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WHITE PAPER

The Critical Importance Regulatory Affairs Serves in the Development and Commercialisation of a Drug

Insights and best practices for pharma/biotech companies to future-proof the continuity of quality, worldwide regulatory support

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Abstract

Clinical Research Organisations (CRO) are recognised as strategic partners for pharma/biotech companies in managing and conducting clinical trials efficiently, with the objective of commercialising a medicinal product. Regulatory compliance is fundamental in navigating the complex regulatory landscape governing clinical research, ensuring the reliability and validity of trial results.

Clinical activities often grab the headlines, but the highest quality regulatory activities are as critically important to obtaining marketing approval as clinical activities, if not more so. Robust connections with agencies are essential and need to be established early and moving vendors disrupts those important relationships.

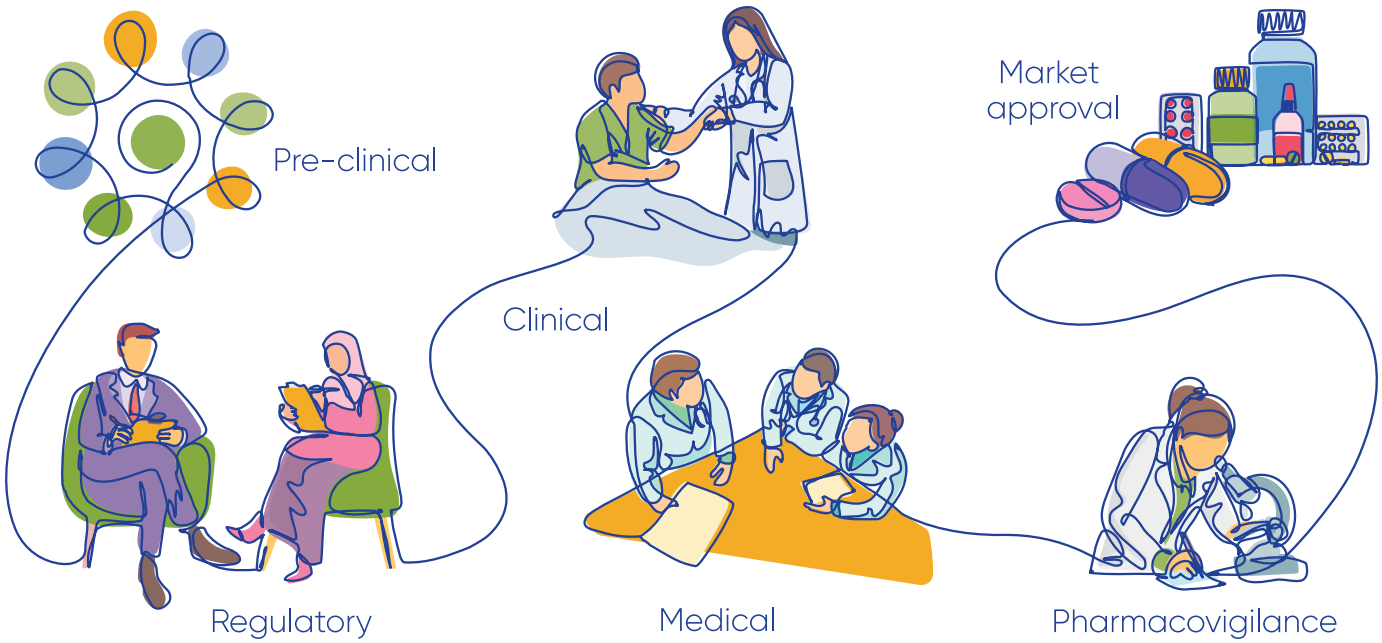
Within this white paper, we discuss some insights and best practices to future-proof the continuity of comprehensive, high quality, worldwide regulatory support.

Introduction

TMC suggests a standalone regulatory partner de-risks and future-proofs a pharma/biotech development programme. For example, if a full-service clinical partner (CRO) fails to deliver a study to quality on time and needs to be replaced, we argue that it would be beneficial to have a regulatory partner outside of clinical. A consistent team navigating global regulatory agency relationships results in highly effective interactions.

Of course, a single vendor could manage both clinical and regulatory aspects, but with a sponsor who has multiple programmes, we would still advise them to consider contracting separately, even if using the same vendor. We believe a regulatory partner that can comprehensively support worldwide programmes, from pre-clinical stage to marketing approval and beyond, is highly beneficial for a sponsor.

Strategy will inevitably change throughout any development programme. Guidance and regulations get updated; 'standard of care' changes; CMC issues arise and the clinical results outcome may not be as desired. A solid regulatory partner team should provide a valuable stream of continuity and seasoned advice. Also, there may be considerable efficiencies, both in time and cost, to apply across programmes, given there are elements of repetition in applications.



How TMC operates

TMC's regulatory team was established over 20 years ago. We employ an expert team of experienced in-house senior personnel, who are supported by a world-class, worldwide group of subject matter experts, our specialist Associates, who work with us across more than 70 countries. Our model hasn't changed in that time, which allows us to support every aspect of regulatory affairs, including:

TMC's Regulatory Services team works in over 70 countries worldwide

- Due diligence and support in pre-clinical – identifying appropriate vendors, reviewing (and auditing) CMC data, supporting animal and toxicity studies, etc
- Acting as sponsor and compiling more than 200 Orphan Drug Designations in EU/USA/Australia/Japan etc
- TMC has supported clients with more than 100 advice meetings with multiple agencies, including EMA scientific advice and FDA meetings
- Authored and successfully negotiated more than 100 Paediatric Investigation Plan (PIP)s, which are a vital early step in the EU approval process
- Qualified Person for Batch Release (EU and UK)
- Global Clinical Trial submissions (Regs & Ethics), inc. IMP label development
- Provision of local Legal Representatives for Clinical Trials (UK, EU, Australia, etc.)
- Small and Medium Enterprise (SME) status in EEA
  - Ex-EEA Clients may 'piggy-back' TMC's SME status to obtain incentives
- Compilation of MAA/NDAs; we have at least two ongoing at any one time
- Acting as Marketing Authorisation Holder in UK, EU and other territories
- Full range of expert pharma/biotech support services in AsiaPac, including Japan
- Other – environmental risk assessments, REMS, local applications for cell/gene therapy, etc

Core team of world-class subject matter experts

	Dr SP, Clinical Regulatory Strategist, achievements of work includes more than 250 Orphan Drug Designations and Paediatric Investigation Plans and 100 MAA/NDA clinical summaries
	Dr JT, Non-Clinical Consultant, has worked with TMC for more than 15 years and has completed countless MAAs, NDAs, CTAs, INDs, PIPs, Scientific Advice, pre-submission meetings and Environmental Risk Assessments
	LB, CMC Consultant, has expertise across all aspects of CMC activities and has worked on multiple applications, including MAAs and IMPDs
	RB, CMC auditor, has completed more than 50 GMP audits, 15 GDP audits, performed six due diligence reviews and nine GMP/GDP rectifications, plus acted as EU Qualified Person for Batch Release for over 15 years
	Significant US-based team supporting the full spectrum of activities, including FDA pre-IND, IND, NDA and post-marketing expertise

Regulatory Associates by expertise

Area of Expertise	Team size
Artwork	3
CMC experts and QPs	10
Devices	10
Pre-clinical	5
Site management contract experts	3
Clinical trial applications	23
MAA/NDAs FDA, EMA, AsiaPac etc	37
Promotional & non-promotional review	5
Varied regulatory experts	35
Translational experts	5
Total Team	**136**

Regulatory Associates by country

Country	Team no.
EU (15 countries)	35
Australia	3
S. America/Brazil	3
Canada	2
Dubai, UAE	1
Israel	3
Japan	5
S. Korea	3
Switzerland	3
Turkey	1
UK	55
USA	13
Total Team	**136**

Examples of outstanding regulatory achievements by TMC over its 20 year history

- With very close agency engagement, **TMC obtained approval in the EU for the first-ever embryonic stem cell study**. We identified cell preparation units, implemented SOPs and organised time-sensitive shipments. This was so groundbreaking that an early evening BBC TV newsflash showed a clip of the first patient enrolled. TMC remained as a trusted full-service partner (Clinical Trial, PV, Medical and Regulatory) and later successfully advised the Sponsor to amend the protocol part-way through the study to achieve 6 months saving in time and cost.
- **TMC rescued a product that had been refused Marketing Approval**. Though the Agency wanted to approve, the data did not fit standard rigid Regulatory rules. The Client decided to discontinue development, then TMC put together a compelling argument (over a weekend) which went back to the Agency and obtained Approval.
- **TMC provided an interim Chief Medical Office (CMO)** at a face-to-face FDA Oncologic Drugs Advisory Committee (ODAC) meeting. The product was approved, despite an EU Authority attendee who actually advised against it.
- TMC has just supported a client with a highly unorthodox data package for a UK MAA in glioblastoma. Our experts re-wrote the dossier and gathered new data. **We have just received validation of the MAA from the MHRA**.
- A number of clients have come to us whilst planning to license products already commercialised in the UK, EU and US. Without a suitable EU or UK entity, the clients' deals were at risk. **TMC stepped in to act as MAH**. In one case, we held the licence for over five years.
- As an example of our problem-solving capabilities, we received a very unusual request from a new client for **Smoke Testing** of a manufacturing facility on a Friday. By Monday, TMC had an expert in place that supported this client.
- TMC has **solid hands-on experience in new EU-CTR and CTIS** systems which became mandatory in

January 2023. We're proud that submissions have been approved more than two weeks earlier than the regulated timelines, due to our strong collaboration between TMC's Reg Lead/PM, our redaction/translation team and the sponsors.

- TMC acts as a trusted partner to our clients and has stepped in to role-fill many positions **including CMO, EU QPPV, Regulatory, CMC and non-Clinical experts etc**.

Conclusion

TMC provides unsurpassed services for its clients when working as a trusted partner; providing bolt-on assistance as required. Having access to TMC's highly qualified team allows sponsor companies to advance development more quickly and effectively than by recruiting internal headcount. It also allows for ramping-up and -down of resource as required.

TMC's regulatory services team can provide the fundamental backbone to a product development programme, with an unlimited and consistently maintained breadth of activities.

About TMC

TMC was founded nearly 25 years ago and is a global product development and clinical research organisation - a CRO with a difference. Utilising a unique business model, TMC's activities are performed by over 900 mature, highly experienced personnel that are subject-matter industry experts, located in over 70 countries. TMC supports pharma/biotech companies that are developing innovative, often life-saving, treatments for niche, rare and orphan diseases. By hand-picking operational teams to match the needs of every project, TMC provides tailored solutions and world-class support that responds uniquely to its clients' requirements..

To learn more about TMC and our focused solutions visit **www.tmcpharma.com** or email us directly at **info@tmcpharma.com**.

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