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BIOCATALYST DEVELOPMENT

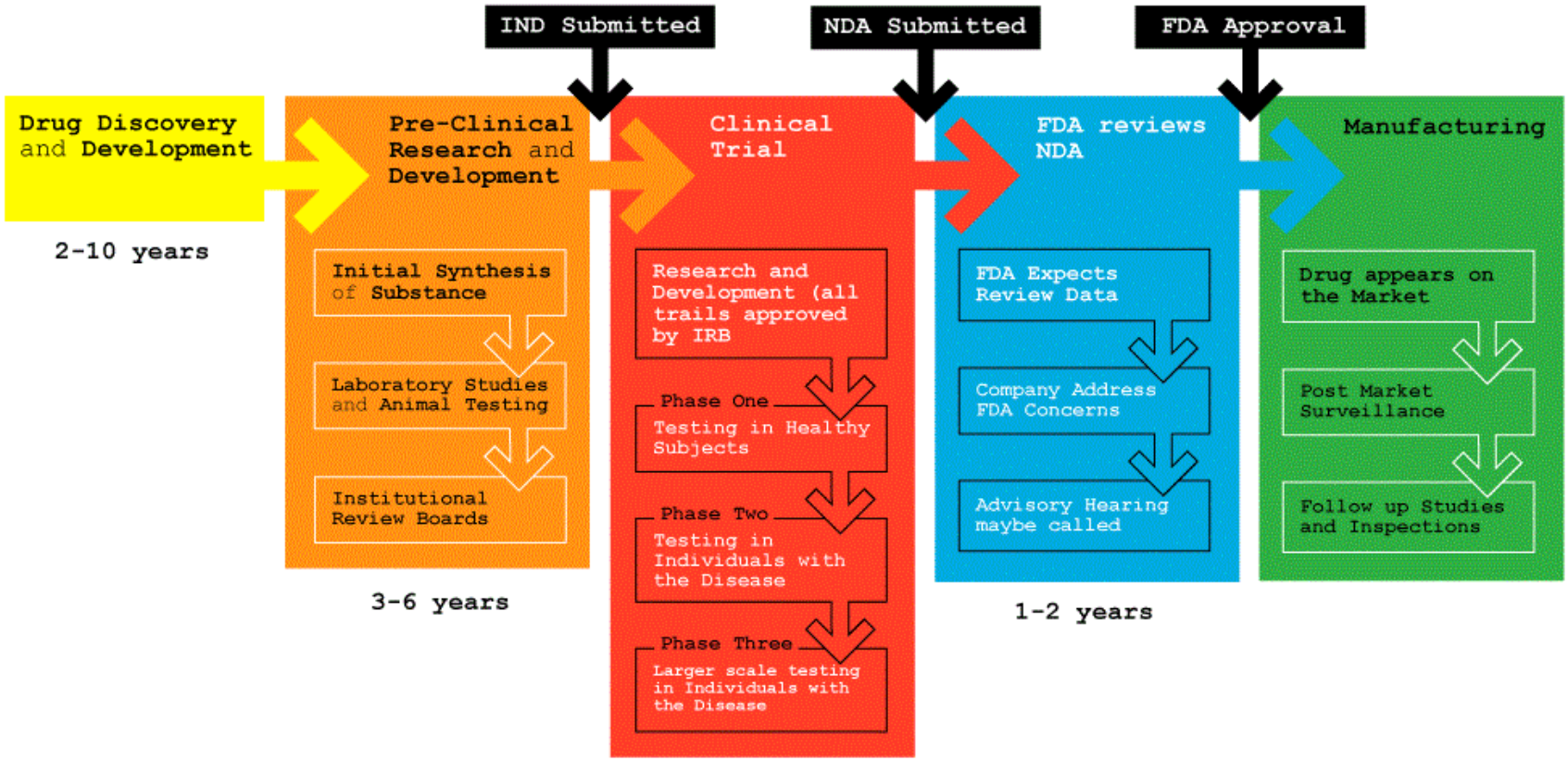
TOWARDS A REGULATORY FRAMEWORK FOR RAPID RESPONSE BIOLOGICS

November 17 2014

Agenda

- Traditional drug development and approval timelines
- Regulations for rapid approvals in major jurisdictions
- Recent joint efforts with respect to expeditious approval of immunotherapies and vaccines for Ebola

Traditional Drug Development and Approval Timelines



FDA = US Food and Drug Administration
IND = Investigation New Drug
NDA = New Drug Application

Rapid Approval - FDA

- Early and frequent consultation between sponsor, end user (if different) and FDA
- Fast track
- Priority review
- Accelerated approval – surrogate
- Approval under "Animal Rule"
- Availability for emergency use under IND or Emergency Use Authorization (EUA) or Expanded Access to investigational drugs

Rapid Approval - EMEA

- Orphan Drug Designation
- Rapid scientific advice
- Fast-track assessments
- Accelerated approvals

BUT….

- Still approvals through separate jurisdictions
- Differing levels of evidence may be required
- Differing opinions of endpoints and clinical trial designs
- Often a sequential process rather then parallel process
- More and more time lost….

The New Emerging Regulatory Paradigm

Global Regulatory Approach to the Ebola Outbreak 2014

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Ethical considerations for the use of unregistered interventions for Ebola

- WHO Advisory panel convened on August 11 2014
- Panel consisted of bioethics experts form both developed and undeveloped regions
- Concluded that "it is ethically acceptable to offer unproven interventions that have shown promising results in the laboratory and in animal models …as potential treatment or prevention."
- Must be in addition to best possible standard of care and include full disclosure and transparency of all aspects of the care
- Safety and efficacy should be evaluated in the best possible clinical trial design understanding the limitations of the setting
- The relevant data generated from the "compassionate" use of these unregistered treatments must be shared with the scientific community

Report of an advisory panel to WHO – Ethical considerations for the use of unregistered interventions for Ebola viral disease August 11 2014

Statement on international regulatory cooperation regarding Ebola

- "..medicines regulators worldwide have committed to enhanced cooperation with WHO and between regulatory agencies to encourage submission of regulatory dossiers and …accelerate access to investigational treatments for patients most in need…."
- "…come up with practical solutions to ensure that meaningful data is collected and assessed so that decisions on the benefits and risks of medicines can be taken on the basis of limited scientific evidence…"
- "…to consider evidence form a wide range of sources to allow for decision-making under a greater degree of scientific uncertainty."

16th WHO International Conference of Drug Regulatory Authorities (ICDRA) Rio de Janeiro, August 24-29 2014

International Coalition of Medicines Regulatory Authorities

- Australia
- Brazil
- Canada
- China
- European Commission
- Ireland
- Italy
- Japan
- Netherlands
- Singapore
- South Africa
- United Kingdom
- U.S.A

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WHO Meeting on Therapies and Vaccines for Ebola

- Purpose: to discuss lead experimental treatments and vaccines for Ebola
  - potential risks and benefits
  - availability in the short and long term
  - potential use and barriers for use
  - key considerations for deployment in West Africa
  - clinical testing, use, ethics, regulation and data collection

WHO Consultation on potential Ebola therapies and vaccines, 4-5 September 2014, Geneva

Key Questions

- What should be the overall objectives of a plan for evaluation and use of unregistered interventions (therapies and vaccines) as a response to the current outbreak and in preparation for the future?
- What are the most important actions to ensure successful evaluation and use (if appropriate) for any of these investigational interventions?
- What kind of support is required to ensure successful implementation of proposed plans for the evaluation and use of these interventions (therapies and vaccines)?

Meeting

- The 2-day meeting involved approximately 200 participants including scientists and commercial drug developers, regulatory agencies and public health agencies
- Participation from the Ebola effected countries
- Included an update for all on developing therapies and vaccines

Meeting Summary of the WHO Consultation on potential Ebola therapies and vaccines, 4-5 September 2014, Geneva

Summary

- Basic care needs to be established first before any clinical testing can occur
- Point of care diagnostics urgently needed and require expedite review and approval
- Vaccines (VSV-EBOV and ChAd-EBOV) in human testing
- Available data on therapeutics limited to in vitro and animal data (insufficient)
- Best candidates are blood-derived therapies

Summary

- Ethically the use of observational studies (including compassionate use) rather than RCT (PL)
- Establish a WHO centrally coordinated multi-stakeholder consortium for ethical review of interventions
- Issues with the multiplicity of regulatory networks (global vs local)
- WHO urged to establish guidance on regulatory pathway for development of products

Summary

- Establishment of an international review body to review data form studies, an independent safety monitoring board and register of clinical trials
- WHO urged to continue Expert Working Groups to support mechanisms for the
  - development of a mechanism for evaluating pre-clinical data
  - design of appropriate clinical trial protocols and ICFs
  - design of a platform for real time data collection and sharing

What is the New Regulatory Model

- Local authority supported by global advisory committees
  - Ethics
  - Data Safety Committees
  - Review of INDs
- Enforced mandatory real time data sharing
- Global regulatory oversight – WHO

Advantages

- Consistency in the development of new therapies and their application
- Reduction in the redundancy of generated data
- Efficiency and effectiveness of approvals for use
- Superior level of approval driven by centralized expert reviews