MAPS
FOR Medical Affairs Professionals
BY Medical Affairs Professionals
Medical™ Affairs Professional Society

eCAdemy

Best Practices for Managing the Life-Cycle of an Investigator Initiated Trial

Gurveen Saberwal, Ph.D.
Former Program Manager, Investigator Initiated Research,
Oncology and Immunology, Shire

Investigator Initiated Research

Investigator Initiated Research (IIR/IIS/IISR/IIT) is defined as unsolicited, independent research where the investigator or the Institution (academic, private, or governmental) serves as the Sponsor and a pharmaceutical or medical device company provides support in the form of study drug/device and/or funding

Sponsor

- Sponsor is the person or organization who takes responsibility for and initiates a clinical investigation. The Sponsor does not actually conduct the investigation unless the Sponsor is a Sponsor-Investigator

Objectives

- Establish an IIT strategy
- Optimize the proposal submission and review process
- Define contract milestones that will ensure the smooth execution of an IIT
- Manage strong relationships with external investigators while maintaining compliance

Overview

- Establish an IIT Strategy
- Optimize Submission and Review Process
- Define Contract milestones for smooth execution
- Manage strong relationships with external investigators while maintain compliance
- Conclusions

Overview

- Establish an IIT Strategy
- Optimize Submission and Review Process
- Define Contract milestones for smooth execution
- Manage strong relationships with external investigators while maintain compliance
- Conclusions

IIT STRATEGY

Strategy for IIT is created under overall GMA plan to better understand benefit/risk profiles of Company's therapies and also address unmet medical needs

- Medical Team-
  - Understanding pre-clinical data
  - Develop IIT Strategy/create a medical plan
- Limit overlap with Company sponsored strategy/studies
  - Should try to not have patient overlap as well
- Consideration of life cycle management
  - Resources
  - Drug supply
  - Budget considerations

IIT STRATEGY: AREAS OF INTEREST (AOIs)

- AOIs are then created under IIT Strategy-For website
  - ➢ Detailed AOIs
    - ○ Detailed: Less proposals, very focused
  - ➢ Brief/Broad AOIs
    - ○ Broad: More proposals to choose from and provides flexibility

- Detailed AOI documents prepared to train field medical personnel for unsolicited discussion with KOLs/external investigators
  - ➢ Gaps by indication/across program (areas of higher interest)
  - ➢ In scope/out of scope

IIT STRATEGY: Prioritization of Products

- Medical Teams plan product strategies for IIRs depending on where they are with life cycle of the product
- This could be based on company's priorities on brands/products
  - Product being launched- High priority
  - Older products might have lower priority
  - Explore use of a marketed drug for new indications, in new populations, in new dosages regimes or in new combinations with other treatments
  - Evaluate biomarkers that could be useful in diagnostic tests or treatment management

IIT STRATEGY: Budget Planning

- Plan for yearly budget based on branding priorities
  - ➢ Committed amount for ongoing studies
    - Easier to control committed funds
  - ➢ New IIRs
    - Based on IIR Strategy/product priorities of company
    - Previous years' budget allocations/spend

IIT STRATEGY: Company Partnerships

- Partnerships with other companies as part of licensing deals may have an impact on the rights and process for approval and support of IIT studies in certain countries

  - Some products are developed in partnerships
  - Collaboration with partner company on IIT strategy by Medical Teams
  - Budgeting for partnership IITs dependent on company strategy
    - Separate strategy/geographical areas
    - Shared budget

IIT STRATEGIES: Acquisitions

- Products acquired for a specific TA/Franchise
  - IIT strategy could be based on the M&A agreement between the companies
  - Based on contractual status of acquired ongoing IIRs

- Usually acquired from smaller companies where the processes are not very detailed/established

- In addition to amendment per new company policy, there is also a need to honor the commitment made by acquired company to the Investigators/Institutions

Overview

- Establish an IIT Strategy
- **Optimize Submission and Review Process**
- Define Contract milestones for smooth execution
- Manage strong relationships with external investigators while maintain compliance
- Conclusions

OVERVIEW

- Submission via Portal

- Different timelines for submission
  - Windows
  - Rolling submission

- Windows submission
  - Once/twice a year or more
  - Cross functional committee reviews all proposals together with a set budget
  - Utilize submission portal website/field team

Rolling Submissions - Process

- Applications accepted throughout the year via submission portal website
  - Timeframes for review meetings communicated on the website

- Brief Applications
  - Decision provided with 45 days of submission
  - No funding decisions

- Full Applications
  - Quarterly review meetings for decision on funding
  - Medical Affairs team reviews with input/feedback as required from cross functional team

OVERVIEW

Medical Affairs Professional Society
FOR Medical Affairs Professionals
BY Medical Affairs Professionals

Window Submissions

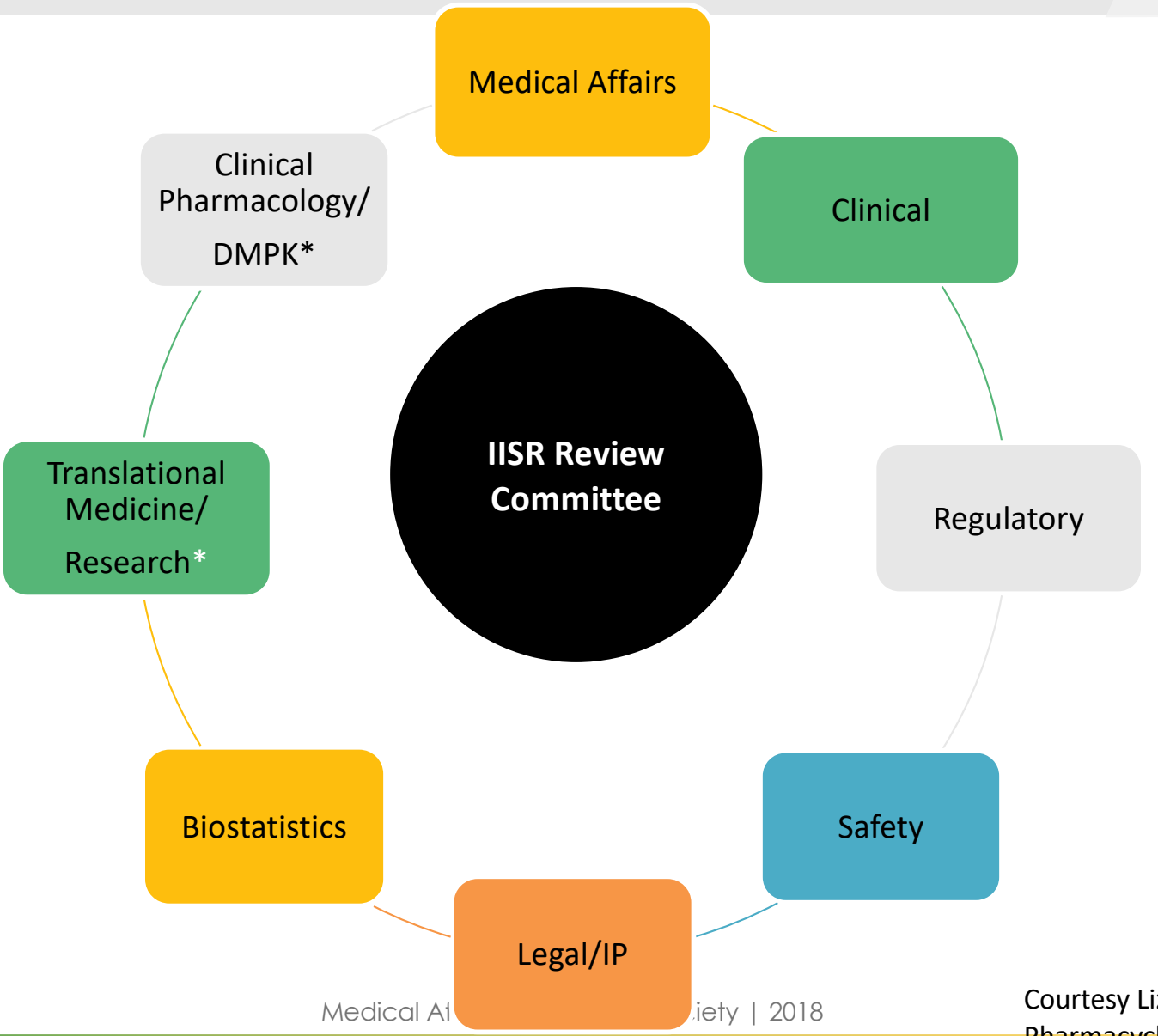
- Advantages:
  - Minimizes trials that are duplicative
  - Best value for program – approving one trial per area in strategy
  - Ensures comparison of all submitted proposals together
- Areas of Caution:
  - Communication of process and expectations to field medical team and external customers
  - All eggs in one basket

Rolling Submissions

- Advantages:
  - High customer satisfaction
  - No need to wait to submit top priority trial
- Areas of Caution:
  - Could lead to greater number of similar trials
  - Cumbersome internal review process
  - Budget allocation and planning for the year

Courtesy Liz Mena, Assoc Dir, Pharmacyclics LLC

Industry Standard Representative Cross-Functional Review Committee



*ad hoc reviewers

Courtesy Liz Mena, Assoc Dir, Pharmacyclics, LLC

Committee Review Assessment

Courtesy Liz Mena, Assoc Dir, Pharmacyclics, LLC

GUIDING PRINCIPLES FOR REVIEW

- They need to address meaningful scientific and clinical objectives supported by valid study designs in which privacy rights, safety and welfare of the patients is of greatest importance
- Good tracking system necessary to identify overlap-(some cases legal/Managers)
- Ethical : Balancing the commitment to high ethical standards against the desire to maximize the investment value
- Promote transparency and disclosure
- Cannot be driven by marketing department (OIG office program guidance for pharmaceutical manufacturers)

Overview

- Establish an IIT Strategy
- Optimize Submission and Review Process
- **Define Contract milestones for smooth execution**
- Manage strong relationships with external investigators while maintain compliance
- Conclusions

Contracting and milestones

- Best practice to have budget approved/contracted in the local currency to avoid fluctuations
  - ➢ Require detailed budget breakdown to allow FMV calculations
    - FMV analysis-use comparators, bench marking tool
    - work closely with compliance to establish ground rules for FMV, develop SOP
    - Exceptions – lack of comparators - different countries, processes etc.
    - Seek expertise from different departments
    - Subject matter experts
  - ➢ Certain costs not supported
    - equipment costs
    - limit on O/H costs
    - SOP important
- Detailed protocol and if any drug distribution/labeling costs
- Set clear expectations with finance

Contracting and milestones

- Milestone payment based on completion of aims in the protocol- hence detailed budget and protocol important
- Typically 4 milestone payments
  - contract execution (including non refundable costs like IRB submission, site start up, pharmacy start up)
  - 50% enrollment (patients)
  - 100% enrollment/last patient enrollment
  - submission of manuscript/final study report (last 10-15% of total budget)

- Modified as necessary depending on size and length of the study
- Study should be funded appropriately to move smoothly/complete on time

Contracting and milestones

- Creating multiple smaller milestones especially for large clinical trials
  - Breakdown bigger milestones into several smaller milestones payments ex execution of contract, submission and approval for Ethical Committee approval, activation of site/s, enrollment of first patient etc.

- These mitigate risks for budget planning as huge sum of money does not get blocked on one milestone

- Helps to clearly set expectations and budget management with finance

- Helpful with internal budget tracking-forecast and spent tracking
  - Consider using specific timelines in the contract for milestone payments

Study Objectives - {IIT STUDY NUMBER}

- **Hypotheses:**
- **Primary/Secondary Objectives:**
- **Primary Endpoints:**

Scientific/Medical Rationale for Study Support - {IIT STUDY NUMBER}

- **Key Data Gap Addressed:**

Investigator/Institution Qualifications- {IIT STUDY NUMBER}

- **Summary of Investigators Qualifications/Experience in this Area of Research:**

- **Institution and Infrastructure Capabilities as it Relates to Feasibility of Completing the Study:**

Overview

- Establish an IIT Strategy
- Optimize Submission and Review Process
- Define Contract milestones for smooth execution
- **Manage strong relationships with external investigators while maintain compliance**
- Conclusions

EXTERNAL ENGAGEMENT – Prior To Submission

- AOI are communicated to PI via submission website – researcher facing

- RFP – launching product or higher priority proposals for unmet needs
  - Used as a tool to raise awareness
  - Work with various congresses to raise awareness for RFPs like a press release

- Field based personnel (MSLs) (based on detailed documents reviewed by compliance)
  - AOI
  - Future research/Treatments available

EXTERNAL ENGAGEMENT: Relationship Building

- Understanding the Investigators:
  - Local involvement important- MSL role central
  - Most Investigators are clinicians along with being researchers
  - Lack of time and administrative process patience

- Developing a good communication and feedback process:
  - Timely and friendly follow ups for efficient budget forecasting
  - Study Updates
  - Reinforcement of company processes and procedures

- Timely payments
  - Be sensitive to situations in external grant run Institutions

Overview

- Establish an IIT Strategy
- Optimize Submission and Review Process
- Define Contract milestones for smooth execution
- Manage strong relationships with external investigators while maintain compliance
- **Conclusions**

Conclusions

- A well developed strategy created before submissions are received allows for the best, unbiased approach to IIT selection
- Both window and rolling submissions have their benefits and the best approach for your company should be taken
- Milestones based on individual study requirement, following basic guidelines lead to timely completion of study
- Strong relationships based on good communication with Investigators/Institutions in a compliant manner, leads to smooth execution of a study

Drug Supply challenges: Operational details

- Managing product life cycle for IIRs
    - Coordination with supply team
    - For global supplies- team structure may vary
- Forecasting of products for IIR trials
    - Forecast as soon as the study is approved
    - Master Planner/Supply Lead for particular product
- Any specific requirement for the product
    - Labeling needs per specific country
- Shipment needs for multi center trials
    - Central Pharmacy or direct shipment- Central pharmacy preferred
    - Central re-labeling before shipment
- Budget planning for such needs
- Product forecast/planning for short shelf life products for large multicenter trials


Thank You

MAPS™
Medical Affairs Professional Society
FOR Medical Affairs Professionals
BY Medical Affairs Professionals

MAPS eCademy

Tweet @MAPSmedaffairs pre-, during and post-Webinar to keep the conversation going. Use #MAPSecademy

Share your best practices, questions & needs 24/7 via our online Forums in the MAPS Community Portal: www.medicalaffairs.org/community