HealthTech Activator

# Regulatory Touchpoint Map Clinical Trials – US FDA

v.2 December 2018



POWERED BY
CallaghanInnovation
New Zealand's Innovation Agency

## REGULATORY TOUCHPOINT MAP CLINICAL TRIALS – US FDA

| PERSPECTIVE OF PERSON/ ROLE | KNOWLEDGE REQUIRED TO OPERATE EFFECTIVELY | RELEVANT REGULATORY FRAMEWORKS | NOTES |
|---|---|---|---|
| **SEED AND EARLY STAGE START-UP – PHARMACEUTICAL ONLY +** | | | |
| Scientist/ engineer/ inventor | Does the technology need evidence of clinical safety and efficacy before it can be marketed as a therapeutic product? | • FDA regulation of drugs, biologics, medical devices, IVDs, complementary medicines and some IT systems means companies need to rely on clinical evidence to substantiate therapeutic claims. | • Any product that claims to have an effect on health, diagnosis or treatment needs to have evidence for this claim. The level of evidence needed depends on the type of claim made. |
| | How does the need for clinical trials impact the optimal target product profile (TPP)+? | • Development of a therapeutic product within a technology platform may be focussed on clinical uses that are most likely to be successful in clinical trials.<br>• Having a clear understanding of the clinical trial requirements at an early stage helps refine the technology into a product with good clinical positioning. | • Identify best route for clinical evidence development with clinicians and regulatory experts experienced in product development through to clinical stages. |
| | Clear clinical strategy ahead<br>Clear milestones identified to clear regulatory hurdles | • Early engagement with regulators<br>• Relevant guidance documents<br>• Relevant standards<br>• Pre-IDE<br>• IDE<br>• 510k/PMA<br>• QSR<br>• Labelling<br>• Protection of Human Subjects<br>• Institutional Review Boards<br>• Good Laboratory Practices<br>• Good Clinical Practices<br>• Confidence that planned studies will achieve regulatory clearance/ approval if scientific/engineering success, or achieve reproducible results that a multinational can utilise in a regulatory application<br>• Stage-gate model | • Review/revise clinical strategy<br>• Research studies<br>• Safety and toxicology profile<br>• Product development<br>• Labelling |
| | Timing of regulatory requirements? | • Pre-clinical provides a platform of safety and efficacy to justify testing in human subjects<br>• Pre-clinical data is a precursor to indication selection | • Scope likely trials while defining target product profile (TPP) for drugs and labelling for devices<br>• Align with overall regulatory strategy |

## REGULATORY TOUCHPOINT MAP CLINICAL TRIALS – US FDA

| PERSPECTIVE OF PERSON/ ROLE | KNOWLEDGE REQUIRED TO OPERATE EFFECTIVELY | RELEVANT REGULATORY FRAMEWORKS | NOTES |
|---|---|---|---|
| **SEED AND EARLY STAGE START-UP – PHARMACEUTICAL ONLY +** | | | |
| | What pre-clinical evidence is needed before trials can commence? | • Based on type or class of product and target indications.<br>• See FDA definitions of:<br>› Drug<br>› Vaccine, blood and biologics<br>› Biosimilars<br>› Combination products<br>› Generic<br>› Medical devices | • Early engagement with regulators to establish submission route, data requirements and clinical track with regulatory, clinical and technical experts |
| Tech Transfer Office (e.g. VicLink, LSNZ, CMDT, WREDA) | Where to seek expert (light touch) advice | • Groups that can advise on clinical trial requirements include:<br>› LSNZ<br>› International CROs<br>› Regulatory/clinical experts<br>› Potential licensing partners (shared interest in getting the clinical trial prerequisites right) | • NZACRES (New Zealand only) |
| | Is clinical team capable of designing and delivering critical data requirements? | • Fill gaps in-house or as external consultants | |
| | How does clinical plan and timeline impact commercialisation strategy? | • Align clinical planning with market launch planning | • Is the company infrastructure experienced and/or adequate to support meeting clinical objectives? |
| | How does clinical strategy and timeline impact IP strategy? | • Optimise patented time on market and data exclusivity | |
| Investor (or TTO) | Ensure runway and budget will achieve critical clinical milestones<br>Ensure research $$$ well spent and align for exit or licensing with the right partner | • Visibility of clear, achievable plan<br>• Early discussion with multinational partner to confirm clinical strategy | |
| Clinical manager | Experience and relevant working knowledge of clinical research and operations in a R&D setting to support pre- and/or post-market approval. | • Relevant guidance documents<br>• Relevant standards<br>• Protection of Human Subjects<br>• Institutional Review Boards<br>• Good Clinical Practices | • Knowledge and experience in clinical research/ operations/compliance |

## REGULATORY TOUCHPOINT MAP CLINICAL TRIALS – US FDA

| PERSPECTIVE OF PERSON/ ROLE | KNOWLEDGE REQUIRED TO OPERATE EFFECTIVELY | RELEVANT REGULATORY FRAMEWORKS | NOTES |
|---|---|---|---|
| **SEED AND EARLY STAGE START-UP – PHARMACEUTICAL ONLY +** | | | |
| Quality manager | Experience and relevant working knowledge of clinical research and compliance in a R&D setting to support pre-market approval. | • Relevant guidance documents<br>• Relevant standards<br>• INDs/IDEs++<br>• Protection of Human Subjects<br>• Institutional Review Boards<br>• Good Laboratory Practices<br>• Good Clinical Practices | • Knowledge and experience in clinical compliance |
| Regulatory manager | Experience and relevant working knowledge of clinical/regulatory compliance to support pre- and/or post-market approval.<br><br>Ongoing monitoring for regulatory updates | • Relevant guidance documents<br>• Relevant standards<br>• INDs/IDEs++<br>• 510k++ / PMA++<br>• Labelling<br>• Protection of Human Subjects<br>• Institutional Review Boards<br>• Establishment and Listing<br>• Good Laboratory Practices<br>• Good Clinical Practices<br>• Adverse Event Reporting | • Knowledge and experience in clinical research/compliance<br>• Revise regulatory strategy |

## REGULATORY TOUCHPOINT MAP CLINICAL TRIALS – US FDA

| PERSPECTIVE OF PERSON/ ROLE | KNOWLEDGE REQUIRED TO OPERATE EFFECTIVELY | RELEVANT REGULATORY FRAMEWORKS | NOTES |
|---|---|---|---|
| **START-UP, LATE-STAGE, PRE- AND POST-MARKET APPROVAL[1]** | | | |
| CEO, CTO, CSO | Data package required before entering first in human (phase 1) clinical trials<br><br>Clear milestones identified to clear regulatory hurdles | • Relevant guidance documents based on therapeutic product type and class.<br>• Relevant standards based on therapeutic product type and class.<br>• Confidence that planned studies and study design will achieve regulatory clearance/approval if scientific/engineering success, or achieve results that a multinational can utilise in a regulatory application<br>• Stage-gate model | • Management need robust knowledge of regulatory pathway to progress commercially<br>• Licensing partners look for professionally developed data package that ensures streamlined entry to clinical trials<br>• Coordinate data requirements in discussion with regulatory experts or with licensing partner early to avoid re-work and inappropriate science studies being undertaken<br>• Review/revise regulatory strategy |
| | What conditions are needed to develop investigational product for clinical trial use? | • Understand regulatory hurdles e.g., investigational drug product used for clinical trials in human subjects must be manufactured in a facility that is FDA registered following GMPs.<br>• Understand regulatory hurdles e.g. investigational devices for clinical trials require that investigational product be manufactured in a FDA registered facility following the principles of elements of QSR, e.g. traceability, design control etc.<br>• IND/IDE++<br>• GMP/QSR++<br>• Product development<br>• Design Controls++<br>• Adverse Event Reporting | |
| | What conditions are needed to develop investigational product for post-market trials? | • Approved drug product used for clinical trials in human subjects must be manufactured in a facility that is accredited for Good Manufacturing Practice (GMP).<br>• IND/IDE++<br>• NDA/BLA<br>• GMP/QSR++<br>• Product development<br>• Design Controls++<br>• Post-market approval requirements<br>• Medical Device Reporting++<br>• Adverse Event Reporting | |

1 Most NZ developed pharmaceuticals are out-licensed at this stage

## REGULATORY TOUCHPOINT MAP CLINICAL TRIALS – US FDA

| PERSPECTIVE OF PERSON/ ROLE | KNOWLEDGE REQUIRED TO OPERATE EFFECTIVELY | RELEVANT REGULATORY FRAMEWORKS | NOTES |
|---|---|---|---|
| **START-UP, LATE-STAGE, PRE- AND POST-MARKET APPROVAL[1]** | | | |
| | Awareness of costs and skills for preparing to undertake clinical trials guides commercial negotiations for licensing or acquisition of R&D programme. | • Clinical trial budgeting should be undertaken in partnership with experts as this impacts on company valuation at this stage (due to the major costs of trials)<br>• CROs<br>• Potential licensing partners | • Trial costs vary greatly by jurisdiction, but company choice of jurisdiction to run the trials has multiple aspects including regulatory efficiency, quality of data etc.<br>• NZACRES has a clinical trial costing tool that can help companies understand the elements of trial costing, but this is only relevant for trials run in NZ and does not include administrative costs of preparing for the trials. http://www.nzacres.org.nz/costing-template |
| | What should the data package contain leading up to clinical trials? | • Early engagement with regulators<br>• Develop data package INDs/IDEs++ includes, but is not limited to:<br>› Manufacturing and controls<br>› Pharmacology/toxicology as applicable<br>› Clinical protocol<br>› Investigator's Brochure<br>› Clinical compliance documents for regulatory submission<br>› Clinical compliance documents for IRB approval<br>› In-vitro/In-vivo testing++<br>› Biocompatibility testing++ | • Identify data requirements early to support licensing or entry to phase 1 trials<br>• Understand IND/IDE requirements for US trials for pharmaceuticals. Note, for investigational devices data is required to support Investigational Device Exemption (IDE) .<br>• PMA with clinical data.<br>• 510(k) may also need clinical data with the type of study dictated by:<br>› Ability of bench and animal testing to demonstrate technological and performance characteristics<br>› Understanding of subject and predicate devices (similarities and differences) |
| | Which guidelines control pharmaceutical clinical trial practices (how trials are run)? | • Pharmaceutical drug trials:<br>› Relevant guidance documents<br>› Relevant standards<br>› Good Clinical Practices<br>› Design Controls++<br>› Product Development | • The ICH Good Clinical Practice guidance provides a standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials.<br>• The guidance and accreditation aims to provide assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are protected.<br>• All clinical trial sites need to comply and be accredited for GCP. |

## REGULATORY TOUCHPOINT MAP CLINICAL TRIALS – US FDA

| PERSPECTIVE OF PERSON/ ROLE | KNOWLEDGE REQUIRED TO OPERATE EFFECTIVELY | RELEVANT REGULATORY FRAMEWORKS | NOTES |
|---|---|---|---|
| **START-UP, LATE-STAGE, PRE- AND POST-MARKET APPROVAL[1]** | | | |
| | Which guidelines control device clinical trial practices (how trials are run)? | • Medical device trials:<br>› Relevant guidance documents<br>› Relevant standards<br>› Good Clinical Practices<br>› Design Controls++<br>› Product Development | • ISO14155 standard outlines the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials.<br>• The guidance and accreditation aims to provide assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are protected.<br>• All clinical trial sites need to comply and be accredited for GCP. |
| Quality manager | Experience and relevant working knowledge of clinical research and compliance in a R&D setting to support pre- and/or post-market approval | • Relevant guidance documents<br>• Relevant standards<br>• INDs/IDEs++<br>• Protection of Human Subjects<br>• Institutional Review Boards<br>• Product Development<br>• Design Controls++<br>• Good Laboratory Practices<br>• Good Clinical Practices | |
| Regulatory manager | Experience and relevant working knowledge of clinical/regulatory compliance to support pre- and/or post-market approval<br><br>Ongoing monitoring for regulatory updates | • Relevant guidance documents<br>• Relevant standards<br>• INDs/IDEs<br>• 510k/PMA<br>• Labelling<br>• Protection of Human Subjects<br>• Institutional Review Boards<br>• Establishment and Listing<br>• Product Development<br>• Design Controls++<br>• Good Laboratory Practices<br>• Good Clinical Practices<br>• Adverse Event Reporting | • Regulatory knowledge and experience in clinical research/operations<br>• Revise regulatory strategy<br>• Knowledge and experience in clinical compliance/ inspection/assessment<br>• Advisory committees |

## REGULATORY TOUCHPOINT MAP CLINICAL TRIALS – US FDA

| PERSPECTIVE OF PERSON/ ROLE | KNOWLEDGE REQUIRED TO OPERATE EFFECTIVELY | RELEVANT REGULATORY FRAMEWORKS | NOTES |
|---|---|---|---|
| **START-UP, LATE-STAGE, PRE- AND POST-MARKET APPROVAL[1]** | | | |
| Clinical manager | Relevant working knowledge of clinical research, operations and compliance with respect to the conduct of regulatory process and environment in product development to support pre- and/or post-market approval<br><br>Clinical expertise in the technology space/clinical application space | • Relevant guidance documents<br>• Relevant standards<br>• Protection of Human Subjects<br>• Institutional Review Boards<br>• IND/IDE++<br>• 510k++ / PMA++<br>• NDA/BLA<br>• Product development<br>• Design Controls++<br>• Lifecycle Management<br>• Good Clinical Practices | |
| R&D manager | Relevant working knowledge of product development to support clinical research<br><br>Regulatory expertise in the technology space/clinical application space | • Relevant guidance documents<br>• Relevant standards<br>• IND/IDE++<br>• 510k++ / PMA++<br>• NDA/BLA<br>• QSR++/GMP<br>• Product development<br>• Design Controls++<br>• Good Laboratory Practices<br>• Good Clinical Practices | • Understand compliance requirements to provide compliant investigational product/unit for testing under clinical protocol |
| Marketing/ Sales manager | Relevant working knowledge of clinical data needed to support label claims to support pre- and/or post-market approval<br><br>Marketing and sales expertise in the technology/clinical application space | • Labelling<br>• Product development<br>• Design Controls++<br>• Good Clinical Practices | • Knowledge and expertise in establishing label claims<br>• Knowledge in market, specifically of competitors for the sector |

## REGULATORY TOUCHPOINT MAP CLINICAL TRIALS – US FDA

| PERSPECTIVE OF PERSON/ROLE | KNOWLEDGE REQUIRED TO OPERATE EFFECTIVELY | RELEVANT REGULATORY FRAMEWORKS | NOTES |
|---|---|---|---|
| **GROWTH, ESTABLISHED, EXPANSION** | | | |
| CEO, CTO, CSO, CMO | Clinical trials (fully or partially sponsored by the company) conducted by researchers who are independent of the company | • Relevant guidance documents<br>• Relevant standards<br>• IND/IDE++<br>• 510k++ / PMA++<br>• NDA/BLA<br>• QSR+/GMP<br>• Product development<br>• Design Controls++<br>• Good Clinical Practices | • Professional outsourced trial organisations and clinical staff within trial sites remain independent of the sponsor company and have a direct responsibility to the patient.<br>• The company remains responsible for regulatory, quality and compliance standards, protocol development and adherence as well as data integrity, analysis and monitoring.<br>• Must balance the risk benefit for fully sponsored versus partially sponsored trials in the US.<br>• Identifying appropriate experience PI's and centres is critical to the success of the clinical trial. |
| Clinical manager | Relevant working knowledge of clinical research, operations and compliance with respect to the conduct of regulatory process and environment in product development to support pre- and/ or post-market approval<br><br>Clinical expertise in the technology space/clinical application space | • Relevant guidance documents<br>• Relevant standards<br>• IND/IDE++<br>• Product development<br>• Good Clinical Practices<br>• Adverse Events<br>• Clinical trial registration++<br>• Post market approval studies<br>• Registry studies++ | • In some cases, e.g. devices, where post-market infrastructure is in place, traditional Post-Approval Study requirements are being replaced with in-market surveillance based requirements e.g. comprehensive/ linked registry based surveillance. |
| Quality manager | Experience and relevant working knowledge of clinical research and compliance in a R&D and commercial setting to support pre- and/or post-market approval studies and registries where applicable | • Relevant guidance documents<br>• Relevant standards<br>• INDs/IDEs++<br>• Protection of Human Subjects<br>• Institutional Review Boards<br>• Product development<br>• Design Controls++<br>• Good Laboratory Practices<br>• Good Clinical Practices<br>• GMPs / QSRs++ | |

## REGULATORY TOUCHPOINT MAP CLINICAL TRIALS – US FDA

| PERSPECTIVE OF PERSON/ROLE | KNOWLEDGE REQUIRED TO OPERATE EFFECTIVELY | RELEVANT REGULATORY FRAMEWORKS | NOTES |
|---|---|---|---|
| **GROWTH, ESTABLISHED, EXPANSION** | | | |
| Regulatory manager | Experience and relevant working knowledge of regulatory process with FDA to support the product development team when required to conduct a clinical trial<br><br>Ongoing monitoring for regulatory updates affecting clinical trials | • Relevant guidance documents<br>• Relevant standards<br>• IND / IDE++<br>• 510k / PMA<br>• Investigational Labelling<br>• Protection of Human Subjects<br>• Institutional Review Boards<br>• Product development<br>• Design Controls++<br>• Good Laboratory Practices<br>• Good Clinical Practices<br>• Adverse Event Reporting<br>• Post-market Approval<br>• Registry studies++ | • Regulatory knowledge and experience in the product technology<br>• Ability to deliver a clinical strategy that is current for the product and regulatory environment which is relevant to the business<br>• Knowledge and experience in clinical compliance<br>• Knowledge and experience in clinical trials/ operations |

+: Pharmaceutical only
++: medical devices only