The Forum HIV Cure Project: Focus on Regulatory Issues

A Collaborative Effort to Map the Regulatory Pathway for HIV Cure Strategies

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Acknowledgments

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Additional project support provided by:

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• Veronica Miller, PhD

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• George Hanna, MD
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Academia:
• John Mellors, MD
• Jintanat Ananworanich, MD, PhD

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Forum Staff

- Erik Lontok
- Nivedha Panneer
- Courtney Hutchison (Year 1)
- Sonia Navani (Year 1)
Accelerated Access to Innovative Medicines for Patients in Need

LG Baird\textsuperscript{1}, R Banken\textsuperscript{2}, H-G Eichler\textsuperscript{3}, FB Kristensen\textsuperscript{4}, DK Lee\textsuperscript{5}, JCW Lim\textsuperscript{6}, R Lim\textsuperscript{5}, C Longson\textsuperscript{7}, E Pezalla\textsuperscript{8}, T Salmonson\textsuperscript{9}, D Samaha\textsuperscript{2}, S Tunis\textsuperscript{10}, J Woodcock\textsuperscript{11} and G Hirsch\textsuperscript{1}

- Current “siloed” system increases development cost, time and risk
- Inefficient use of accelerated access programs
- FDASIA Legislation (2012): apply principles more broadly
- Increased cross-jurisdictional and cross-functional interaction
- Increased engagement of all stakeholders

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Forum “Process” in Drug Development

- HIV
  - Clinical trial design
  - Recognition of new toxicities
  - Long term safety monitoring
  - Immune based therapies
  - Introduction of new drug classes (CCR5)
- HCV
- CMV-transplantation
- Liver fibrosis/NASH

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**Context**

- Benefit-risk is cornerstone of regulatory process
- Enthusiasm balanced by efforts to ensure safety, decrease/manage risk
- Requires:
  - Clarity of purpose (clear communication of goals)
  - Consensus + evolving consensus
  - Maximum research efficiency through collaboration
  - Each patient’s data contribution as valid and informative as possible

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Specific AIMS – Year 1 & 2

• Facilitate and advance HIV cure research by clarifying and resolving regulatory issues through multi-stakeholder dialogue
  – Provide an ongoing neutral and independent platform for targeted discussions with multi-stakeholder experts
  – Provide a productive mechanism for broader, public input on questions of acceptable risk, ethics, informed consent and appropriate populations

• FORUM NICHE
  – Regulatory Pathway: Facilitate FDA efforts for more systematic patient input on benefit-risk decision making (PDUFA V)

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Year 1: Working Groups

- #1: Biomarkers & Endpoints
  - John Mellors & Michael Miller

- #2: Clinical Trials – Benefit – Risk
  - Jintanat Ananworanich & Joe Eron

- #3: Patient education, recruitment & informed consent
  - David Evans & Tim Henrich
Working Group Members

Jintanat Ananworanich  David Evans  Richard Jefferys  John Mellors  Seema Shah
Rachael Anatol  David Favre  Rowena Johnston  Mike Miller  Matt Sharp
Chuka Anude  Susan Fiscus  Filip Josephson  Veronica Miller  Jeff Sheehy
Jose Arribas  Kevin Fisher  Andy Kaytes  Ron Mitsuyasu  Adam Sherwat
Mark Bagarazzi  Joe Fitzgibbon  Damian Kelly  Paris Mullen  Neil Shortman
Stephen Becker  Charlie Flexner  Hans-Peter Kiem  Rob Murphy  Janet Siliciano
Gwen Binder-Scholl  Yuman Fong  Richard Klein  Jeff Murray  Kim Struble
Jacques Bollekens  Nicole Frahm  Rick Koup  Charles Nicolette  Jeremy Sugarman
Nicolas Chomont  Victor Garcia  Dan Kuritzkes  Una O’Doherty  Geoff Symonds
Mike Cohen  Sam Garner  Diane Lawrence  Lars Ostergaard  Winson Tang
Giulio Maria Corbelli  Romas Geleziunas  Michael Lederman  Cecile Peltekian  Jeff Taylor
Liza Dawson  Sara Goldkind  Sandi Nusinoff Lehrman  Deborah Persaud  Pablo Tebas
Lynda Dee  Cynthia Grossman  Yves Levy  Chris Petropoulos  Randy Tessler
Steve Deeks  George Hanna  Sharon Levy  Carla Pettinelli  Kati Vandermeulen
Jim Demarest  Patrick Harrington  Jeff Lifson  Sarah Read  Mark Wainberg
Damon Deming  Mark Harrington  Bernard Lo  Harriet Robinson  Chris Ward
Carl Dieffenbach  Daria Hazuda  David Margolis  Anna Laura Ross  Carol Weiss
Tri Do  Gail Henderson  David A Margolis  John Rossi  James Whitney
Karine Dube  Tim Henrich  Javier Martinez-Picado  Asier Saez-Cirion  Celia Witten
Michael Egan  Carey Hwang  Steve Mason  Paul Sato  Brian Woodfall
Joe Eron  Ilan Irony  Julie McElrath  Tim Schacker  Jerry Zack

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## Working Group Members

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Academia | Community/Advocacy | Federal Government | Foreign Government | Foundation | Industry

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Charge to Working Groups

- Formulate, review, and discuss specific questions
- Establish baseline: where is the field now?
- Record consensus where possible
- Recommend path forward for future consensus

Motto: Need to start somewhere

Take small steps – build on success
Regulatory Path?

• Effect of strategy vs. “CURE”
  – Intermediate steps vs. end-goal
• Combination of strategies
  – What, when, how?
• Combination of experimental + approved
• Combination of experimental + experimental
Progress

• Document current status of field from a regulatory perspective
• Measurable definition of “cure”
• Risk mitigation strategies for clinical trials
• Components of appropriate informed consent
• Guidance on survey instruments to collect patient perception of benefit-risk
June 17: Public Input

- Opening by CBER director Karen Midthun
- Working groups reports and discussion
- Case studies
- 180+ in person /200+ webcast participants
- Post June 17
  - Project evaluation
  - Publication plan
  - Review/re-align
Specific Aims ‘14 – ‘15

• Clarify & resolve regulatory issues through multi-stakeholder dialogue
  – Independent/neutral platform for targeted discussions
  – Mechanism for broader public input of what is acceptable risk

• Community perception of HIV cure research & willingness to refer/participate

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Specific Activities: WG Evolution

- WG 1: Animal model working group
- WG 2: Network for focused/targeted discussion on specific strategies
- WG 3: Interdisciplinary research interaction
Other Potential Activities

- Perceptions, beliefs and knowledge among patients, providers, communities and researchers
  - Influence on willingness to participate/refer
- Recruitment strategies for different patient populations
- Research interaction between social scientists, decision making science, behavioral economics, etc.
Advantages/Contribution

• Increased efficiency of development
  – All parties in the room vs. one-one

• Signal that field is structured/poised to move ahead
  – Recruitment of new partners and collaborators

• Support and synergize with other ongoing efforts
  – Annenberg group, IAS, etc.