Global Development in Asia: a PhRMA Perspective

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Introduction

- Simultaneous Global Development (SGD): T*he ability to study patients in all regions at the same time under the same protocol resulting in a single database for analysis and review by the relevant regulatory authorities at the same time.* (SGD does not mean that separate clinical trials are conducted in a given market at the same time as the global studies, nor that all portions of clinical development will contain subjects from each market.)

Introduction

- Intellectual Underpinnings of SGD: Although ethnic differences among populations may cause differences in a medicine's safety, efficacy, dosage or dose regimen, many medicines have comparable characteristics and effects across regions. Requirements for extensive duplication of clinical evaluation for every compound can delay the availability of new therapies and unnecessarily waste drug development resources (ICH E-5: 1).

The Current Situation

- Staggered Development and Launches = Drug Lags
  - Why? For a variety of reasons, including, but not limited to country-specific regulatory requirements, clinical trial infrastructure limitations, concerns over intellectual property protection, and uncertainty of achieving a price that fully recognizes the value of innovation.
  - Result? Innovative pharmaceuticals have been largely developed and introduced in the U.S. and Europe and then come later (sometimes much later) to Asia. This is not a good model for Asian patients because it means that they must wait for the latest pharmaceutical treatments. It is also not a good model for the multinational pharmaceutical industry because it stretches limited research and development resources on often duplicative testing, adding little, or no scientific value.
- Encouraging Signs – APEC, Japan, China, South Korea, Chinese Taipei, Singapore, Thailand, ASEAN and India

Critical Success Factors – General, not Country Specific

- Total Support for the Cycle of Innovation – R&D/Clinical to Regulatory to Pricing and IPR
- Key Regulatory Considerations
  - Regulatory Agencies need to evolve regulatory processes and criteria to enable pharmaceutical development in their country to progress from Phase 1 studies through approval at a pace comparable to that in the US and EU. Early discussions with the sponsor as to overall development strategy is extremely important even in the absence of actual clinical data.

Critical Success Factors – General, not Country Specific

- Key Regulatory Considerations
  - Clinical trial systems needs to increase their rates of growth in capacity and capability to deliver high quality, timely and cost effective clinical trial data.

Critical Success Factors – General, not Country Specific

- Key Regulatory Considerations
  - Clinical investigators, IRBs, patients, and regulatory authorities need to be willing to accept the risks in having sites participate in SGD and to accept safety data generated in other regions.

Critical Success Factors – General, not Country Specific

- Key Regulatory Considerations
  - Companies need to modify their internal processes so that they can conduct studies in Asian markets with the same degree of real time safety evaluation, dose escalation, and phase transition processes and standards as accepted by US and EU regulatory authorities.

Key Regulatory Considerations

- Specific Regulatory Recommendations
  - Because SGD is a “break-through” in drug development in Asia in that it prepares for the future, participation of regulatory agency leadership in the consultation / discussion related to SGD projects is seen as an important key to success. Participation and “approval” is sought from regulatory agency Director Level leadership to assure the global spirit permeates all levels of an agency’s review teams.
  - Once a SGD project is identified, special priority access to the regulatory agency needs to be provided in order to keep pace with global development. It is important to acknowledge that information will many times not be in a formal report form and interactions will be both written and verbal – consistency and adherence to advise are critical.
  - An early (Pre-Phase 1) interaction between sponsor and the regulatory agency needs to be made available rapidly to enable quick decision making on key development plans.
  - Following Phase 1 in Asian subjects (but not necessarily conducted in Asia), additional “country-specific studies” are not needed since dose proportionality, Population PK, etc, will be addressed in common global data-bases. This will maximize the use of limited individual country clinical trial sites to conduct cutting edge development studies.

Key Regulatory Considerations

- Specific Regulatory Recommendations
  - Regulatory environments for governing investigational new drugs need to ensure that they can keep pace with global development. For example, if it is not possible, regulatory agencies should consider allowing continuous Phase 1 studies in which Single Ascending Dose (SAD) studies would transition into Multiple Ascending Dose (MAD) studies in an overlapping fashion and without administrative interruption following similar procedures already in place in many US and EU centers.
  - Where the results of Phase 1 studies in Asia and in the US/EU are similar, differential response in terms of efficacy and safety is not expected and regulatory agency requirements for additional studies in specific markets would result in those markets not being able to join Global Phase 3 programs.
  - Key to SGD is a market's participation in Global Phase 3 studies. The requirements to include patients (for example: demonstration of safety and tolerance, characterization of PK, demonstration of dose response, etc) in such studies need to be consistent with, and not more rigorous than, those used globally.

Key Regulatory Considerations

- Specific Regulatory Recommendations
  - Careful and meaningful deliberations with the regulatory and relevant government groups already established to address clinical data requirements are needed to assure maximum benefit and scientific value with minimal duplication.
  - An open dialog between Asian regulatory agencies and appropriate FDA and EU regulators should be encouraged to assure information, issues, and decision sharing across the regions.
  - A joint working group of Asian regulatory officials, experienced domestic and multinational (PhRMA, EFPIA) company drug development experts needs to be organized to prepare recommendations that will result in a regulatory environment that enables SGD.

The Future

- Challenging but Optimistic – Timing and Risk
- Experience and Interaction will facilitate positive change
- It is a race to change – Who will be left behind?
- Working from a default of SGD, based on data and scientific evaluation the principle of “sameness” will direct the development path.