Assessment of the Contraceptive Research Activities of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

Key Recommendations of the Panel

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Panel Members

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- William J. Bremner, MD, PhD, The University of Washington
- Melissa Gilliam, MD, MPH (Co-Chair), The University of Chicago
- Carolyn Tucker Halpern, PhD, The University of North Carolina at Chapel Hill
- Daniel S. Johnston, PhD, Pharmaceutical/Scientific Consultant
- Gregory S. Kopf, PhD (Co-Chair), FHI 360
- John R. McCarrey, PhD, The University of Texas at San Antonio
- Patricia L. Morris, MS, PhD, Population Council
- Ken Muneoka, PhD, Tulane University
- Paul Wise, MD, Stanford University

NICHD Contraceptive Research Activities

- Identification contraceptive targets and development of drugs/devices
- Behavioral research
- Training

The Charge

- Assess past accomplishments, impact, and current status of contraceptive R&D activities at NICHD

- Identify areas for improvement and innovation, making specific recommendations for increasing the likelihood of future success

The Approach

- Six months, two phases:
  - Review previous two decades of contraceptive R&D activities
  - Make recommendations for improvement
- Discussions held among the Panel, with NICHD staff, and with experts in the field
- Focus was primarily on the three NICHD branches most closely aligned with contraceptive research programs:
  - Contraceptive Discovery and Development Branch (CDDB)
  - Fertility and Infertility Branch (FIB)
  - Population Dynamics Branch (PDB)

Overall Assessment

- Contraception critically important and the Panel fully supports NICHD's mission
- Current R&D activities are not a sufficiently coherent and strategic response to lack of private sector engagement
- NICHD needs to assume leadership role in the development of new research paradigms or methods of operation to achieve success
- **NICHD must assume a more focused strategic and leadership role by promoting cutting-edge scientific discovery, product development, and studies of end user needs and acceptance**

Cross-Cutting Recommendations

Recommendation #1: **Improve Communication**

- Among branches (i.e., CDDB, FIB, PDB)
- Between branches and NICHD leadership
- Between branches (especially the CDDB) and other NIH institutes, scientific community, peer review panel members, private industry, non-profit sector
- Between branches and PIs both pre-application and during funding cycles

Cross-Cutting Recommendations

Recommendation #2: **Restructure Application and Peer Review Process**

- More specific language in RFAs/RFPs to increase alignment with goals
- Create standing peer review subcommittee within NICHD for contraceptive R&D proposals to ensure alignment with goals
- Develop dedicated Contraceptive Development Review Panels under the auspices of NICHD charged with well-defined areas for review of research/development proposals to ensure that reviewer expertise is aligned with proposal content

Cross-Cutting Recommendations

Recommendation #3: **Foster Closer and More Productive Interactions with Industry**

- Engage industry to reinvigorate interest and maximize opportunity/possibility for products in development to be licensed to industry for further development
- More aggressive and effective use of SBIR and STTR funding to stimulate collaborations between investigators and entrepreneurs
- Explore indemnification of products (i.e., through a product liability exemption)

Cross-Cutting Recommendations

Recommendation #4: **Foster Training Relevant to Contraceptive Development**

- Increase career development award annual salary caps from $75,000 to at least $100,000 (preferably $125,000)
- Continue and increase funding of training programs devoted to family planning and contraception research
- Increase number of K24 grants for mid-career basic and clinical scientists whose research targets contraception development and related behavioral issues

Cross-Cutting Recommendations

Recommendation #5: **Improve Monitoring & Evaluation (M&E) and Tracking of Progress**

- Develop progress metrics and M&E criteria tracked by both investigators and NICHD to assess performance and process

Cross-Cutting Recommendations

Recommendation #6: **Increase Diversity**

- Strive to increase diversity of researchers through minority supplements, career development awards, and training programs that target underrepresented populations
- Strive to increase workforce diversity at all levels by hiring diverse staffs, ensuring regular cultural competency training, and working closely with HR to learn best practices
- Create robust relationships with community organizations representing diverse populations (e.g., racial, ethnic, religious, sexual orientation) to better understand contraceptive concerns and needs
- Increase consideration of diversity issues within research by ensuring that diverse groups are represented in research populations in clinical and behavioral studies

Cross-Cutting Recommendations

Recommendation #7: **Inclusion of Global Populations**

- Keep global populations in mind when developing strategies and product pipelines – overpopulation and unwanted pregnancy are global issues
- Increase communication and strategy integration with other international global health/human development agencies and NGOs

Cross-Cutting Recommendations

Recommendation #8: **Pursue Innovative Devices**

- Assume a leadership role in bringing new drug delivery technologies and platforms to market and supporting post-marketing device and related behavioral research

Branch-Specific Recommendations: Early Development

Recommendation #9: **Improve Early Development Pipeline**

- Increase emphasis on target ID and validation with focused RFAs
- Actively monitor FIB grant portfolio for new potential targets
- Encourage any NICHD-funded bioinformatics analyses of identified target strategies to include mining publicly available data and data repositories
- Develop RFA to curate all potential contraceptive targets from large-scale national/international consortia designed to understand gene function

Branch-Specific Recommendations: Early Development

Recommendation #9: **Improve Early Development Pipeline (con't)**

- Consider multiple funding approaches for contraceptive target ID and related activities
  - Shorter funding periods (e.g., 1-2 years) and smaller budgets (e.g., $100-200K) with milestones and go/no-go decision criteria to be met for renewal
  - R21, R33, SBIR, administrative supplements, centralized IDIQ-type contract
- Commit to programs until they fail to meet go/no-go criteria
- Implement a modified scoring mechanism for drug development program reviews, including criteria recognized by industry/regulatory agencies and/or criteria to promote maximum acceptance/utilization among end users

Branch-Specific Recommendations: Early Development

Recommendation #10: **Strengthen Target Selection and Validation Processes**

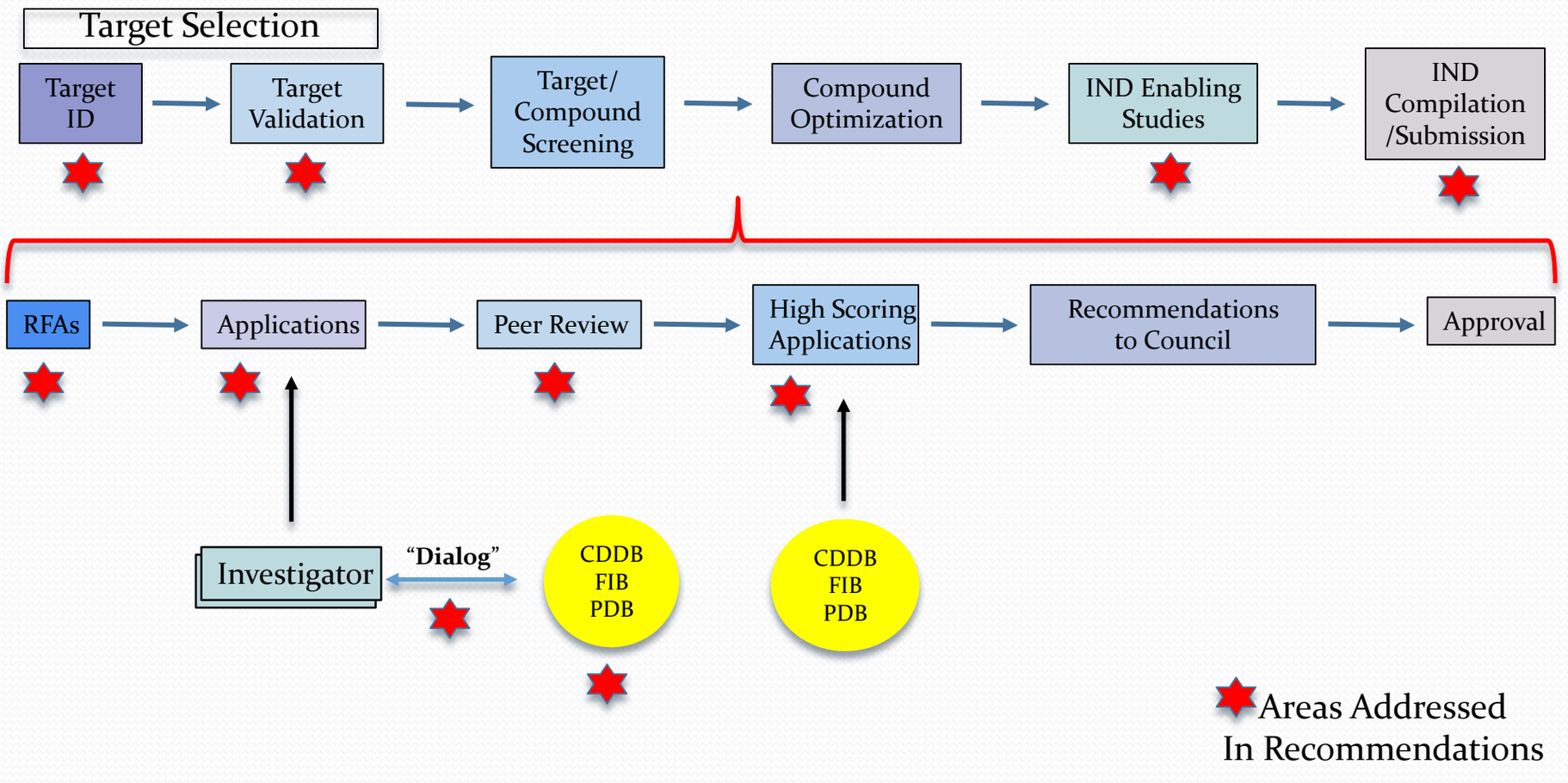
- Pursue targets that have a highly promising, “druggable” mechanism of action and those validated with specific and convincing methodologies
- Evaluate novel methods that strongly suggest that pharmacologic modulation would lead to a contraceptive effect, including models of reduced target function (e.g., knockdowns) as opposed to complete loss of function (e.g., knockouts)

Branch-Specific Recommendations: Early Development

Recommendation #11: **Target Areas of Focus for Early Stage Drug Development Programs**

- Male hormonal methods and non-hormonal targets
- New or reformulated female hormonal methods
  - Specific populations (e.g., adolescents, obese women, women who have infrequent sex)
  - Multiple purposes (e.g., contraception and HIV protection)
  - Non contraceptive health benefits (e.g., protection against cancer, bone loss)
- Female non-hormonal targets
- New delivery and device technologies that can be applied to contraception

Summary of Areas in Drug Program Initiation and Pre Clinical Product Development Addressed in the Recommendations of the Panel



Branch-Specific Recommendations: Clinical Studies and Training

Recommendation #12: **Contraceptive Clinical Trials Network (CCTN)**

- Re-evaluate number of female sites to maximize efficiency and effectiveness
- Leverage CCTN for training and cultivating expertise in contraceptive development, creating more opportunities for meetings and collaboration among the female sites and between the female and male sites
- Establish and utilize a single centralized Institutional Review Board (IRB) that would serve all CCTN sites
- Engage industry to develop best practices to make CCTN sites more attractive to industry-sponsored trials

Branch-Specific Recommendations: Social and Behavioral Research

Recommendation #13: **Better Integrate Behavioral Research Throughout Contraception Development**

- Better incorporate behavioral research in strategic development of contraceptive pipeline, both on the front end and back end
- Support new/expanded areas of research that incorporate:
  - Systems / policies that affect contraception acceptance, use, discontinuation
  - Men and women's priorities for their contraceptive use and their partners' use
  - Individuals' physical and social contexts
  - Quality of life issues (e.g., behavioral/mood effects of hormonal contraceptive methods)
- Continue / increase attention to the needs and contraceptive use of diverse populations (e.g., adolescents, minorities) in diverse settings

Branch-Specific Recommendations: Social and Behavioral Research

Recommendation #13: **Better Integrate Behavioral Research Throughout Contraception Development (con't)**

- Leverage the National Survey of Family Growth (NSFG), the National Longitudinal Study of Youth (NLSY), and the National Longitudinal Study of Adolescent to Adult Health (Add Health) datasets to inform all aspects of contraceptive behavior and use
- Expand diversity of study samples through CCTN-supported post-marketing and behavioral studies
- Focus strongly on communication, translation of findings, implementation science

Conclusions

- NICHD's contraceptive R&D programs serve a critical research and training role needed for product development in the field of family planning
- NICHD must be a leader in the development of new and innovative contraceptives to fill the void left with the exit of industry
- NICHD must evolve and adapt its current approaches to meet the dynamic changes and challenges in this field