

Workshop - Mercoledì 10 giugno

Risk-based thinking come vera intelligenza per il mondo farmaceutico

Moderatori

Piero Iamartino
AFI

Paolo Mazzoni
PTM Consulting



SIMPOSIO EFT



Informed decisions
for better process

Workshop schedule

10:10 – 10:40

La nuova era dell'intelligenza del rischio

10:40 - 11:10

Nuova ICH Q1: product intelligence per un approccio innovativo alla stabilità

11:10 – 11:35

ICH Q3E: approccio risk-based integrato per la valutazione di E&L

11:35 – 12:00

Il dato come bussola: l'analisi statistica a supporto del rischio

12:00 – 12:25

Dalla teoria alla pratica: dalla gestione dello studio di stabilità all'analisi dei dati

12:25 – 12:30

Conclusione dei lavori



ICH Q3E: integrated risk-based approach for E&L evaluation

Giorgia Romagnoli

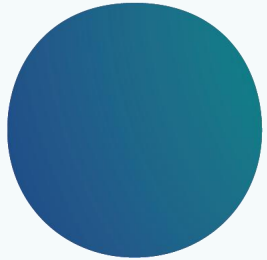
Professional Consultant - PTM Consulting Srl

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#1 - Introduction

#2 – Operative framework

#3 – Conclusions and take-home messages



Introduction

E&Ls are everywhere and it is a risk

TYLENOL® Paediatric 2010



- 2,4,6-Tribromophenol from 2,4,6-Tribromoanisole (wood preservative)
- Nausea, vomiting, diarrhea
- Product recall, authorities actions

EPREX® prefilled syringes 2002



- Silicone oil from syringes
- Immunogenicity, pure red cell aplasia (PRCA), deaths
- Global product recall, regulatory investigation

SINGLE-USE BIOREACTOR 2008-2012



- Release of additives from components
- Toxicity, cell culture death
- Economic damage, review of single-use components

SUPOR® FILTER 2000

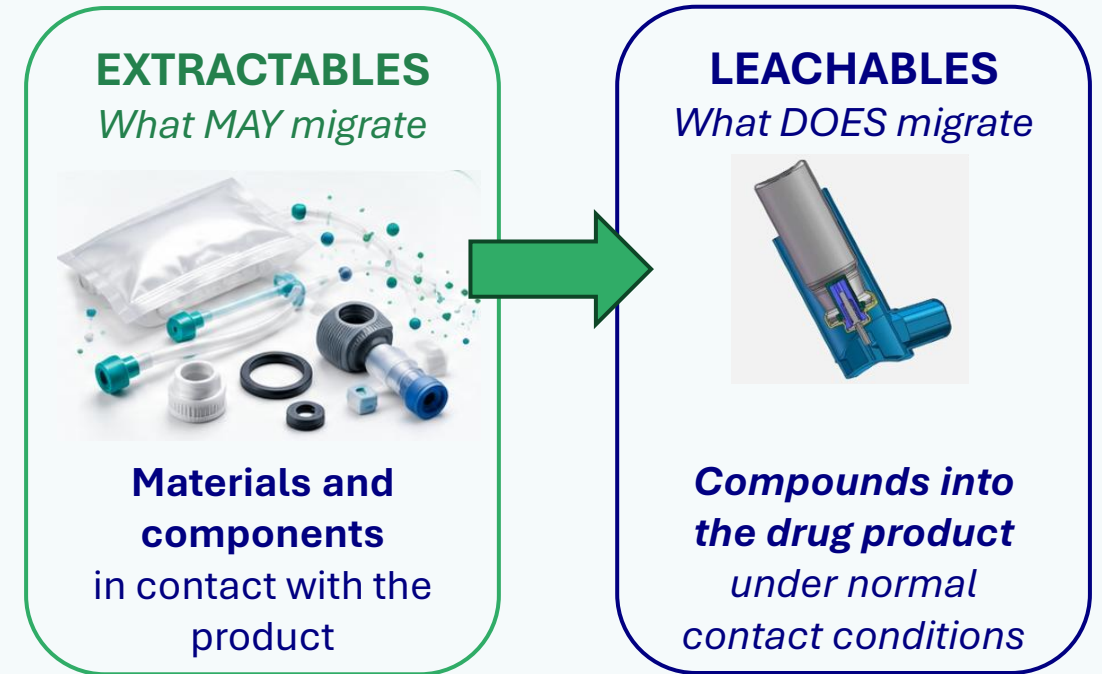


- Oxidant component release from PES membrane
- Protein oxidation, biological activity damage
- Change in protocols (pre-flusing), filter qualification

Why E&L matters today

Impacts:

- Patient safety
- Product quality
- Regulatory expectation



What is really in scope?

- Manufacturing equipment
- Single-use systems
- Packaging components
- Combination products
- Drug delivery device components

“Any material potentially interacting with the product **across the lifecycle.**”



Regulatory requirements

European Commission, EUDRALEX Volume 4, «Good Manufacturing Practices, Medicinal Products for Human and Veterinary Use», Chapter 3 «premise and Equipment»

*“Production equipment should not present any hazard to products. Parts of production equipment that come into contact with the product **must not be reactive, additive or absorptive** to such an extent that it will affect the quality of the product and thus present any hazard”*

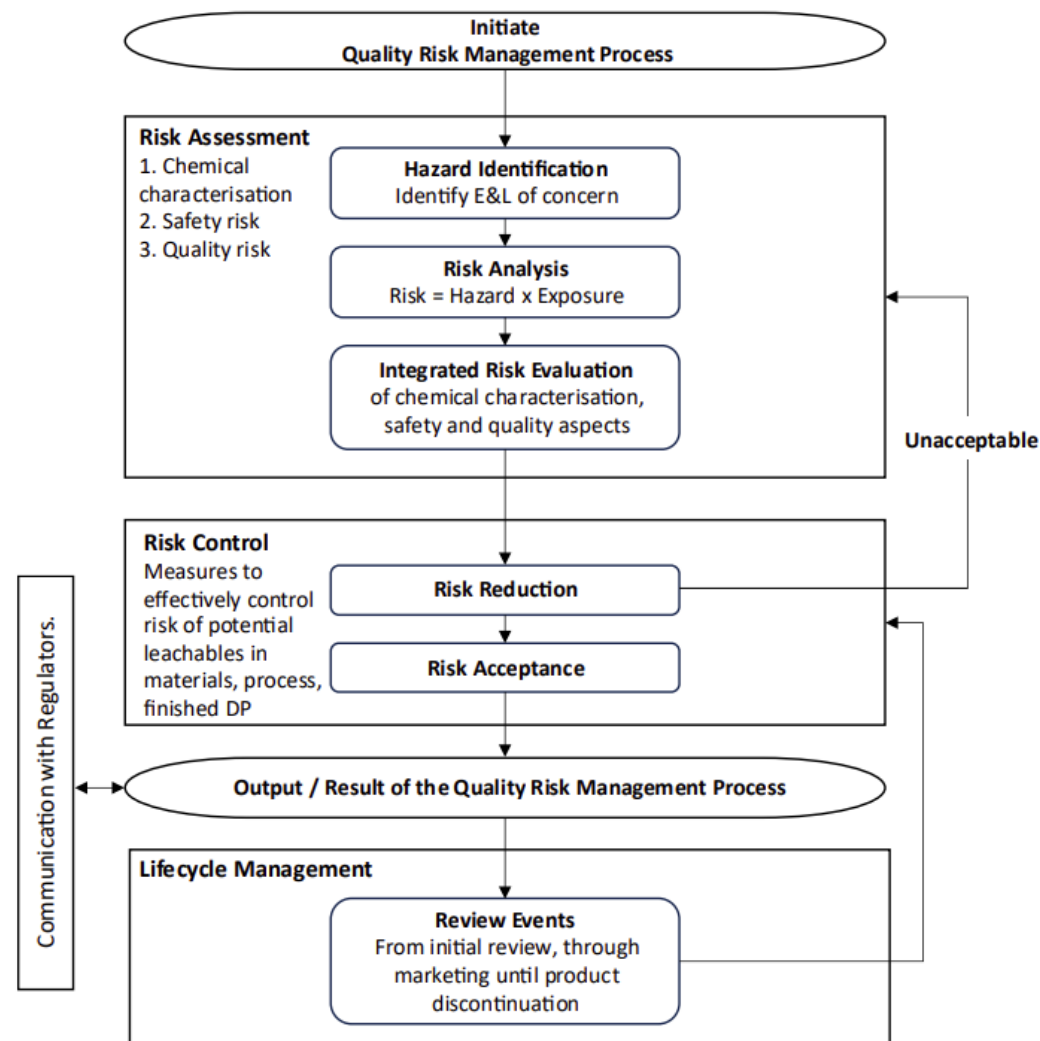
FDA, 21 Code of Federal Regulations, Part 211, «Current Good Manufacturing Practise for Finished Construction»

*“Equipment shall be constructed so that surfaces that contact components, in-process materials, or drug products **shall not be reactive, additive, or absorptive** so as to alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.”*

What changes with ICH Q3E

- **Harmonize** global regulatory expectations for E&L assessment
- Align E&L management with **QbD**, and existing ICH impurity guidelines
- **Integrate safety assessment** with exposure- and route-based qualification thresholds
- The focus is no longer only identifying compounds, but understanding and **controlling patient-relevant risk**
- Promote a holistic, science- and **risk-based control strategy** with Application of **ICH Q9** QRM principles

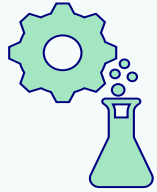
E&Ls became part of product knowledge





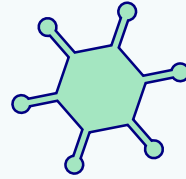
Operative framework

The four pillars of the integrated approach



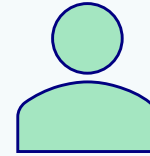
Product/process understanding

Materials interaction
Process conditions



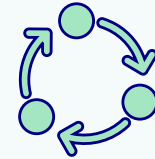
Chemical characterization

Extractables profile
Analytical understanding



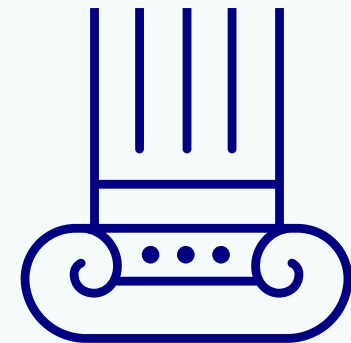
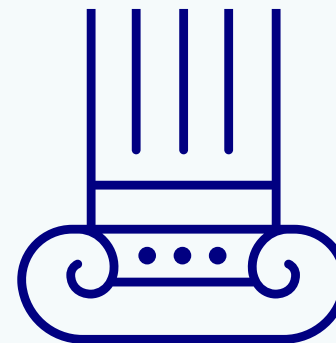
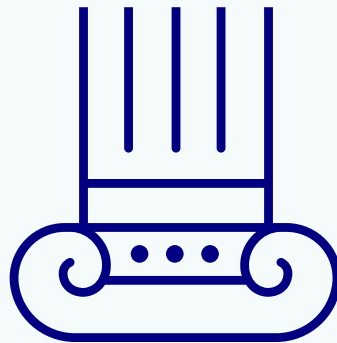
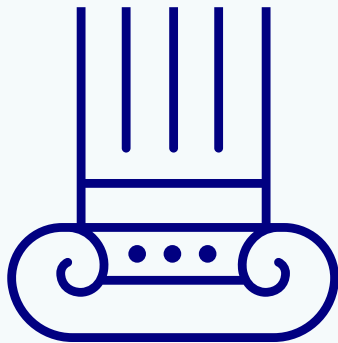
Toxicological assessment

Exposure-based qualification
Patient safety

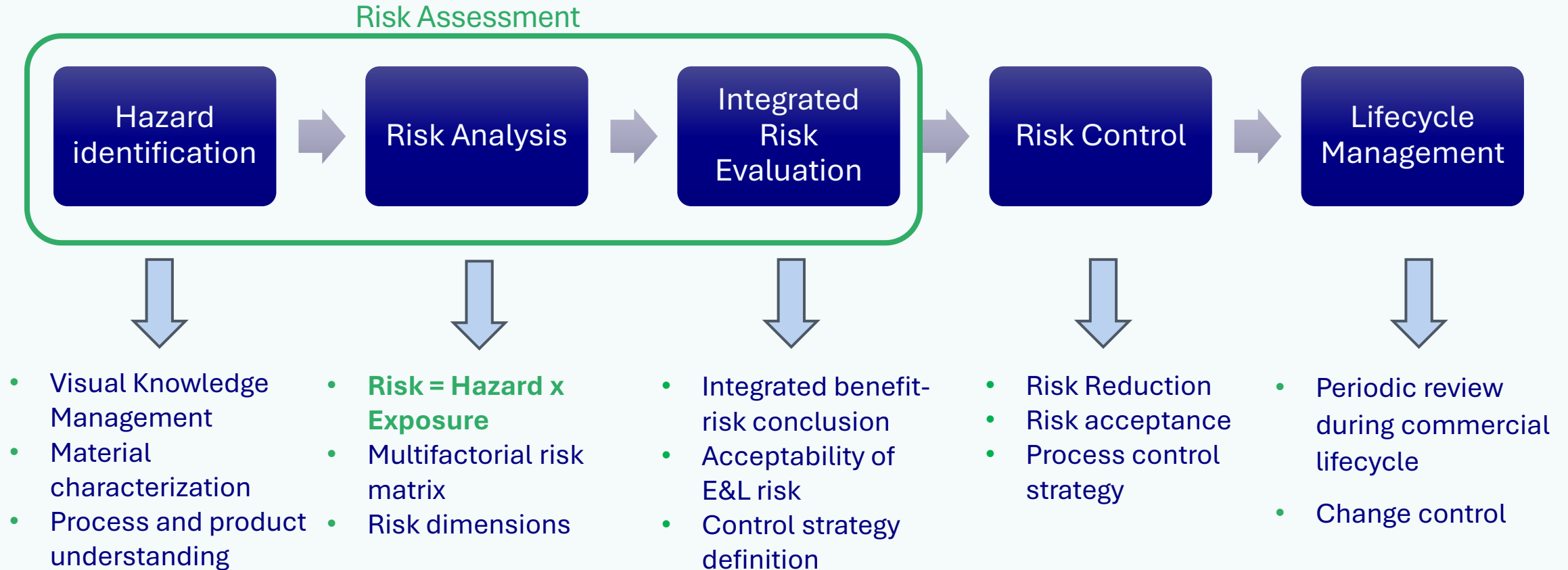


Lifecycle risk management

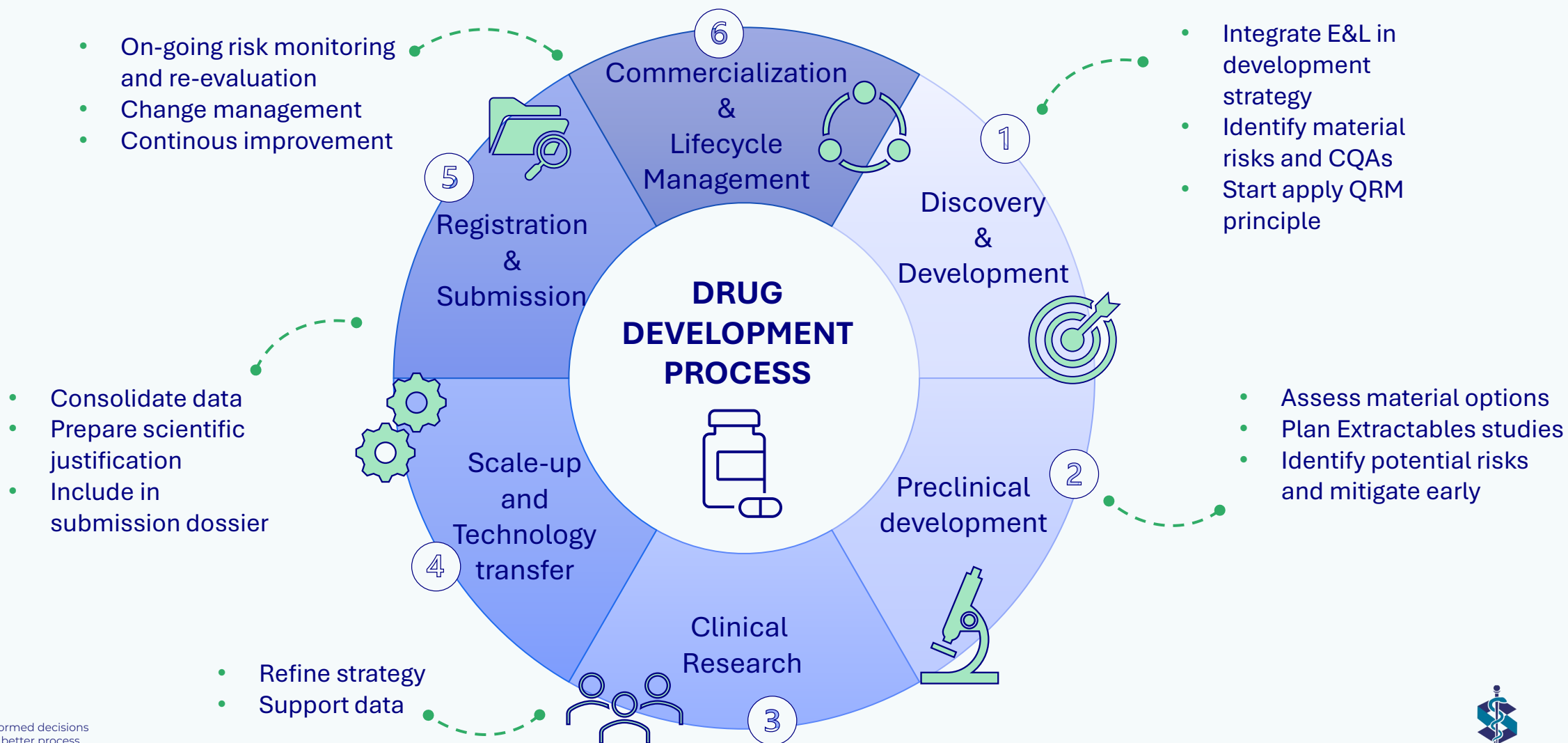
Risk assessment
Continuous evaluation



Quality Risk Management Process for E&L

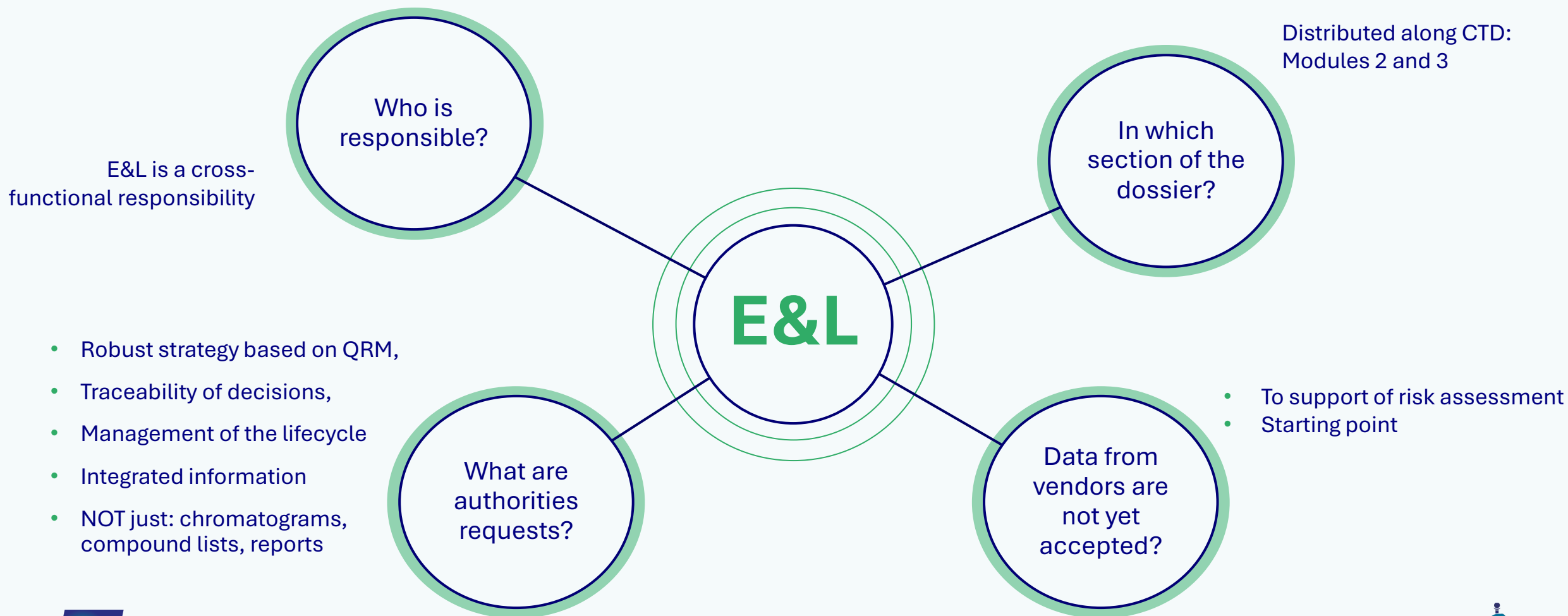


When should you start thinking about E&L?



ICH Q3E: integrated risk-based approach for E&L evaluation

Building an E&L Strategy: The Critical Questions





Conclusions and take-home messages

E&Ls are everywhere and it is a risk...under control

TYLENOL® Paediatric 2010



- VOC monitoring during storage
- Screening TBA in packaging materials

EPREX® prefilled syringes 2002



- Formulation-materials interaction evaluation
- Change of material

SINGLE-USE BIOREACTOR 2008-2012



- Multi-technique screening
- Validated pre-flushing

SUPOR® FILTER 2000



- Harsh extraction tests
- Change materials
- Enhanced quality controls

Take-home messages

ICH Q3E is a key reference for a responsible and science-based management of E&L risk



ICH Q3E promotes an integrated management of E&L risk



Quality decision matters more than the quantity of data



A risk-based approach enables:

- More focused studies
 - Greater scientific robustness
-



Solid approach is challenging but essential and highly beneficial

- Implementing ICH Q3E requires expertise, experience and a structured method.

Thanks for listening

ICH Q3E: approccio risk-based integrato per la valutazione di E&L



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Any questions?

Do you need any information?

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