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Meet Our Speakers

James Biddlecombe

Business Transformation and CTR Lead
DLRC Ltd, DLRC Group

James's journey with the EU CTR started in 2017, working at the EMA in the CTIS business team. Over the last six years, he supported the development of the regulation and guidance and the development of CTIS and has supported clients with CTR readiness and CTA submissions. He has supported numerous clients in getting them ready for the CTR Go-Live through training, redesign of operating models, and updates to processes and procedures. More recently, he supports clients with strategic direction for trials submitted under the CTR and helps to navigate EU CTR guidelines and ensure CTA document compliance with the regulation.

Contact James | Connect with James on LinkedIn

Wafa Bouaziz

Managing Director & Head of Regulatory Affairs, Orphix Consulting GmbH, DLRC Group

Wafa is a global regulatory professional with a broad experience across various therapeutic areas including rheumatology, anti-infective, dermatology and oncology. With her strong scientific, regulatory, and managerial expertise, she successfully led early development projects (CTA and IND submissions) and full development programs (MAA and NDA/BLA). She has supported clients with several investigational products through their European regulatory journey, advising on CTA requirements from a strategic perspective. She also acts as the EU legal representative under CTR and helps companies ensure compliance with the new regulation.

Contact Wafa | Connect with Wafa on LinkedIn

Today’s Agenda

What do you really need to know about CTR and related legislation?

CTR in the current EU Regulatory Landscape

Can you summarise the new EU Clinical Trial Regulation, on one slide?

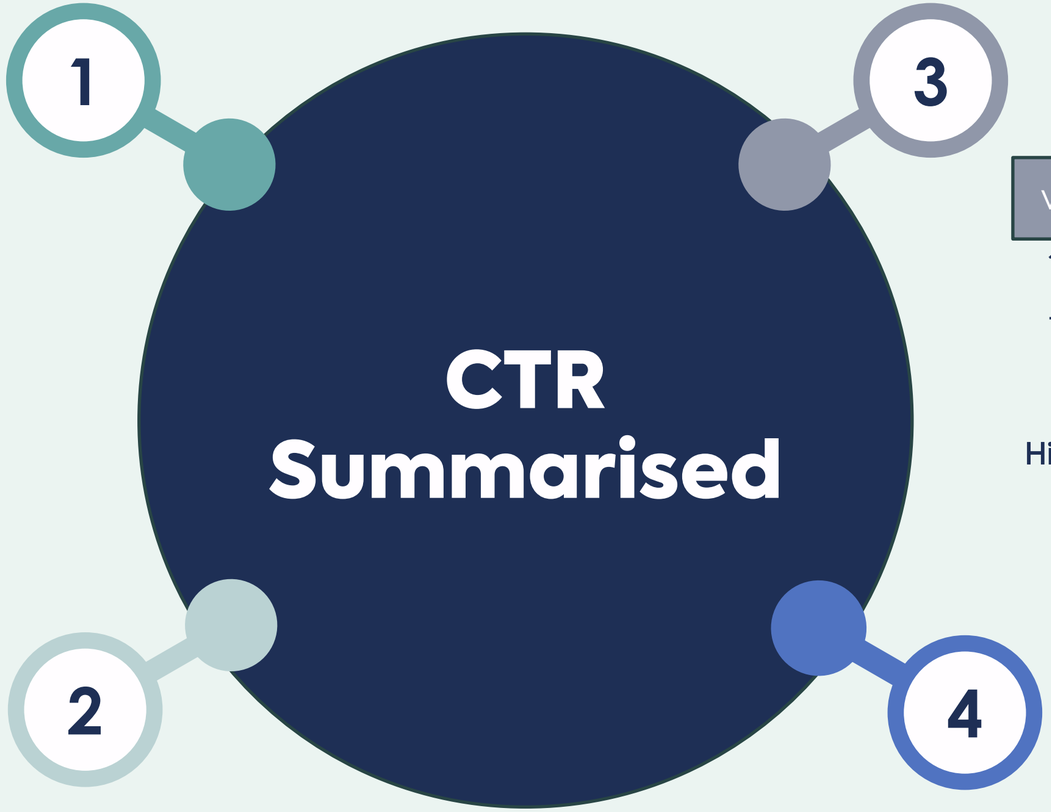
We will certainly give it a try…

Aim and Targeted Outcomes

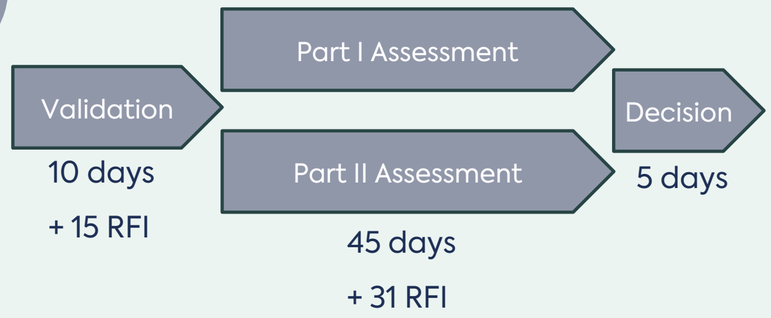
1. Ensure high standard of safety and efficacy for trial subjects
2. Harmonize the process of conducting clinical trials across the EU.
3. Facilitate cross-border collaboration in research
4. Promotes transparency and accountability.

Challenges

1. Implementation complexities
2. Compliance with new requirements
3. Stakeholder adjustments



The Application



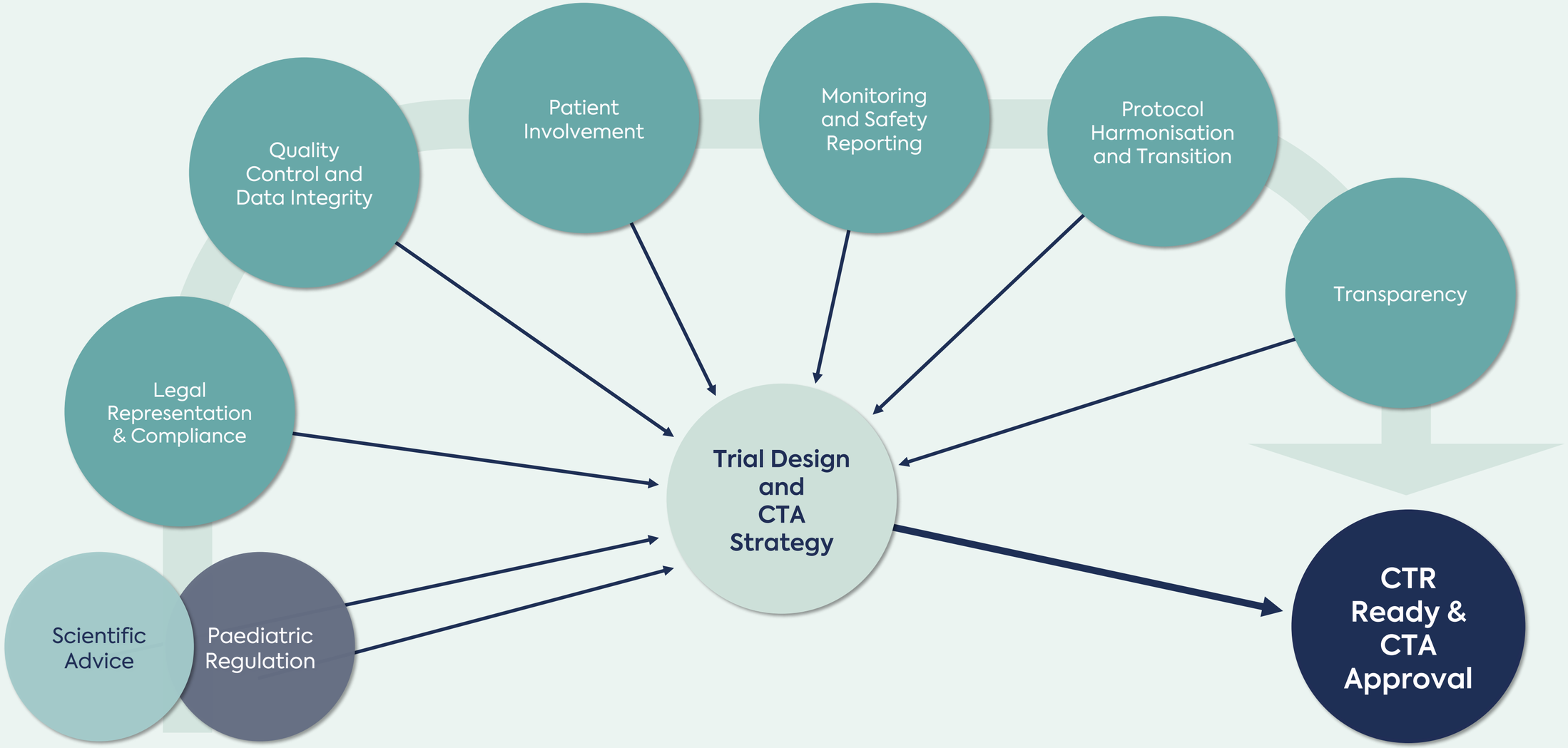
High Risk – RFI response times:
10 calendar days (validation)
12 calendar days (assessment)

Before you can submit…

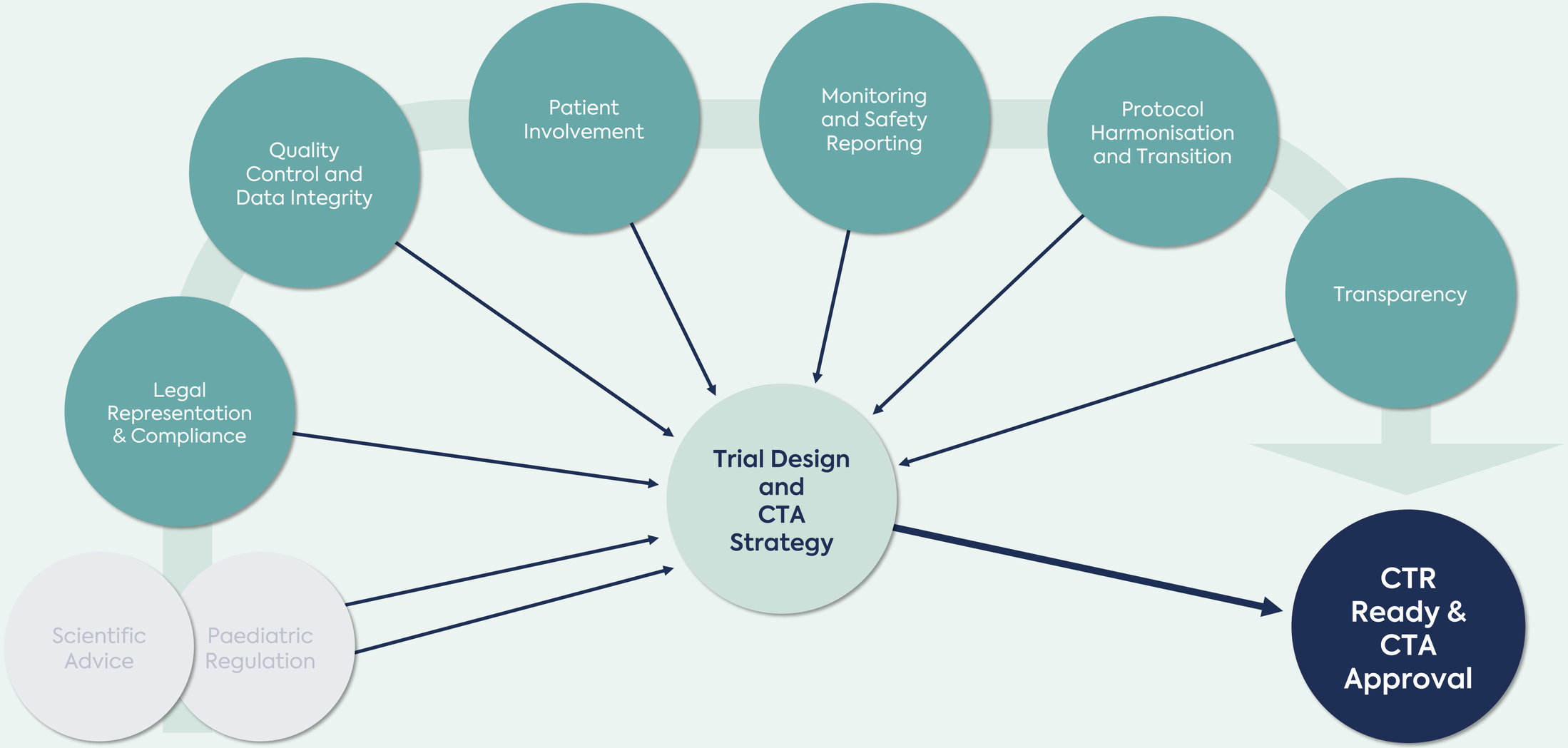
1. Establish your EU Legal Representative
2. Register the Sponsor in EudraVigilance
3. Register the Sponsor in OMS (SPOR)
4. Register the IMP(s) / AxMP(s) in xEVMPD

What do you really need to know about CTR impact on clinical trial and EU development strategy, Compliance and Best Practices?

How does CTR impact trial design and clinical development strategy?



Spotlight: What do you really need to know about the role of the EU Legal Representative?



Things have changed.
What is the responsibility of the EU legal representative under CTR?

CTD (2001/20/EC) – Article 19:

"…..the sponsor or a legal representative of the sponsor must be established in the Community……"

CTR (536/2014) – Article 74:

"Where the sponsor of a clinical trial is not established in the Union, that sponsor shall ensure that ***a natural or legal person*** *is established in the Union as its legal representative. Such legal representative shall* ***be responsible for ensuring compliance with the sponsor's obligations pursuant to this Regulation and shall be the addressee for all communications with the sponsor provided for in this Regulation.*** *Any communication to that legal representative shall be deemed to be a communication to the sponsor."*

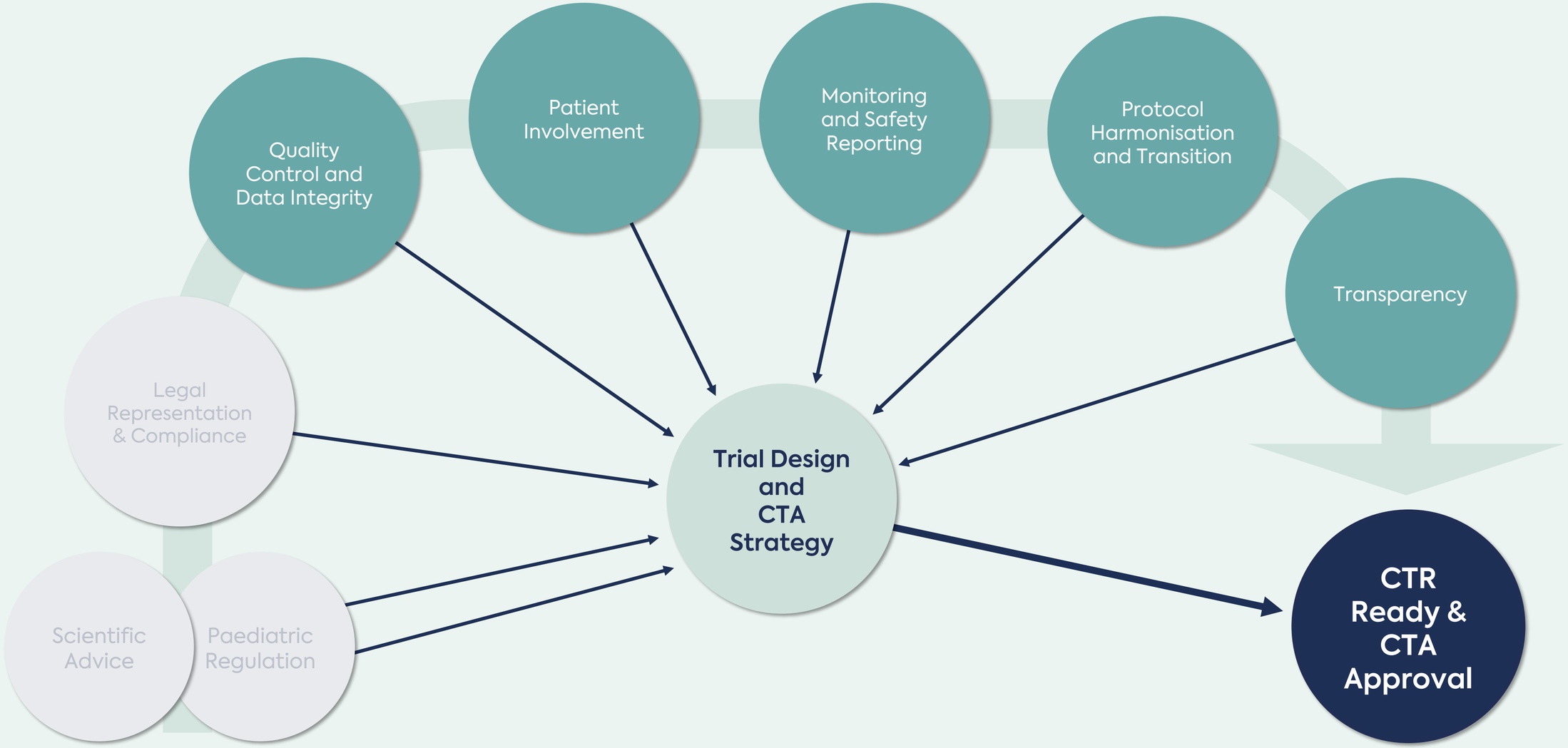
Our experience as a legal representative and how to not make mistakes that may cost you time

Common shortcomings that we have experienced when conducting Compliance Gap Analysis:

- Lack of clarity about the end-to-end responsibilities of various business partners involved in the planned trial.
- Insufficient evidence that Sponsor or its CRO's standard operating procedures cover all the necessary Sponsor's trial related duties under the GCP and the CTR (data protection, redactions, study milestone notifications, result preparation and posting etc.).
- Insurance certificates do not always cover the legal representative

➢ **Under the CTR, the EU legal representative becomes an additional safeguard for CTR and GCP adherence and is an integral part of the sponsor´s compliance strategy and best practices**

What do you really need to know about Quality Control and Data Integrity?



Quality Control and Data Integrity

"The reliability and robustness of the data generated in the clinical trial" is mentioned multiple times in the regulation!

Expected impact: Rigorous data collection procedures and controls are needed when setting up a trial to meet regulatory requirements

How to effectively ensure "the reliability and robustness of the data generated in the clinical trial"?

Guideline on computerised systems and electronic data in clinical trials

- Standardized Processes
- Data Security Measures
- Validation Requirements
- Audit Trails
- Data Backup and Recovery
- Electronic Signatures

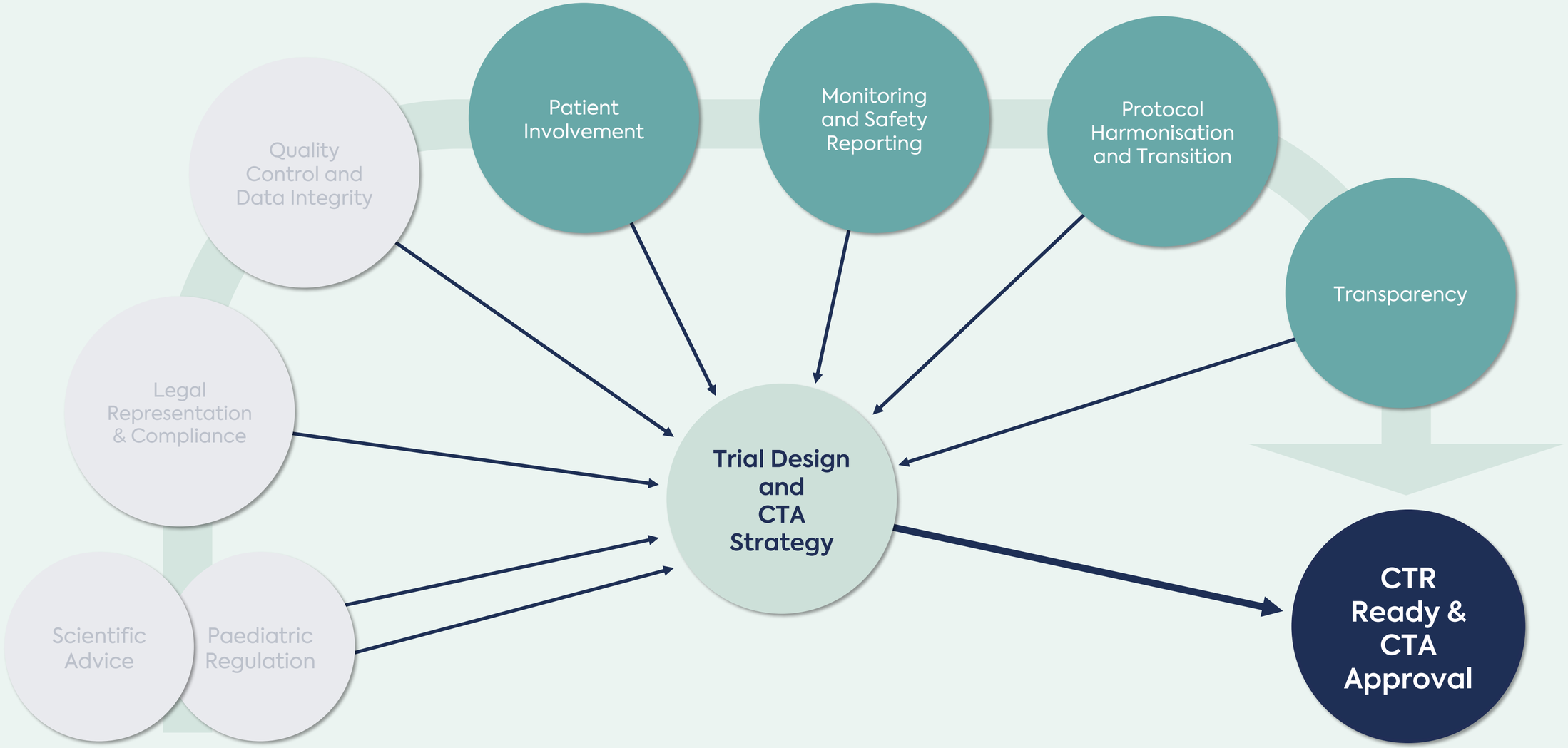
CTR Provisions

- Detailed protocols and documentation
- Informed Consent
- QMS
- Adherence to GCP
- Data Collection and Monitoring

ICH E6 (R3) - GCP

- Ensure clarity in end-to-end responsibilities
- Risk-based approach
- Fit for purpose protocols
- Evidence based decision making
- QMS
- Data management
- Monitoring and Oversight

What do you really need to know about Patient Involvement?



Patient Involvement

The regulation emphasises the importance of patient involvement in the design, conduct, and evaluation of clinical trials

Expected impact: 1) promoting inclusion of patient-reported outcomes, 2) enhancing participant recruitment and retention strategies, and 3) improving overall trial relevance and feasibility.

How to efficiently involve patients and promote their engagement?

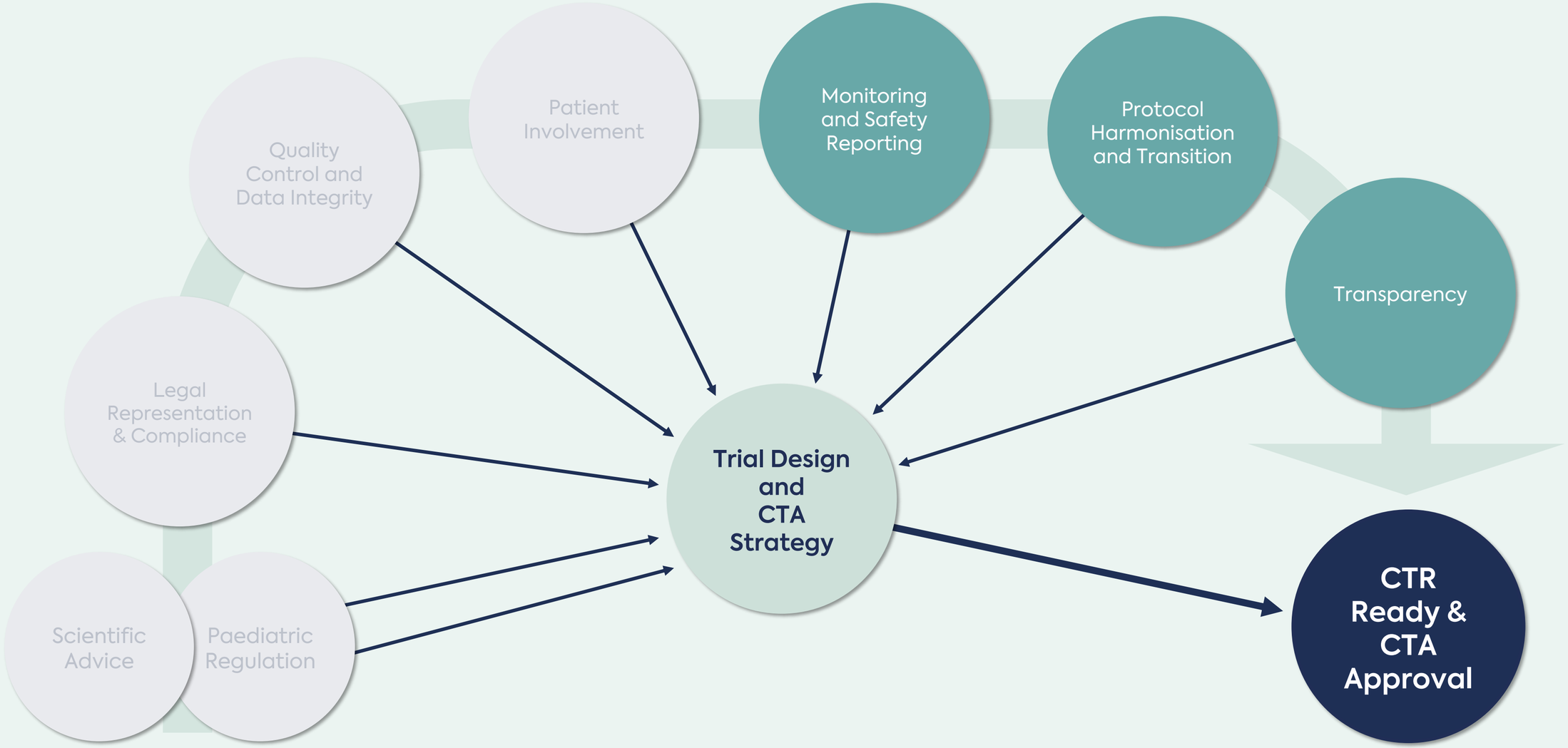
CTR Provisions

- Informed Consent (Article 5)
- Lay Summary of Results (Article 34)
- Access to Clinical trial Data for lay summaries (Article 37)
- Access to Clinical trial Data (Article 38)

Additional strategic considerations

- Patient centred approach
- Use of PROs and clinically relevant endpoints
- Fit for Purpose Protocol
- Builds for the JCA and HTA assessment

What do you really need to know about Patient Monitoring and Safety Reporting?



Patient Monitoring

Rigorous safety monitoring procedures to meet regulatory requirements (Article 48)

Expected impact: Promoting of risk-based approaches, leveraging remote monitoring technologies and adopting patient-centric approaches.

CTR and GCP Provisions

- Frequency and Intensity of Monitoring - a risk-based approach focusing on safety and data integrity
- Remote Monitoring Technologies – use of electronic data capture systems and centralized monitoring
- Patient-Centric Approaches – facilitate patient engagement and input

Resource intensive if a risk-based approach is not appropriately used

Safety Reporting

CTR puts greater emphasis on patient safety within various procedures

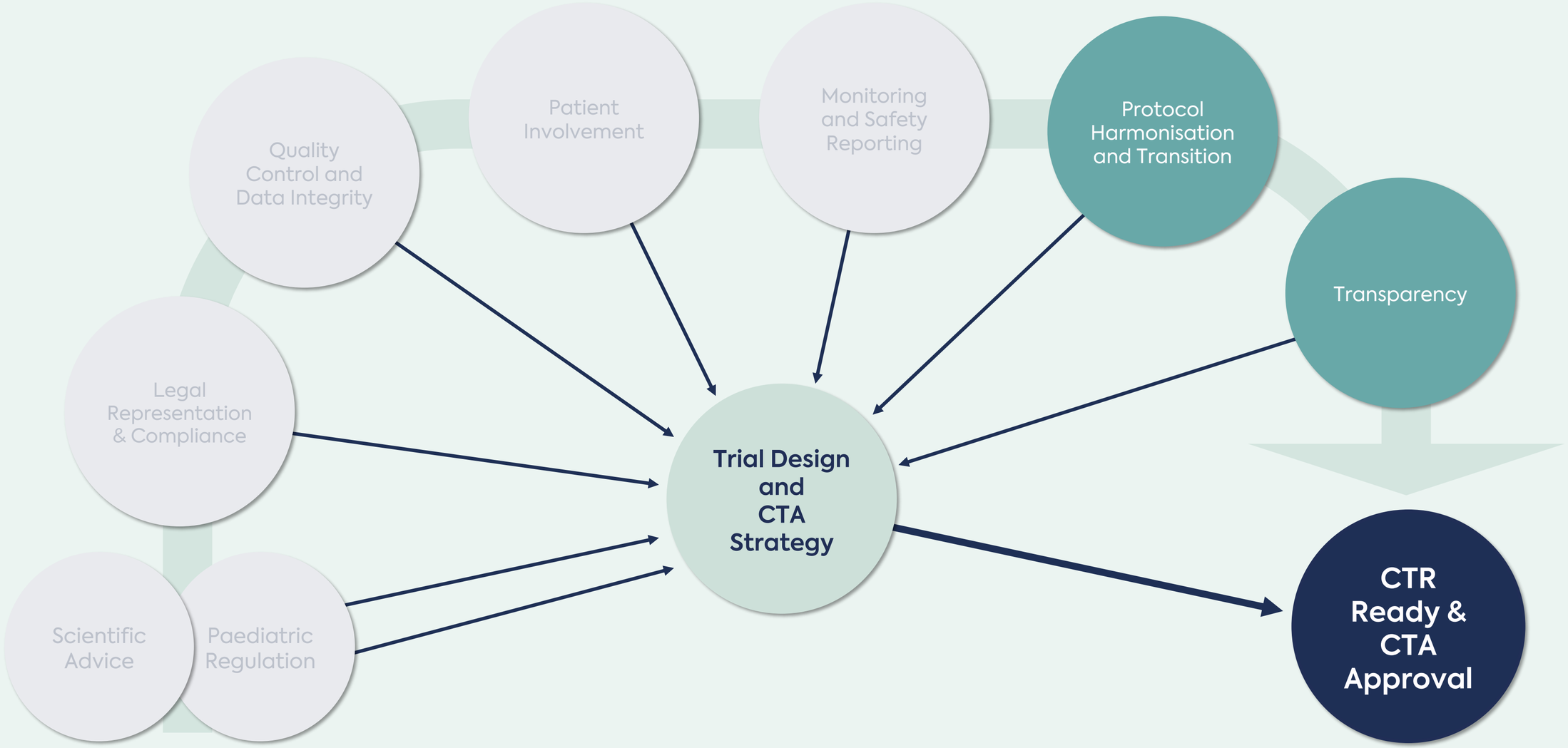
Expected impact: Promoting proactive risk assessment, timely safety reporting, and appropriate risk mitigation strategies throughout the clinical trial lifecycle.

CTR Provisions (Annex III)

- Safety Monitoring Plan
- Risk Assessment
- Safety Reporting Timelines
- Safety Monitoring Committees
- Protocol Modifications

Ensure your QMS captures all new reporting requirements and that responsibilities are clearly identified

What do you really need to know about Protocol harmonization and CTD to CTR transition?



CTD to CTR transition…tick tock, you're on the clock!

We break down a CTD to CTR transition into three distinct 'stages' to help with understanding

The authorisation in Stage 2 **must be completed before end of January 2025**

Stage 1 – Pre-Transition activities

- Harmonise / Consolidate protocol
- Prepare 'minimum' dossier
- Register in EMA systems
- Approve EU Legal Rep

1

Stage 2 – Application in CTIS

- Expedited review timeline
- Requests for Information

2

Stage 3 – Alignment

- At the time of the first CTR substantial modification

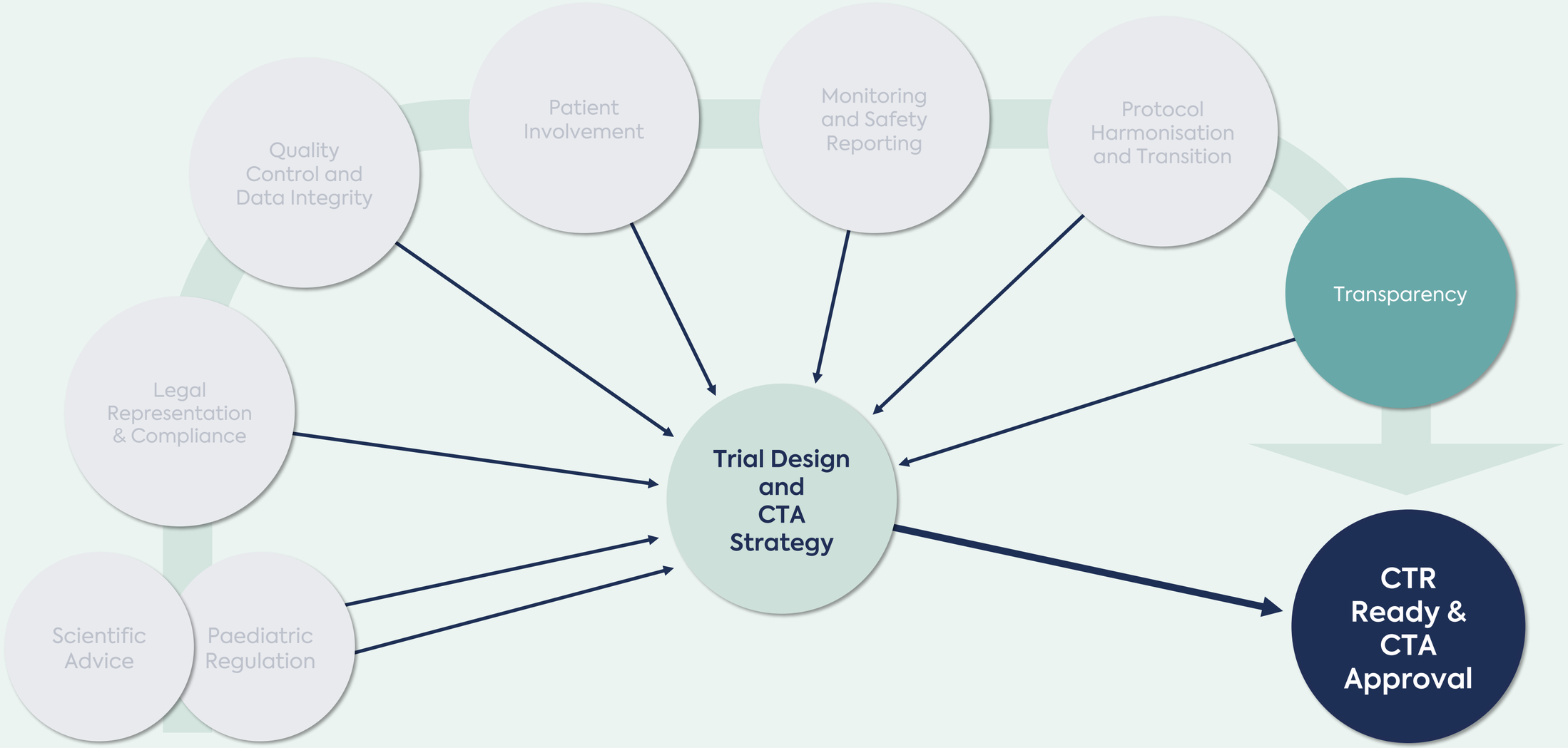
a) If Part I SM, align Part I

b) If Part II SM, align Part II

c) If Part I & Part II SM, align Part I and Part II

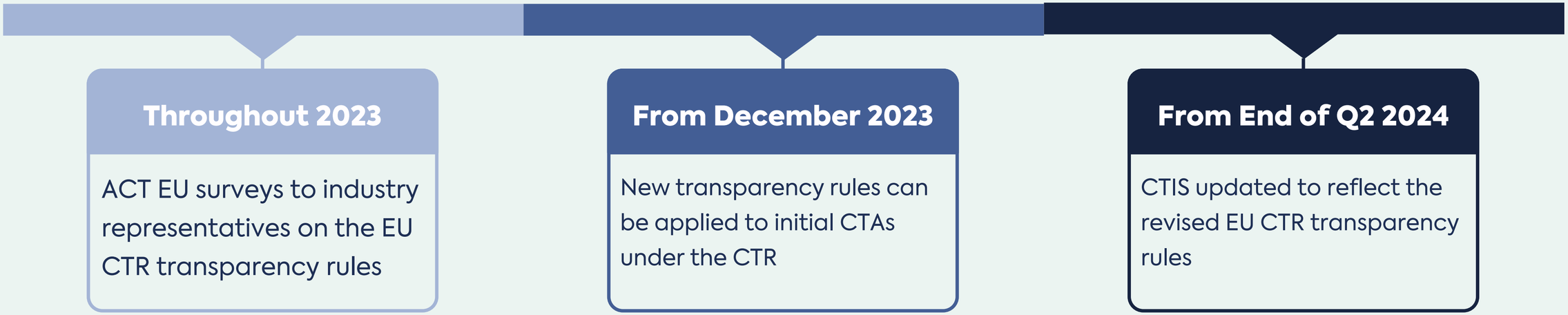
3

What do you really need to know about EU CTR transparency?



EU CTR Transparency

Our best advice is take advantage of the revised transparency rules **now**!



In practice, this means that:

- Fewer documents are subject to publication; it's now a 'patient focus'
- The deferral mechanism is removed
- RFI responses are never published - **be careful of this before the CTIS update in 2024**

Any questions?

Can we summarise the overall impact of CTR on EU clinical development strategy, on one slide?

We think we have got this one covered…

Have you considered….

- Positioning the EU Legal Representative as an additional safeguard for CTR and GCP adherence and an integral part of the sponsor´ s compliance?
- Ensuring rigorous data collection procedures and controls to ensure the generated data's reliability, robustness and integrity?
- Promoting patient involvement and engagement when designing the key elements of clinical protocols?
- Advocating for a risk-based approach rather than a one-size-fits-all?
- Necessitating timely safety reporting, and appropriate risk mitigation strategies throughout the clinical trial lifecycle?
- Transitioning ongoing CTD studies to the CTR, leveraging the expedited review process?
- Protecting your confidential information and personal data in documents made public under the revised CTR transparency rules?

Thank you

How can DLRC help you maximise your products' and company's potential?

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