UN Panel Discussion on Climate Change and Its Impact on Children's Health

The View from FDA and Biotech World

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Global Climate Change and Health

- The need for development of new vaccines
  - Insect-borne diseases are the major causes of morbidity and mortality in several tropical and subtropical countries
  - Climate, i.e. temperature, precipitation, humidity, wind, etc. can influence various aspects of an arthropod vector's life cycle, including survival, arthropod population numbers, vector pathogen interactions, pathogen replication, vector behavior and of course vector distribution
- Control of vector-borne diseases is becoming a great challenge
- Need improved efficiency and efficacy of existing interventions and their combinations, such as vector control, diagnosis, treatment, and vaccines

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Role of Biotechnology

- Traditional vaccination strategies use weakened or inactive forms of microorganisms to mount the initial immune response
- Modern techniques use the genes of microorganisms cloned into vectors to mass produce the desired antigen
  - May include nucleic-acid based (DNA) vaccines, viral-vectored vaccines, recombinant fusion protein vaccines and genetically altered attenuated live vaccines
- The antigen is then introduced into the body to stimulate the primary immune response and trigger immune memory

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Role of FDA

- Significant experience in review and approval of vaccines, which can benefit vaccine developers
- A number of regulatory pathways are available to expedite the development of vaccines
- FDA can license vaccines to protect against infectious diseases or conditions that are not endemic or have not been reported to occur in the U.S.
- The regulatory pathways to U.S. licensure for the development of vaccines for neglected diseases of the developing world are the same as for diseases endemic to the U.S.

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Regulatory Pathways

- Food and Drug Administration Amendments Act of 2007 (Public Law 110-85) dated September 27, 2007 (FDAAA) added Section 524 which authorized FDA to grant priority review for products to treat and prevent tropical diseases that disproportionately affect poor and marginalized populations and for which there is no significant market in developed nations
- Accelerated approval may be granted for certain biological products that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments (21 CFR Part 601, Subpart E)
- The Animal Rule (May 2002) allows appropriate studies in animals in certain cases to provide substantial evidence of the effectiveness of new drug and biological products when definitive human efficacy studies are not ethical or feasible.

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Foreign Clinical Studies

- Foreign clinical studies are likely to be necessary if the disease of interest has a low incidence in the U.S.
- FDA regulations permit the acceptance of foreign clinical studies in support of a BLA
- FDA will accept well-designed and well-conducted foreign clinical studies if
  - The study was conducted under GCP
  - Were reviewed and approved by an independent ethics committee

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Human Challenge Studies

- In some situations, it may be possible to conduct challenge studies in human subjects during early development or in lieu of clinical trials in an endemic area
  - Human challenge studies could suffice to demonstrate efficacy of a cholera vaccine provided that studies were adequate and well-controlled and conducted under the provisions of GCP
- Because of unique issues, sponsors should discuss plans for human challenge studies with FDA

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Pediatric Development

- For many global diseases (e.g., malaria), the pediatric population may face greater mortality or morbidity than the adult population because adults may already be immune
- If the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, FDA may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults with supplementary information from pediatric studies

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Pediatric Development

- Pediatric development should be discussed with FDA at an End of Phase 2 meeting, or earlier if it is the predominant patient population of interest
  - A Pediatric Study Plan is required to be submitted for FDA review and agreement within 60 days of the End of Phase 2 meeting
- EMA requires submission of a paediatric investigation plan earlier in the development program
- If the EMA and FDA consider the product to be of major importance they may initiate cross-agency discussions early in the development program

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Challenges of Conducting Clinical Trials in Developing Countries

- Possibility of scarce health resources in the region
- Cultural issues with obtaining voluntary, legally acceptable, informed consent
  - Language
  - Different understanding of the cause of disease
  - Paternalistic society where male community or family members make all decisions for the women and children
- Available of resources to pay for the treatment once it is developed

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Conclusion

- Global climate change will increase the requirement for the development of new vaccines and other products for use around the world, especially in developing countries
- Regulatory Agencies in developed countries are eager to facilitate development of vaccines and other products for use in developing countries, particularly in children.
- It is important for developers of these products to engage in discussion with these agencies early in the development process and take advantage of their experience and advice

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