# Conducting CNS Clinical Trials in the Developing World

## Summary

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## M Page: *Clinical Trials in the Developing World: Background and Changing Role*

- Global clinical development programs make sense
- Single integrated data base is more efficient for pharma
- Challenge is how to respect cultural diagnostic, pharmacokinetic diversity
- Different outcome measures
- Trend is of global development going from West to DW; what about the reverse?
- Is there a role for WHO in guidelines for regulatory bodies?

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## A Kiev: *Multi-National Trials in the Developing World: Conceptualizing the Trials—An Academic Perspective*

- **Importance of awareness of local diagnostic traditions, care taking issues**
- **Importance for inclusion of local PIs and physicians in protocol design issues; inclusion of anthropological expertise**
- **Low placebo response rates**
- **Does that mean also higher study medication response rates?**

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## R Anand: *Multi-National Trials in the Developing World: Conceptualizing the Trials—An Industry Perspective*

- **What does it mean "Developing World"?**
- **A comprehensive review of all issues involved in conducting CTs in the DW**
- **Need to involve local PIs and local opinion leaders EARLY in the protocol design phase**
- **Need to focus on drug dosage issues, related to weights and metabolic issues; lack of preliminary MTD studies**
- **Question: food drug interactions; example curcumin in India;**
- **Issue of concomitant herbal medicine?**
- **ICF in local language and reviewed by independent observer**
- **Concept of independent capacity evaluation; does it exist?**
- **Traditional outcome measures may not be applicable**
- **Western pharmacoeconomic questionnaires may not be applicable**

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## *A Kalali: Setting Up and Implementing Protocols in the Developing World*

- **The CRO experience in the DW**
- **Need for adequate local CRO infrastructure**
- **Knowledge of local regulations, medication importing regs, blood sample export regs, DNA sampling**
- **Availability of comparators, generic quality**
- **Questions: What about the site infrastructure? Research pharamcists, research RNs, biostatisticians, cognitive psychologists?**

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S Khanna: *Reviewing the Protocol Submissions: An Indian Regulatory Perspective on Issues to Be Considered in Approving a Global Trial*

- **Review of Indian Regulatory Procedures**
- **Significant procedural changes are taking place**
- **Some stream lining of the steps required, such as a time line**
- **Procedural standards for ECs**

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# JK Trivedi: Setting Up And Implementation The Protocol: A Site Perspective On How To Adapt It For The Developing World

- A comprehensive view from the trenches by an Indian PI
- Issue of funding of research being mostly by outside agencies
- Issue of validity of western developed instruments
- Problems with inquiries of “tabou” subjects in rating scales
- Issue of IQ assessment in illiterate patients
- Remedy: Exclusion of patients during screening
- Issue: Different social and functional normative standards
- Remedy: Inclusion of culturally sensitive social function scales

# T Sharma/ R Mohs: Case Studies: Evaluating Cognition In Multi-National in Developing World Trials

- **Computerized, paper and pencil tests are doable in other cultures,**
- **Although computer literacy may not be available in some countries**
- **Problem is the assessment of IQ in illiterate patients**
- **Cognitive tests are applicable, but may have to be modified, e.g. for illiterate patients or making them locally applicable ("what a normal person in that particular culture would know")**
- **Maintain the concept of cognitive function tested and scoring rules**
- **What is the validity of the modified tests, particularly for regulators?**
- **Test retest validity?**

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# N A Khin: Reviewing Data from Multi-National Trials in the Developing World: FDA Perspective

- **Overview of review process of non US data by FDA**
- **FDA can approve data conducted in non US countries without IND**
- **FDA can approve non US data for marketing approval**
- **Possibility of FDA site inspections in non US countries**
- **Low number of non US sites are FDA inspected with comparable results to US sites in CNS studies**
  - **Exception: low reporting of AEs**
- **FDA will not rely exclusively on pivotal trial data from non US sources**
- **FDA will accept data from long term placebo controlled non US studies**
- **Excellent case studies**

- **For use of culturally adapted or modified assessment instruments….ask the Division before getting into it.**

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# G Pons: Reviewing Data from Multi-National Trials in the Developing World: European Regulatory Perspectives

- **There is a regulatory EU frame work for the acceptance of CT data from results from one Region to another Region, provided ther no intrinsic or extrinsic differences in the two populations:**
- **Need for a bridging study:**
  - **Dose response study**
  - **pK study**
  - **Full clinical study**
- **Case study of EU: CT data was accepted in a substantial number of trials and indications for new drugs in minors**
- **Significant numbers of completed GPC inspections**
- **Most concerns came from sponsors and not from hosting countries**

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