Worldwide Clinical Trials

Infographic

Maximizing Simplicity in Complex First-in-Human Studies

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Simple and straightforward First-in-Human (FIH) study designs are a thing of the past, as a need to address additional hypotheses early in clinical development becomes dominant, and exploratory endpoints expand to address increasingly complex questions.[1,2] This infographic highlights ways to address these complex questions more efficiently.

The primary goal of an FIH study remains unchanged: to assess safety and tolerability as well as pharmacokinetics and biodisposition of a novel compound. However, sponsors and a diverse spectrum of stakeholders increasingly demand assessments in Phase I of target engagement and clinical efficacy, prompting the emergence of "hybrid" clinical studies that include patients and healthy volunteers.[3]

Traditional FIH

- Safety
- Tolerability
- PK/Biodistribution

Contemporary FIH

- Safety
- Tolerability
- PK/Biodistribution
- Target Engagement
- Preliminary Clinical Efficacy

Senior-Level Engagement

Tailored Solutions

Operational Agility

Streamlined FIH Programs

To address an emerging need for hypothesis generation and testing early in clinical research, differentiated early phase CPUs offer **senior-level engagement, operational agility, and tailored solutions** that incorporate both early as well as late phase subject matter experts to enable more informed decision-making in Phase I. This hands-on execution, combined with **specialized expertise and infrastructure** required for advanced modalities and innovative study designs, helps to streamline and derisk FIH programs.

Design Element	Precedent	Complex Design	Solutions
Treatment Modality	Small Molecule	Advanced Therapy Medicinal Products (ATMPs) such as Cell/Gene Therapies and Biologics	• Implement **modality-specific operational "playbooks"** with mock runs prior to FIH dosing to reduce execution risk and protocol deviations. • **Onsite pharmacy** with sterile compounding and a suite for radiolabeled compounds permitting real time, adaptive dosage modification.[4]
Route of Administration	Oral, SC/IM Injection, IV, Topical, Intranasal	Inhalation, Intranasal, Sublingual, Long-Acting/ Depot Systems, Nasogastric, and Transdermal	
Product Profile	Standard Noncompartmental Toxicokinetic and PK/PD Analysis	Multi-Stage, Non-Linear PK with Multiple Analytes/Metabolites PD Effect vs. Concentration Modeling Diverse Drug Partitioning and Elimination Pathways Extended/Near-Nonexistent Drug Half-Life[5]	• **Singular integration** of operations, bioanalytics, biostatistics, and pharmacometrics. • **Experienced team** of PK scientists fully integrated with operational and design staff.
Participant Population	Healthy Normal Participants	Healthy Participants with Age/Ethnic Diversity, and Diverse Conditions (i.e., overweight, high cholesterol, with/without stable concomitant medication).	• **Established participant relationships** accelerate recruitment and maximize retention. • **Operationalize seamless protocol** architectures with predefined transition criteria and governance committees.
Study Design	SAD + MAD	SAD + MAD + Accelerated Dose Escalation, Recursive Backfilling, and Bayesian Precepts	• **Bioanalytical methods are a priority, not an afterthought**. In-house capabilities facility adaption. • **Remote data review and real-time safety outputs** support informed escalation and expansion without operational pauses.
Preliminary Efficacy/Clinical Assessments	Safety, Tolerability, PK, and Biodisposition	Safety and Tolerability, PK and Biodisposition + Specific Imaging, Advanced PD, and Disease-related Biomarkers and Clinical Assessments	• Collaboration with clinical specialists and vendors to provide insight and **evaluate risks during protocol/program development**. • Integration of clinical systems (i.e., telemetry) with a cloud-based e-source/EDC system (i.e., ClinSpark®) **minimizes manual data entry and streamlines data management**.

Beyond the Transaction

Our scientific, medical, and operational teams consider the sponsor's corporate objectives, regulatory requirements, and patient management to tailor operations accordingly (e.g., speed, cost, and signal-detection capabilities).

Change Isn't Avoided, It's Expected

Our operational teams anticipate opportunities and challenges and respond with agility. We anticipate and discuss potential regulatory and medical feedback with subject-matter experts across Worldwide, and present this to sponsors for review.

Why Worldwide?

Direct Lines of Communication

Worldwide's structured governance, including executive steering, a joint operating committee, and project teams, working closely with the sponsor's decision-makers, expedites change, enabling rapid adaptability.

Building a Continuum

Collaboration between early and late phase provides a comprehensive, seamless clinical development plan that accelerates timelines while ensuring data integrity, participant safety, and informed decision-making.

References

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