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The Safety Journey for Advanced Therapies – Innovation Over Effort

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Introduction & Objectives

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Supports pharmaceutical and biotech organisations with practical, inspection-ready pharmacovigilance across the advanced therapy lifecycle.

Session Overview

Advanced therapies are reshaping safety expectations. This session explores how evolving science and regulation challenge traditional pharmacovigilance models — and how smarter design supports scalable, defensible oversight.

Objectives

- Understand why traditional PV models misalign with ATMPs
- Recognise where effort increases without improving oversight
- Consider how evolving legislation reshapes expectations
- Explore innovation-led approaches for complex modalities
- Take away practical, scalable safety strategies

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What We'll Cover Today

- Why advanced therapies challenge traditional PV models
- Where key unknowns and legislative gaps sit
- How safety complexity differs from pharmacological products
- Where effort increases without improving oversight
- What proportionate, innovation-led safety design looks like

Setting The Scene

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Advanced Therapies Represent a Structural Shift

1. Advanced therapies are not simply new products but a different safety paradigm
2. Risk evolves differently across the product lifecycle
3. Scientific uncertainty remains significantly higher than traditional medicines
4. Most safety frameworks were built on pharmacological principles
5. Existing PV systems rely heavily on statistical signal detection

ATMPs challenge the foundations of traditional PV design

Setting The Scene

From Pharmacology to Biological Complexity

Traditional PV Assumptions
Dose-response predictability
ADME-based understanding
Population-scale datasets
Defined exposure duration

ATMP Realities
Persistence and irreversibility
Scientific unknowns
Long-term uncertainty
Individualised treatment response

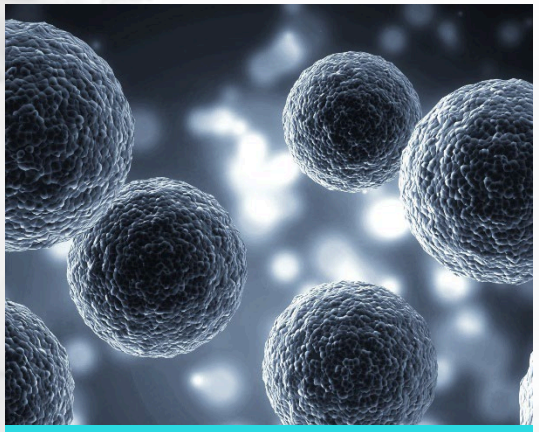
Safety models built for pharmacology do not naturally translate to ATMP complexity

Setting The Scene

What Are ATMPs?

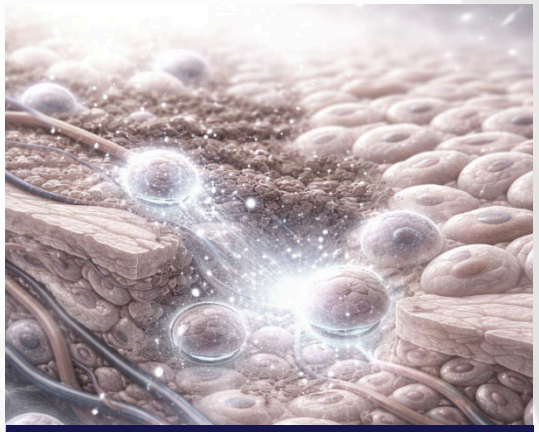
Gene Therapies

Introduce recombinant genetic material to achieve therapeutic, prophylactic or diagnostic effects.



Somatic Cell Therapies

Use manipulated cells or tissues to change biological function or treat disease.



Tissue-engineered Medicines

Repair, regenerate or replace damaged human tissue.

Combined ATMPs

Integrate medical devices, adding further complexity to safety monitoring.

Curative intent introduces new safety oversight demands

Why This Matters Now

The Emerging ATMP Safety Landscape

Advanced Therapies Introduce New Safety Pressures:

- Novel and often poorly understood mechanisms of action
- Long-term and delayed safety risks requiring extended follow-up
- Small, heterogeneous patient populations limiting signal detection
- Accelerated development timelines with reduced clinical exposure
- Evolving legislation adapting to new scientific realities

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Why This Matters Now

Where The Unknowns Sit

Key Areas of Uncertainty Across ATMP Oversight:

- Long-term genetic and biological effects remain uncertain
- Manufacturing variability can significantly influence outcomes
- Real-world heterogeneity complicates safety interpretation
- Predictive preclinical models remain limited
- Geographic follow-up presents operational challenges

ATMP oversight requires decisions despite incomplete evidence

Why This Matters Now

Additional Complexity Drivers

Beyond Scientific Unknowns, Operational Realities Increase Complexity:

- EU centralised approvals require rapid cross-border coordination
- Global patient follow-up creates sustained operational burden
- Combined ATMP/device oversight adds monitoring complexity
- Long-term registries demand consistent data governance

Oversight complexity is operational as well as scientific

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Traditional PV vs ATMP Reality

Structural Contrast

Traditional PV structures do not naturally align with ATMP oversight needs

Traditional PV vs ATMP Reality

Unique Safety Challenges

Clinical Challenges

- Long-term surveillance for delayed toxicity
- CRS and ICANS management complexities
- Limited clinical exposure at approval stage

Scientific Challenges

- Small and selective datasets
- Interpreting causality in evolving evidence
- Uncertainty around long-term outcomes

Operational Challenges

- Manufacturing consistency pressures
- Complex follow-up programme delivery
- Resource demands across extended timelines

Traditional PV vs ATMP Reality

Industry Responses Emerging

Emerging Approaches Across ATMP Oversight:

Long-term patient registries supporting lifecycle surveillance

Real-world evidence strengthening safety understanding

Advanced PV tools improving consistency and traceability

Greater integration across clinical, safety and quality functions

The direction is clear – but consistency and sustainability remain challenges

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Where Effort Replaces Strategy

Industry Reflex Under Uncertainty

Common Industry Responses Under Uncertainty:

1. Additional manual review layers introduced
2. Expanded SOP frameworks beyond operational need
3. Duplicate documentation across systems
4. Conservative oversight behaviours emerging

More effort does not automatically improve compliance or accuracy

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Where Effort Replaces Strategy

Risks of Overcorrection

Overcorrection Can Introduce New Risks:

- Inconsistent coding and MedDRA interpretation
- Variable triage and case assessment decisions
- Process inefficiencies that reduce overall consistency
- Manufacturing quality oversight becoming fragmented

Defensive systems often create new compliance vulnerabilities

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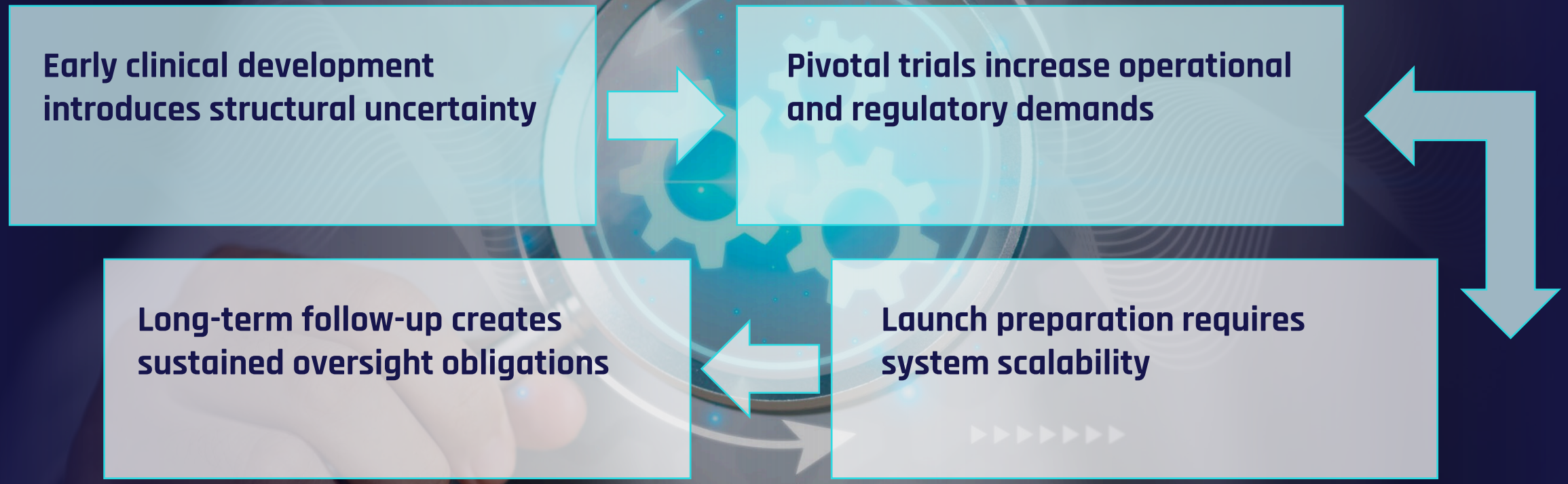
Designing for Complexity, Not Volume

ATMP Safety Requires a Lifecycle-based Approach:



Effective oversight depends on design, not workload

Designing for Complexity

What Smart Design Looks Like

Key Characteristics of Proportionate ATMP Safety Design:

- Structured intake ensuring consistent case capture
- Automated routing and QC supporting operational efficiency
- Embedded audit trails strengthening inspection readiness
- Workflow-enforced consistency across activities
- Alignment with registries and long-term data systems

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Regulatory Lens

What Inspectors Expect

Inspection focus in ATMP oversight:

- Validation aligned to intended system use
- End-to-end traceability across the product lifecycle
- Transparent and defensible oversight structures
- Clearly defined operational accountability

Well-designed systems demonstrate control without defensive explanation

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Innovation Over Effort

A Practical Framework

- Identify structural misalignment
- Remove unnecessary variability
- Automate rule-based processes
- Preserve scientific expertise
- Build scalable long-term systems

Innovation strengthens oversight — effort alone does not

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Closing Summary

Recap & Key Takeaways

- ✓ Advanced therapies require models designed for complexity
- ✓ Scientific unknowns and evolving legislation must shape oversight
- ✓ Complexity demands different operational approaches
- ✓ Effort alone does not strengthen compliance
- ✓ Innovation enables scalable, sustainable safety systems

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Q&A

Key Question:

Are our systems evolving with the science?

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