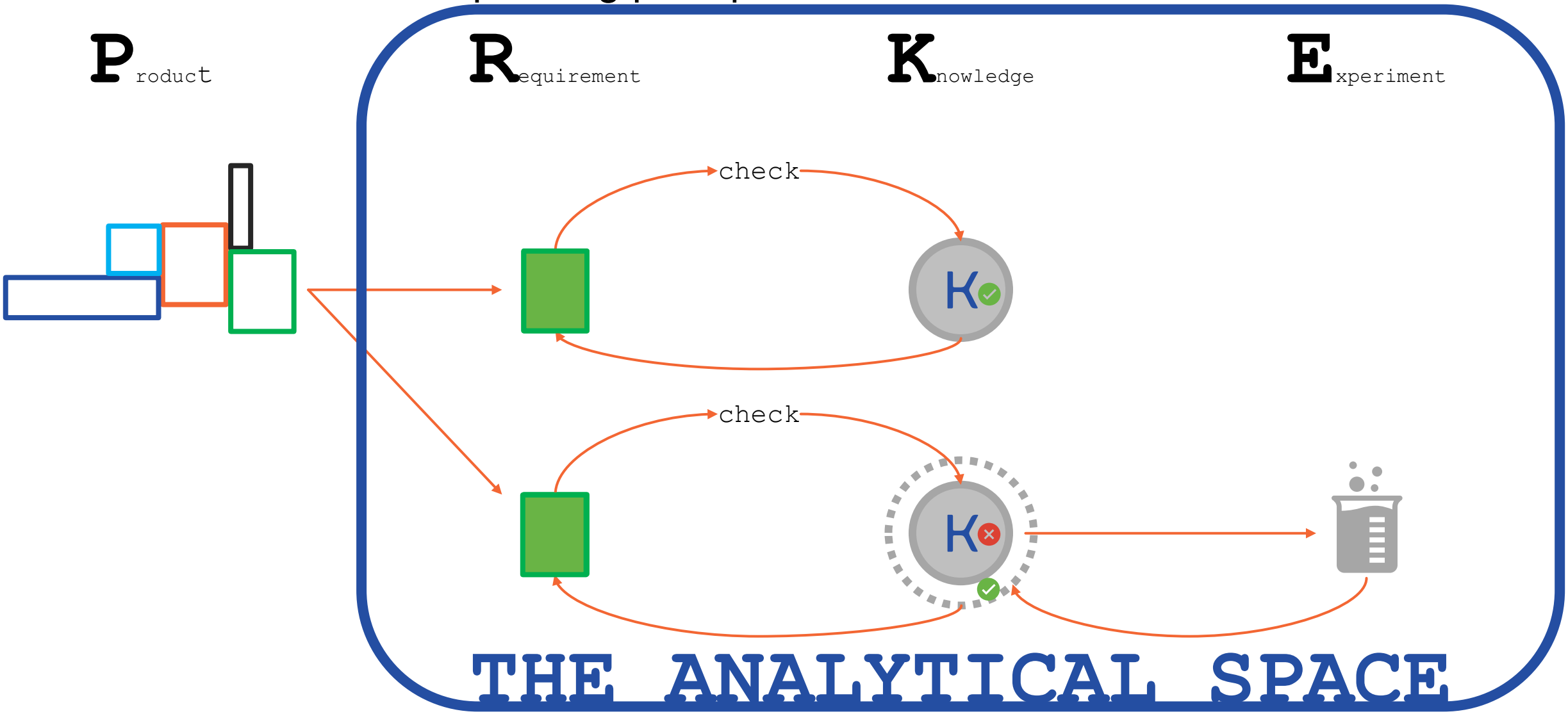
A schematic vision of the operating principles

Product **R**equirement **K**nowledge



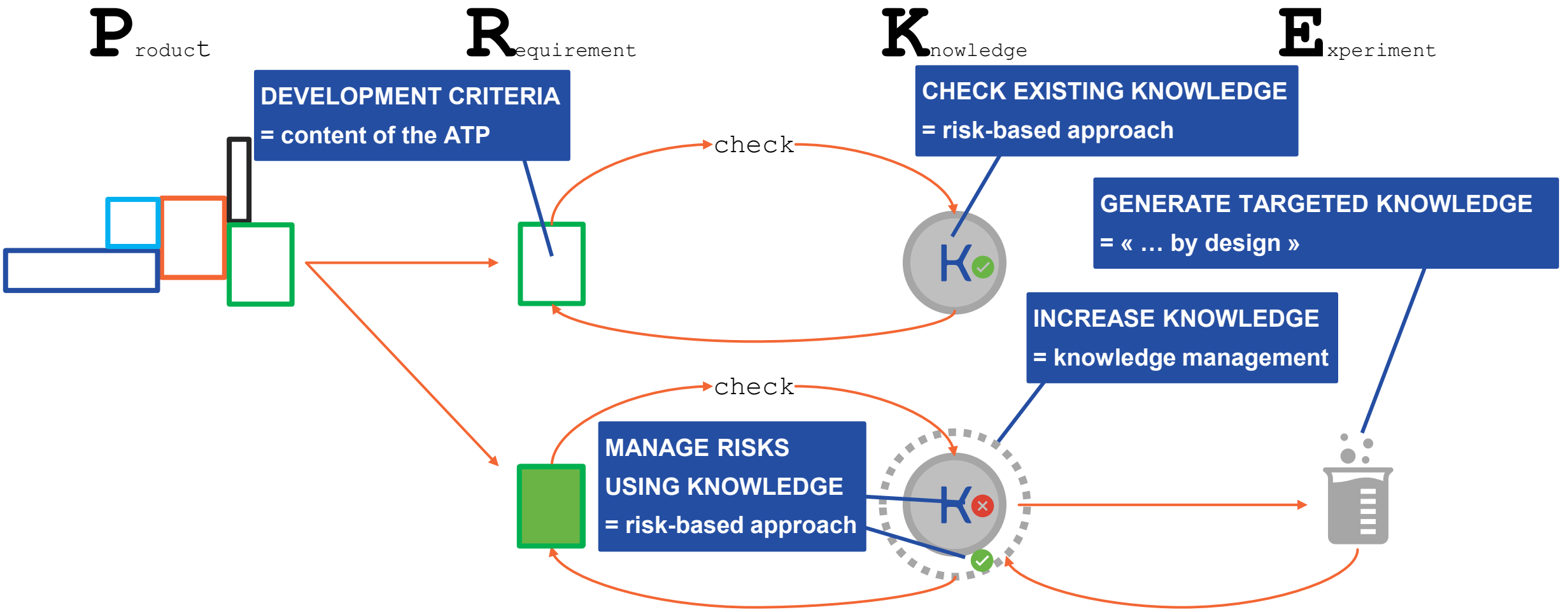
ICHQ2 (R2) and ICHQ14, what's new?

A schematic vision of the operating principles



ICHQ2 (R2) and ICHQ14, what's new?

A schematic vision of the operating principles



ICHQ2 (R2) and ICHQ14, what's new?

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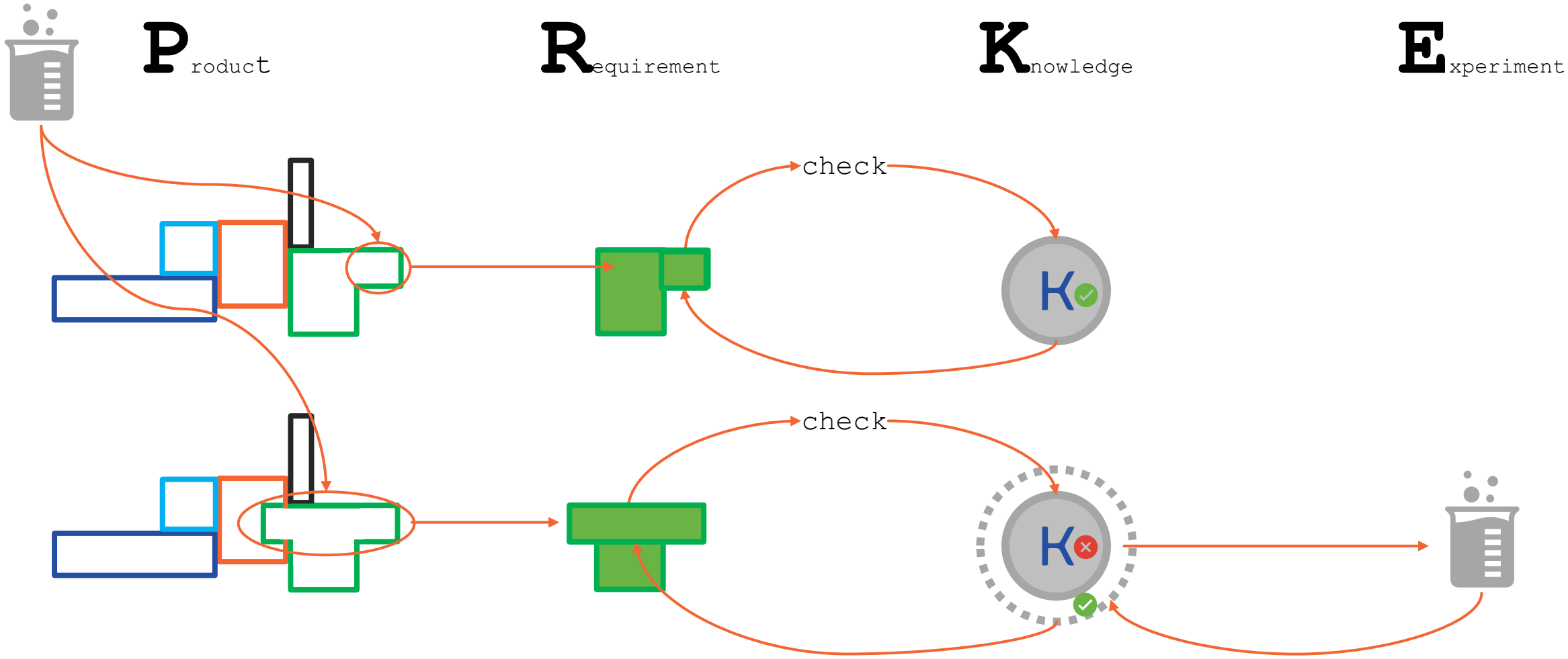

ICHQ2 (R2) and ICHQ14, what's new?

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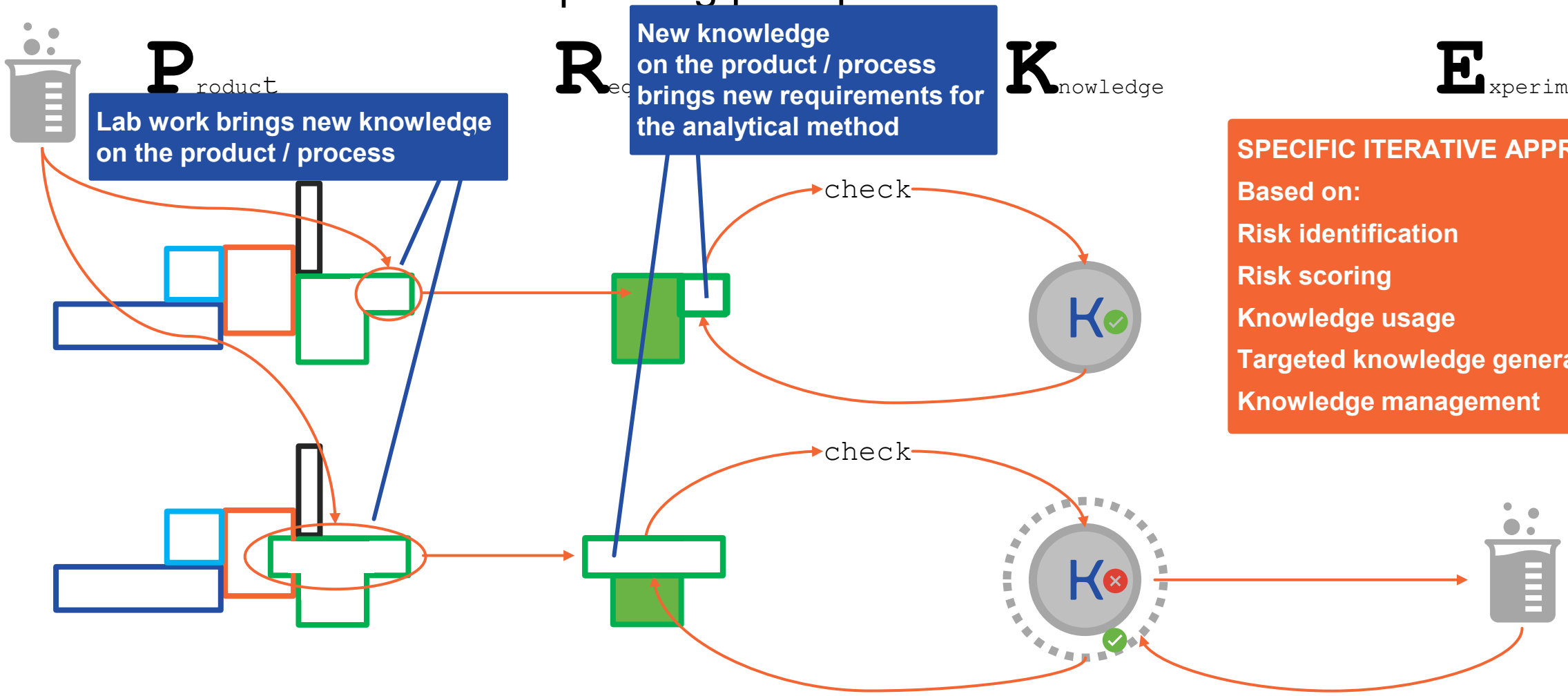


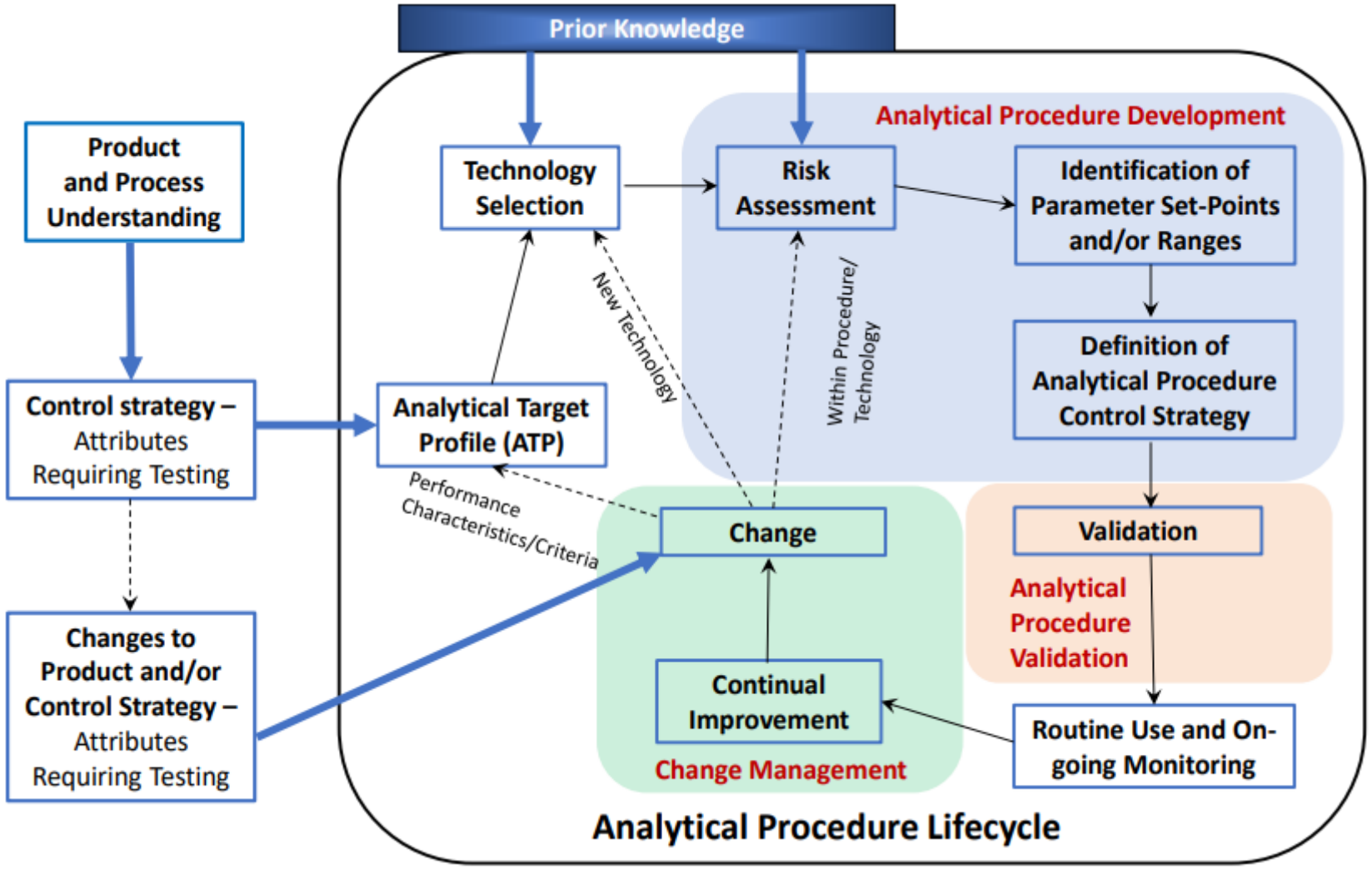
SPECIFIC ITERATIVE APPROACH

Based on:

- **Risk identification**
- **Risk scoring**
- **Knowledge usage**
- **Targeted knowledge generation**
- **Knowledge management**

ICHQ2 (R2) and ICHQ14, what's new?

Vision of the analytical lifecycle



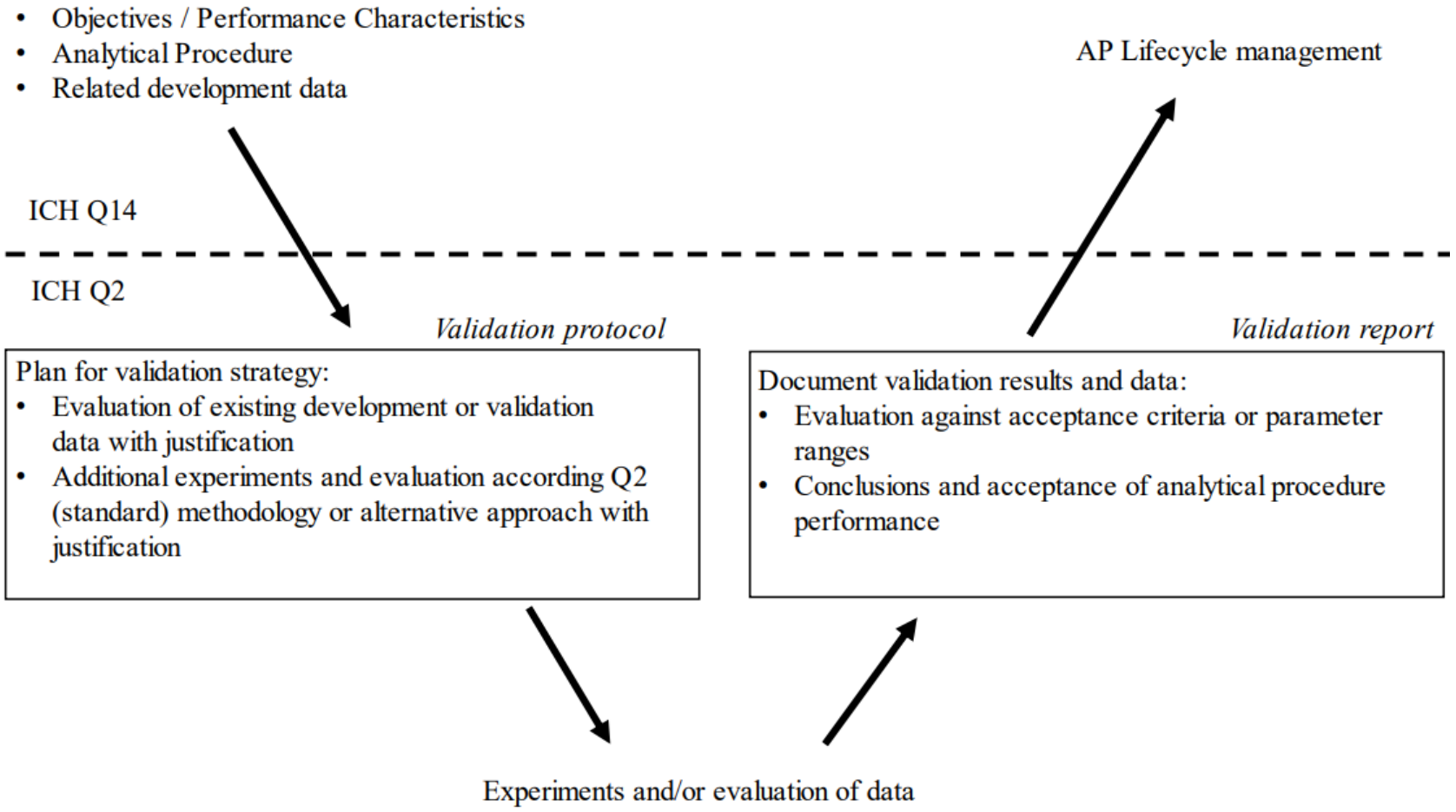
Extracted from ICH Q14 draft guidance

These operating principles are used all along the analytical lifecycle described in ICH Q14:

- Development of Analytical Procedure
  - Technology selection
  - Characterization of method parameters
  - Definition of set points for method parameters
  - + *Iterative dimension*
  - Establishment of Analytical Procedure Control Strategy (APCS)
- Validation of Analytical Procedure
- Definition of Established Conditions for an Analytical Procedure
- Post-Approval Changes management

ICHQ2 (R2) and ICHQ14, what's new?

Validation of Analytical Procedure



Extracted from ICH Q2 (R2) draft guidance

Same operating principles are proposed:

- Consider development data for re-usage as validation data

= Check if the existing knowledge covers the risks

  - Justify usage of development data
  - Performance characteristics come from development

  = "criteria"

- Perform additional experiments

Acquire additional targeted knowledge if required

- Evaluate performance according to ICH Q2 methodology and against criteria

- Conclude on acceptance of analytical procedure performance

ICHQ2 (R2) and ICHQ14, what's ready now, ready soon or may be for later?

Items considered

- Procedure Development
- Procedure Validation
- Analytical Procedure Control Strategy and Ongoing Procedure Monitoring
- Established Conditions, change management and Post-Approval Change Management Protocols

ICHQ2 (R2) and ICHQ14, what's ready now, ready soon or may be for later?

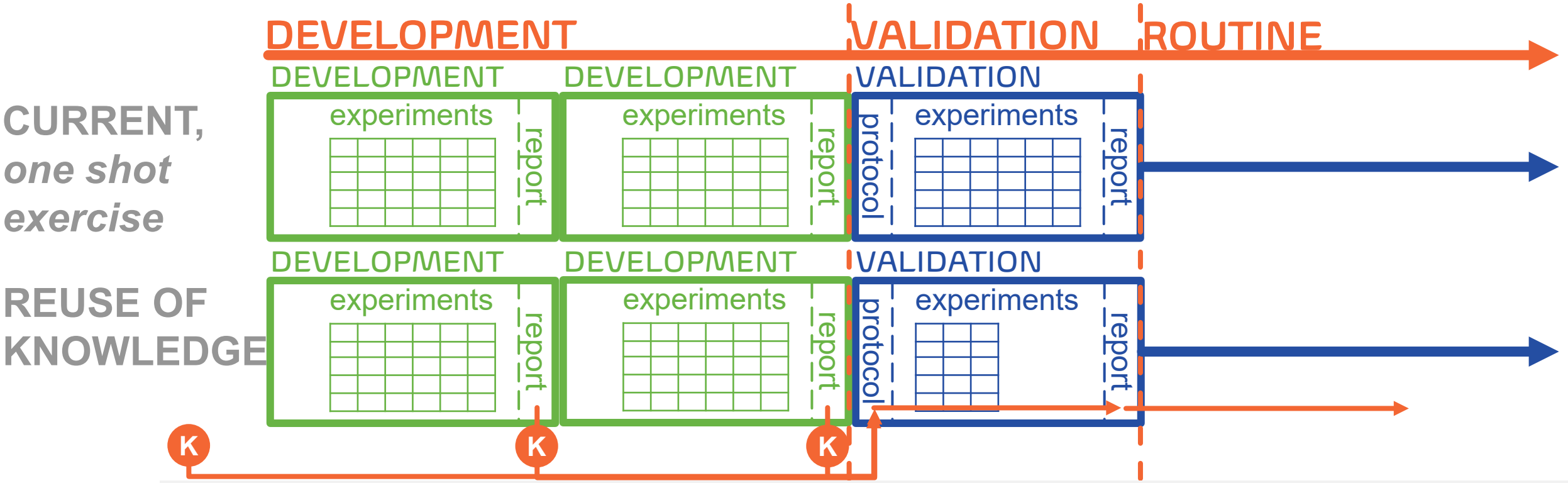
Procedure Development

- Technically speaking, the principles of AQbD are widespread and well understood in the field.
- It is also acknowledged that applying these principles brings robust procedures.
- Sometimes there is the perception that applying the enhanced approach proposed by ICH Q14 relies (only/mainly) on huge Designs of Experiments (DoEs) that consume a lot of resources and this, for outcomes similar than those obtained when using the minimal approach and scientific expertise.

  This perception should evolve towards a systematic approach of risk management through the use of prior knowledge (including scientific expertise) and the generation of targeted knowledge (potentially through DoEs). This would lead to focusing resources and efforts where needed.
- The value of the knowledge generated during development for the validation and commercial spaces is still not fully understood from an operational perspective (see further).

ICHQ2 (R2) and ICHQ14, what's ready now, ready soon or may be for later?

Procedure Validation



- Knowledge is transferred and reused from one stage to the next. (Knowledge = conclusion from previous study)
- The conditions of acquisition of knowledge must be auditable and justified as representative of future procedure.
- More difficult to apply on quantitative performance parameters: Precision, Accuracy, Linearity and Range

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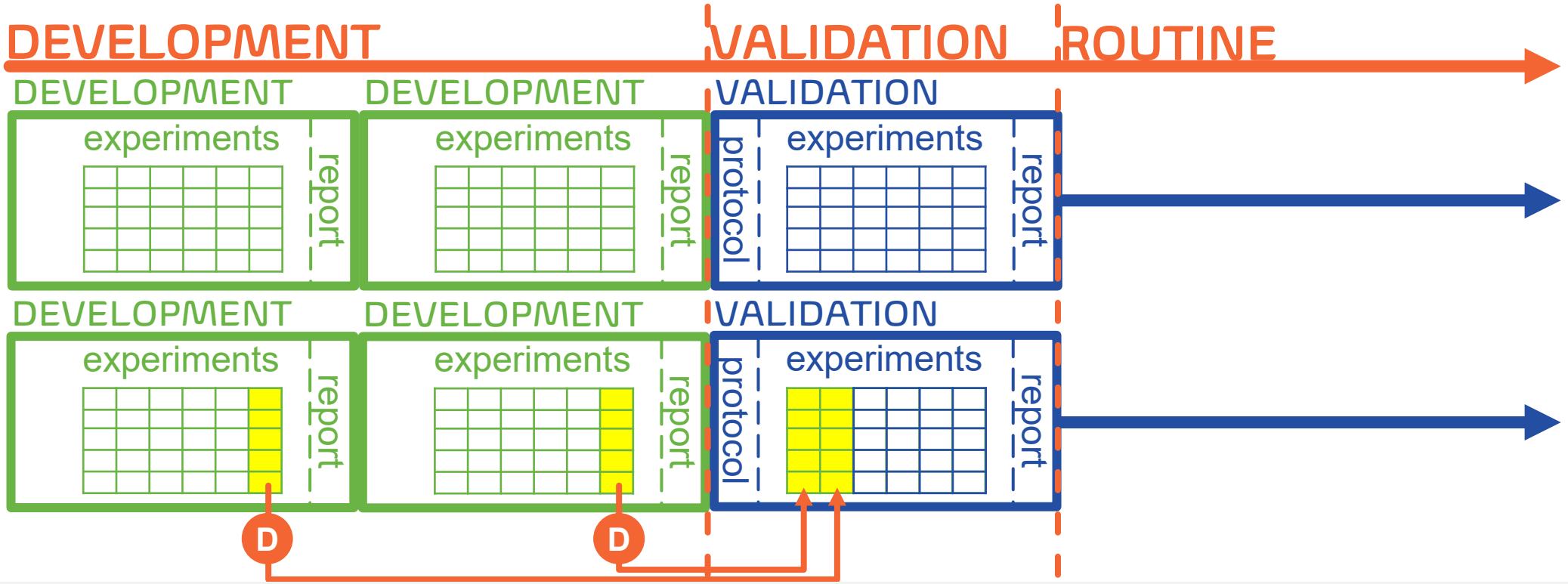
ICHQ2 (R2) and ICHQ14, what's ready now, ready soon or may be for later?

Procedure Validation

CURRENT, ***one shot exercise***

REUSE OF DATA



- Data from one stage are used, together with data from a further stage, into a statistical analysis.
- The conditions of acquisition of data must be auditable and justified as representative of future procedure.
- Same samples must be available and stable across the different stages.
- Applicable to quantitative performance parameters.
- Will require evolution of current paradigms and development of specific processes, statistics and digital tools.

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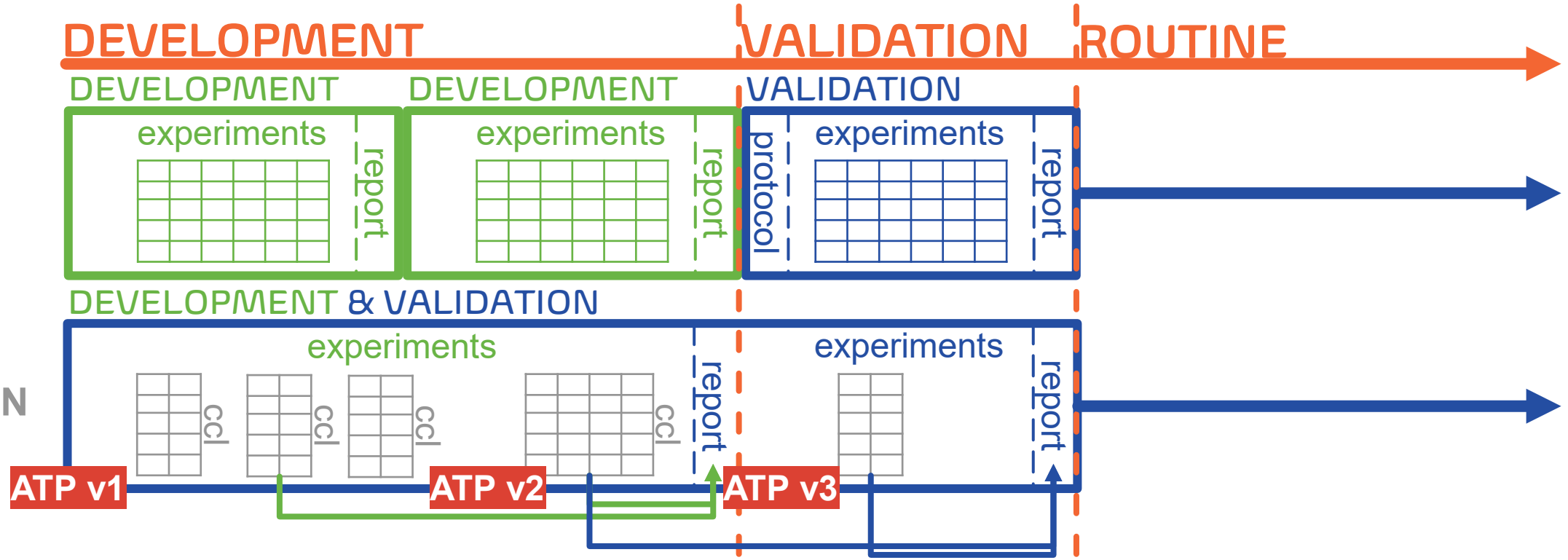
Procedure Validation

CURRENT, ***one shot exercise***

ONGOING VERIFICATION



- Main elements from the validation protocol are covered by a systematic iterative ATP process + pre-defined and conditionned experimental designs and supported by a Quality Risk Management Process.
- The conditions of acquisition of data and knowledge must be auditable and justified as representative of future procedure.
- Will require significant evolution of current paradigms and development of specific processes, statistics and digital tools.

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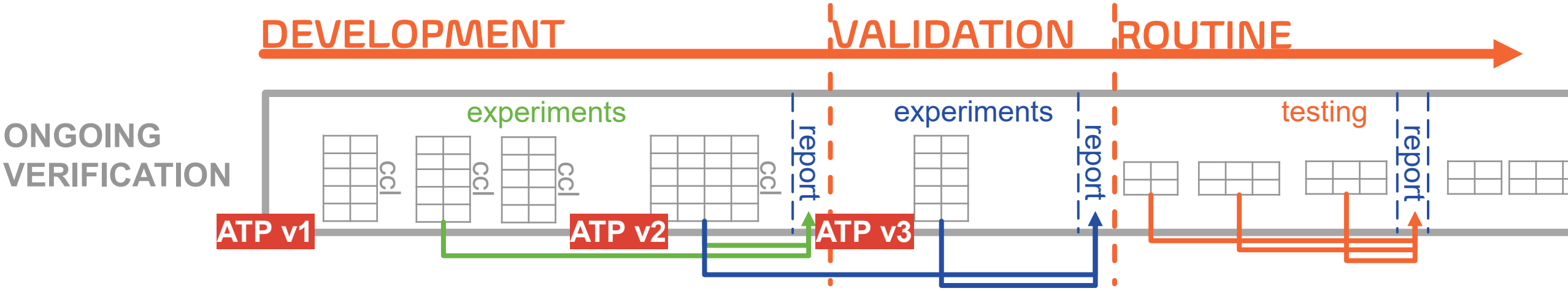
ICHQ2 (R2) and ICHQ14, what's ready now, ready soon or may be for later?

Procedure Validation



- The performance of the procedure is evaluated in a continuous fashion using data acquired during routine testing. The validated status can be verified at anytime
- Will require significant evolution of current paradigms and development of specific processes, statistics and digital tools.
- Better understanding of the effect of procedure parameters on performance elements are provided by an evolved application of enhanced approach with the (additionnal) intention to prepare solid Analytical Procedure Control Strategy (APCS) and procedure performance monitoring.
- This considers that knowledge is also produced during routine use of the procedure.

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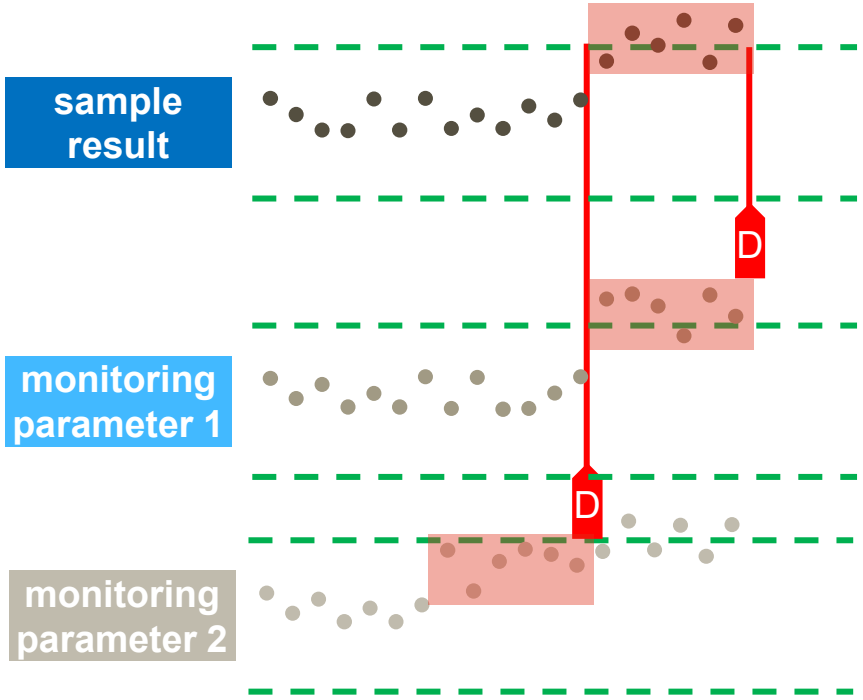
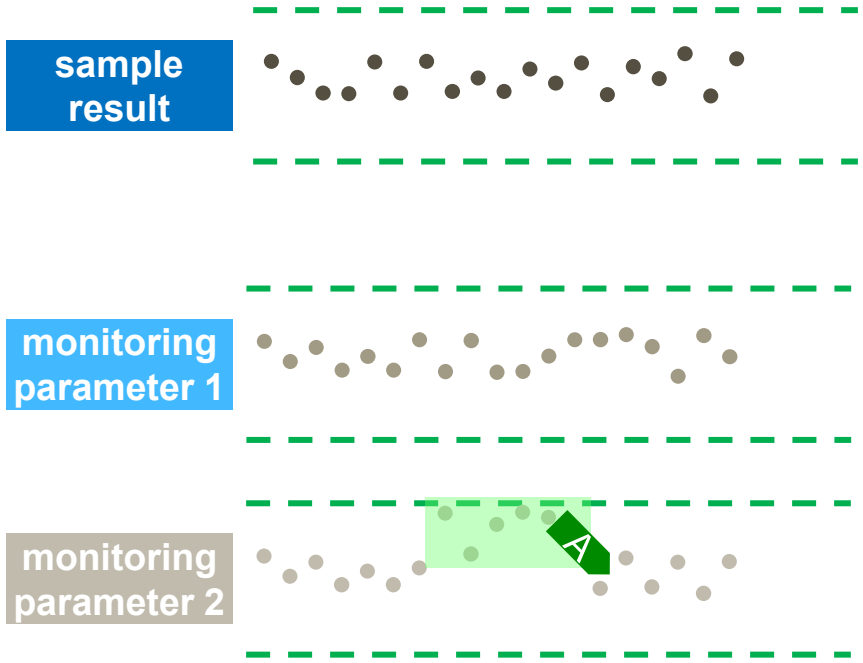
ICHQ2 (R2) and ICHQ14, what's ready now, ready soon or may be for later?

Analytical Procedure Control Strategy and Ongoing Procedure Monitoring

Towards advanced monitoring



Up to anticipactive monitoring



- The performance of the procedure is evaluated in a continuous fashion using data acquired during routine testing. The validated status can be verified at anytime.
- Potential drifts and shifts can be anticipated and action can be taken in order to ensure the maintenance of the performance of the procedure before any unacceptable evolution.
- Such approach would also ensure full control of procedure performance upon changes.

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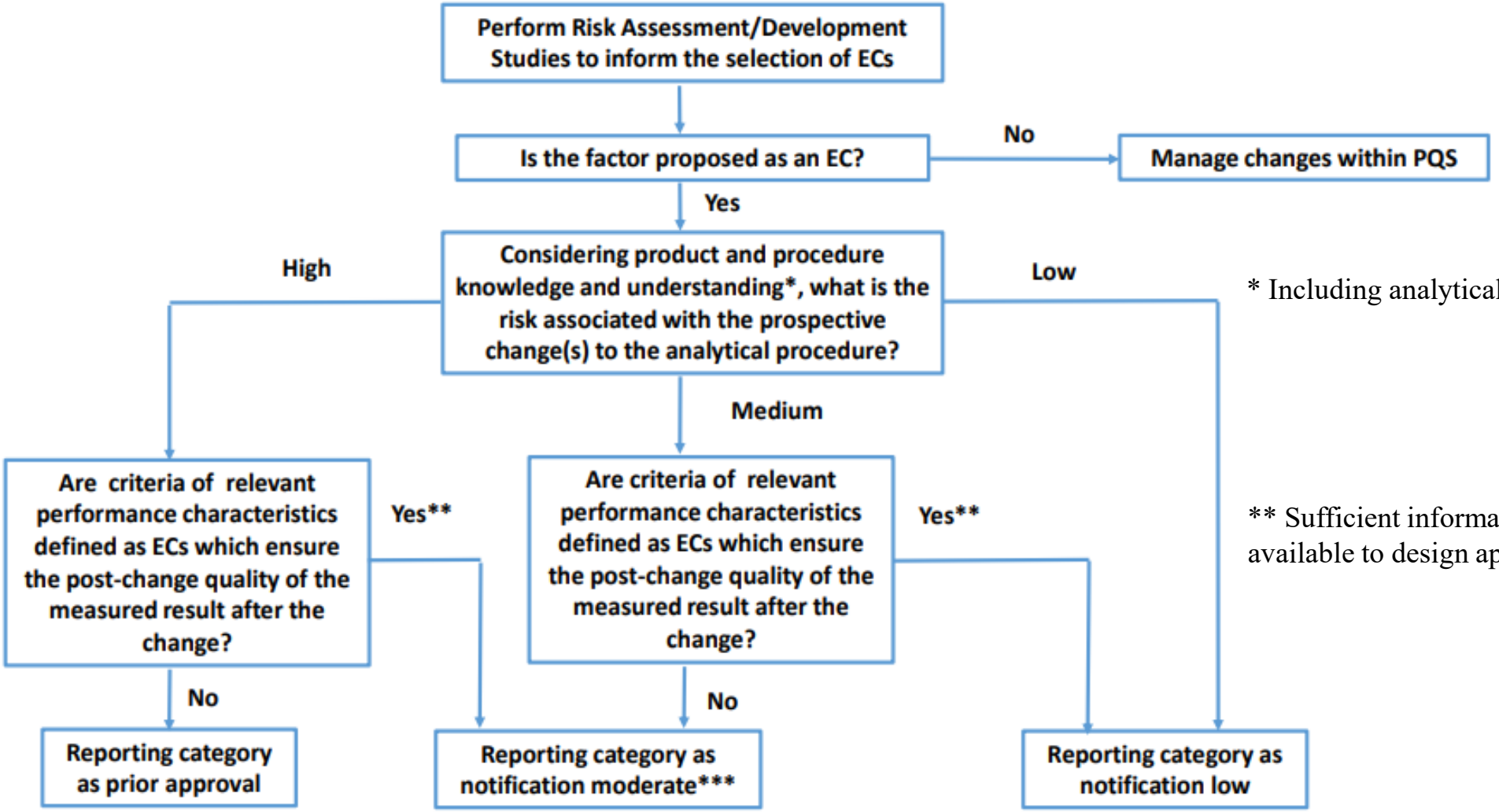
Established Conditions and change management



* Including analytical procedure control strategy

** Sufficient information or prior knowledge should be available to design appropriate future bridging studies

Extracted from ICH Q14 draft guidance

*** In some cases, moderate risk changes proposed by the company may require prior approval based on health authorityfeedback

ICHQ2 (R2) and ICHQ14, what's ready now, ready soon or may be for later?

Established Conditions and change management

- The concept of Established Conditions (EC) is well understood in the field as well as the expected inputs from development phases in order to establish EC.
- While the application of the enhanced approach is recognized to lead to better characterized and more robust procedures; the registration of EC defined using the same enhanced approach might not yet be perceived to its full potential.

  Indeed, A) the parameters from the procedure covered by EC, in most cases, are anticipated as being totally under control and not subject to changes along the analytical lifecycle.

  B) exploring, validating and registering other parameters from the procedure, that are anticipated to be potentially subject to changes along the analytical lifecycle, is associated with a negative cost-benefits balance.

  This will evolve when the perception of ECs will have evolved to established performances characteristics
- The registration of Post-Approval Change Management Protocols another, as valuable approach for the preparation of prospective management of changes along the analytical lifecycle.

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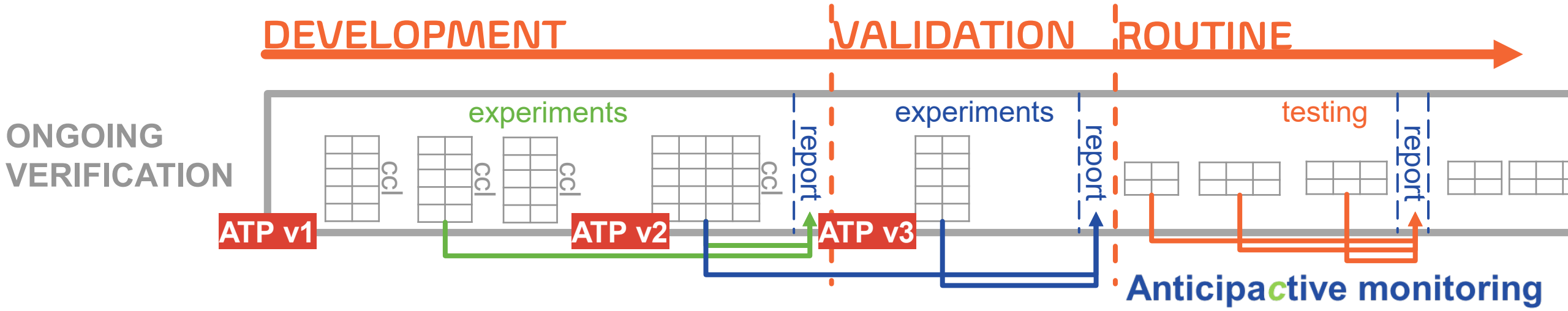
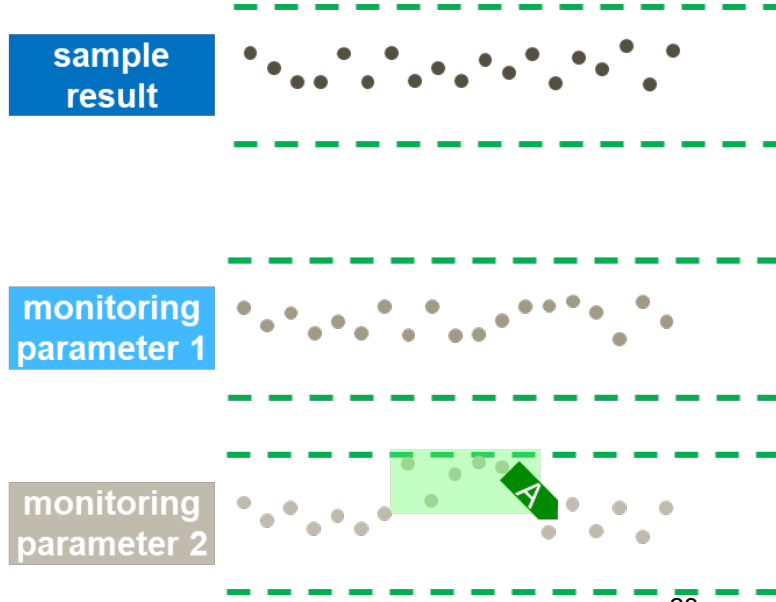
ICHQ2 (R2) and ICHQ14, where may it lead us?





- Could the development of continuous validation and anticipactive monitoring lead us to an enhanced paradigm for the validation and the control of analytical procedure performance?

- Could we move

from **Established Conditions** to **Established Performances?**

THANK YOU,

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The Analytical R&D LT

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