

National Institute of Allergy and Infectious Diseases



# Forging New Partnerships to Advance Pediatric Formulations Development: An Overview of NIH Resources Spanning the Formulation Development Lifecycle

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NIAD



National Institute of  
Allergy and  
Infectious Diseases

# What are the Goals of This Presentation?

- Describe the mission of the U.S. National Institutes of Health (NIH) and available NIH resources to advance pediatric formulations
- Demonstrate our intention to use these resources to develop a new age-appropriate formulation for HIV or TB
- Highlight the opportunity to use these resources to supplement existing efforts and strengthen partnerships across organizations

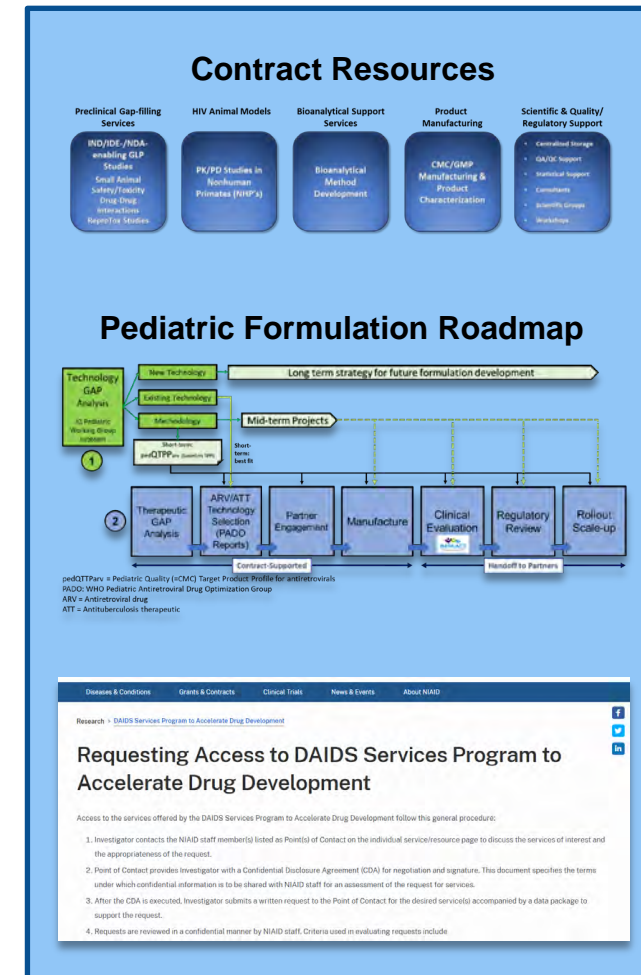


IQ DPLG Pediatric Working Group



# Outline of Presentation

- Present an overview of NIH and a new NIAID contract to be awarded in July 2023
- Describe how **contract resources** to advance HIV prevention products have been expanded to include pediatric formulations for HIV treatment
- Explain how current contract resources have been used to start developing a **Pediatric Formulation Roadmap**
- Provide information on how to **access these contract resources**
- Invite interested stakeholders, including industrial partners, to join us and provide your expertise and guidance in supporting prioritized areas of pediatric formulation development



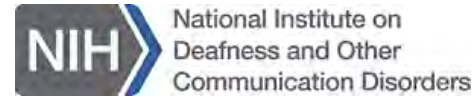
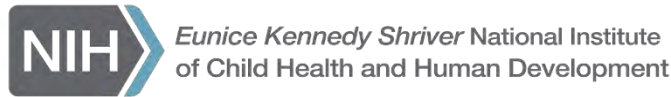
# Who is NIH and What Do We Do?



Source: <http://www.nih.gov/>

- The National Institutes of Health (NIH) is one of the world's foremost medical research centers.
- 168 NIH-supported scientists from around the world have been sole or shared recipients of 99 Nobel Prizes for their groundbreaking achievements in Physiology or Medicine, Chemistry, Physics, and Economic Sciences.
- NIH is one of 11 agencies in the Department of Health and Human Services and the federal focal point for health research in the United States.
- NIH is organized into 27 Institutes and Centers with the following goals:
  - Foster fundamental creative discoveries, innovative research strategies, and their applications as a basis to advance significantly the capacity to protect and improve health
  - Develop, maintain, and renew scientific human and physical resources that will assure the capability to prevent disease
  - Expand the knowledge base in medical and associated sciences in order to enhance the economic well-being and ensure a continued high return on the public investment in research

# Multiple NIH Agencies are Interested in Development of Pediatric Formulations



## National Institute of Allergy and Infectious Diseases (NIAID):

- Development of long-acting or extended-release antiretroviral products for HIV treatment and prevention in infants, children, and adolescents
- Contract and other resources to support the development and advancement of age-appropriate formulations for HIV and associated co-morbidities such as tuberculosis

## National Institute of Child Health and Human Development (NICHD):

- Development of appropriate pediatric formulations and pediatric drug delivery systems
- An understanding of the scientific, technical, and regulatory barriers for the development of pediatric formulation
- Taste, smell, and flavor research in infants and children
- Use and application of new drug delivery systems in pediatrics

## National Institute on Deafness and Other Communication Disorders (NIDCD):

- Studies of the chemical senses—taste, smell, and chemesthesis (chemically provoked irritation) -- to enhance our understanding of how individuals communicate with their environment
- Research on the development of bitter-taste blockers to identify compounds that can mask the bitter taste of essential medications, especially for young children.

# New NIAID Contract: Resources to Advance Pediatrics and HIV Prevention Science (\*RAPPS)

## ■ Purpose

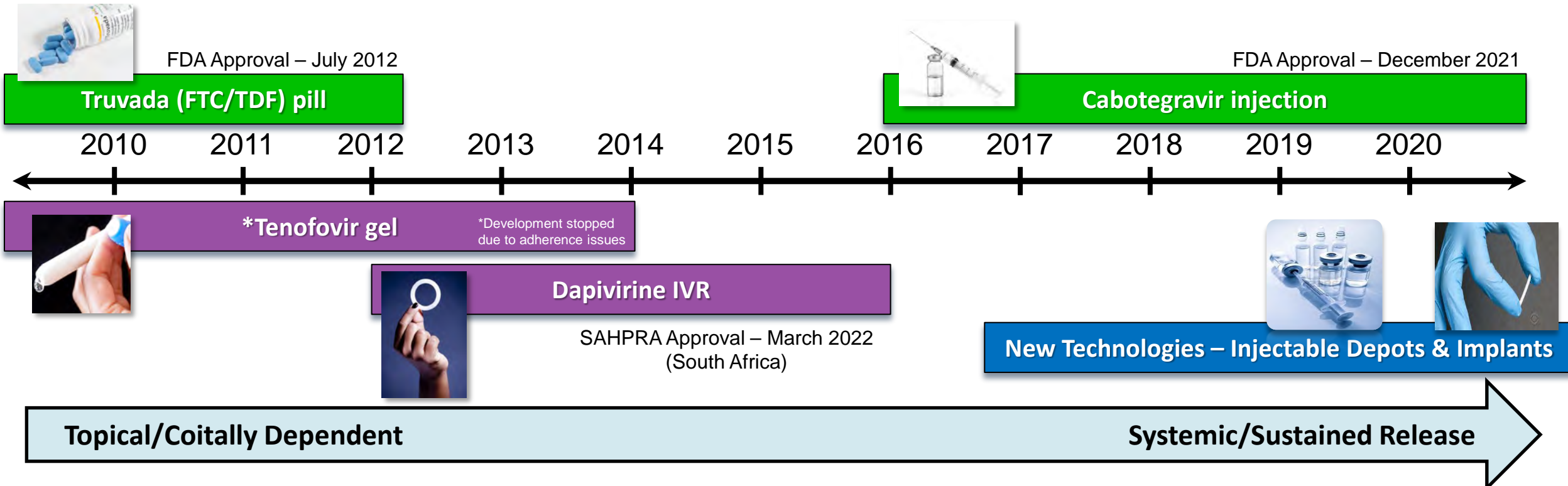
- To provide drug development resources to support advancement of the next generation of HIV biomedical prevention products and **HIV treatment and prevention strategies in maternal (pregnant or breastfeeding women) and pediatric populations**

## ■ Objectives of the Program

- Advancement of promising next generation non-vaccine HIV biomedical prevention products into human clinical testing
- Expansion of user preference studies to better understand desire/choice and how best to engage women and men in HIV treatment or prevention
  - Emphasis on adolescent girls and young women (AGYW) ages 14-25 years old
  - **Potential for studies in caregivers of pediatric populations**
- Provision of gap-filling resources to support **HIV treatment and prevention strategies in maternal and pediatric/adolescent populations**
  - **Includes age-appropriate formulations and co-infections/co-morbidities**
  - **Includes treatment/prevention strategies in newborns/infants**

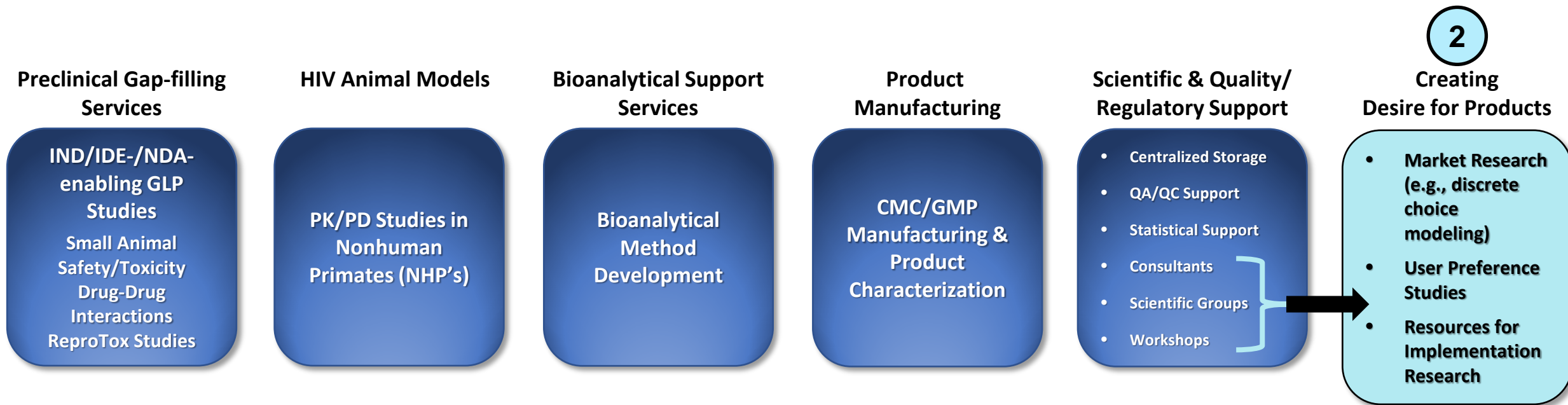
# NIAID Contracts Have Supported Formulation Development for the Evolving Landscape of Non-Vaccine HIV Prevention

- Over the past 12 years, NIAID contracts have supported the development of 12 product IND's – leading to the activation of multiple clinical trials.
- Supported formulation types have included topical gels, films, intravaginal rings (IVR's), a long-acting injectable, and an implant.
- As products have evolved from early topical microbicides to more advanced sustained-release formulations, our contracts have adapted to support the ongoing needs of product developers.



# How Can the RAPPS Contract Be Used to Support Pediatric Formulation Development?


- 1 RAPPS contract resources will be based on those in a current DAIDS contract but expanded to include HIV treatment and prevention strategies/age-appropriate formulations in maternal and pediatric populations
- 2 RAPPS contract will include greater emphasis on use of contract resources to better understand desire/choice and how best to engage women and men in HIV treatment and prevention (e.g., caregivers for infants and adolescents)



- 1 The resources available in these key task areas will allow expansion of the contract to support the range of preclinical activities that are necessary to develop age-appropriate formulations.



# Pediatric Formulations for HIV and TB – Activities Initiated under a Current DAIDS Contract



Engage Outside Experts  
as Consultants  
&  
Establish Objectives  
of NIH Initiative

- Establish expertise to supplement NIAID programs in the development and optimization of age-appropriate drug formulations for infants, children, and adolescents (Drs. Dixit, Hoag, and Schaufelberger)
- Assist NIAID in planning contract activities to support development of age-appropriate formulations
- Plan NIAID-sponsored consultations to bring together relevant stakeholders to:
  - Discuss key gaps and challenges
  - Identify potential gap-filling activities for a prioritized pediatric drug formulation
  - Discuss potential ways to leverage private-public partnerships to advance pediatric HIV drug formulations
- Develop an IP strategy with originators and generic manufacturers to accelerate global access to new molecules, formulations, and drug delivery technologies

# Research Strategy for the Development of Child-Friendly Formulations

**Technology Gaps**  
(the July 2021 workshop)

**Technology/  
Therapeutic Selection**  
(following expert group prioritization, e.g., PADO)

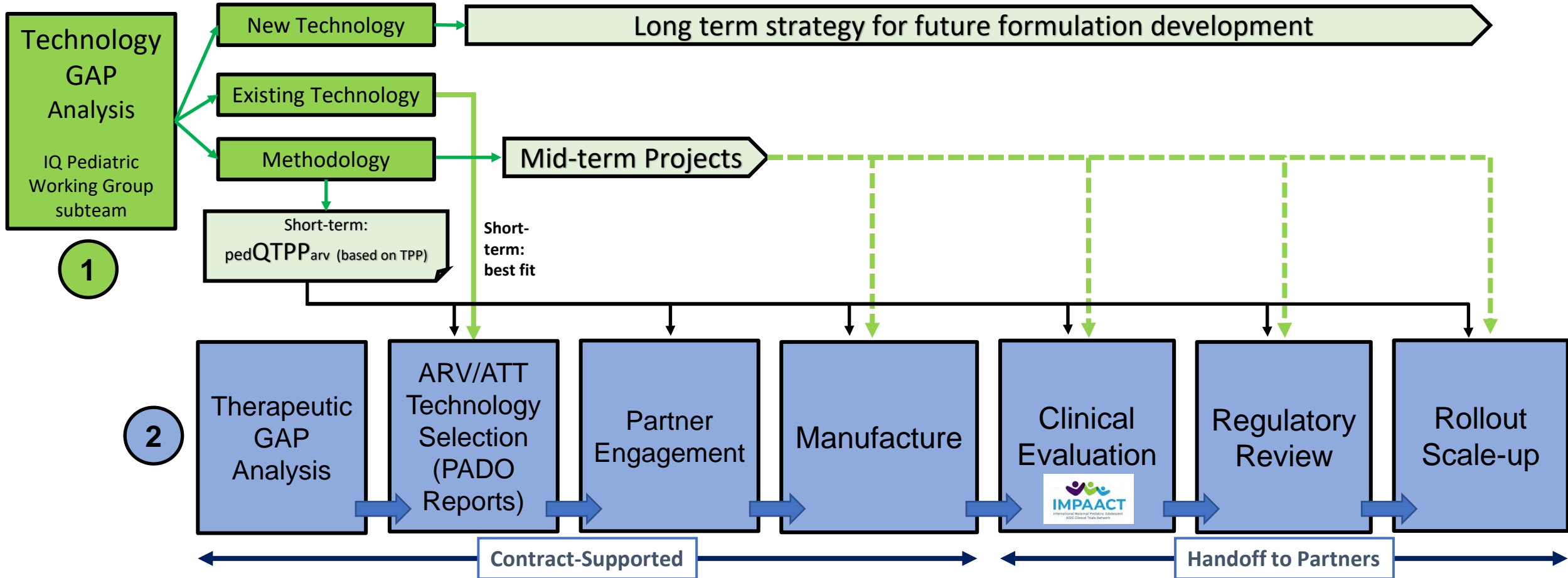
**Partner Engagement**  
(to identify partners)

**Manufacturing**  
(to identify necessary resources)

**New Child-Friendly Formulations**

- Feedback and recommendations from outside experts at these workshops is meant to supplement NIH expertise and aid in identification of key gaps and necessary resources to address these gaps.
- For any funding mechanisms used to support these activities, NIH Program staff will work independently to ensure a fair competition for NIH funding and avoid any potential conflicts of interest.

# Development of a Pediatric Formulation Roadmap: Technical & Therapeutic Gap Analysis



pedQTPParv = Pediatric Quality (=CMC) Target Product Profile for antiretrovirals  
PADO: WHO Pediatric Antiretroviral Drug Optimization Group  
ARV = Antiretroviral drug  
ATT = Antituberculosis therapeutic

# Identifying Partners & Relevant Stakeholders

## Past Partners (HIV Prevention)



Leveraging Relationships



Identifying Opportunities

## Future Partners (HIV Prevention & Pediatric Formulations)

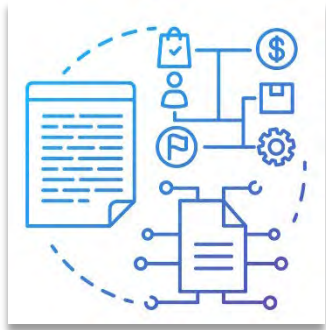


## Future Contract Expansion

- **Pediatrics**
  - Age-appropriate formulations
  - Co-morbidities (TB)
  - Cure research
- **Marketing Science/Human Centered Design**
  - Integrating concepts into product development

# NIAID Funding Process for Accessing Pediatric Formulation Resources under the RAPPS Contract

## Identify Specific Needs (Outside Groups)



- Universal gaps and challenges:
  - Working groups
  - Workshops
- Specific formulations (i.e., API and drug delivery platform)
- Pilot projects to advance the pediatric formulation field

Request Support

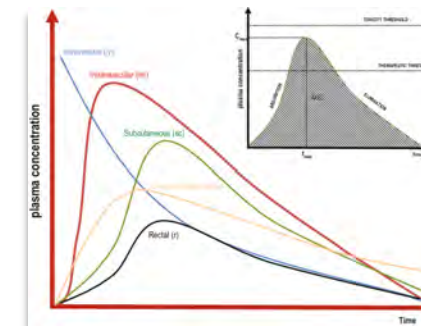
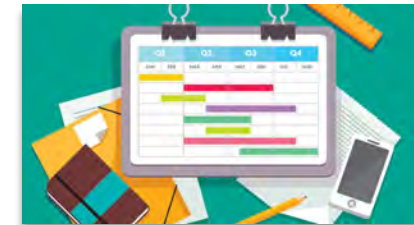
## NIAID Program Review



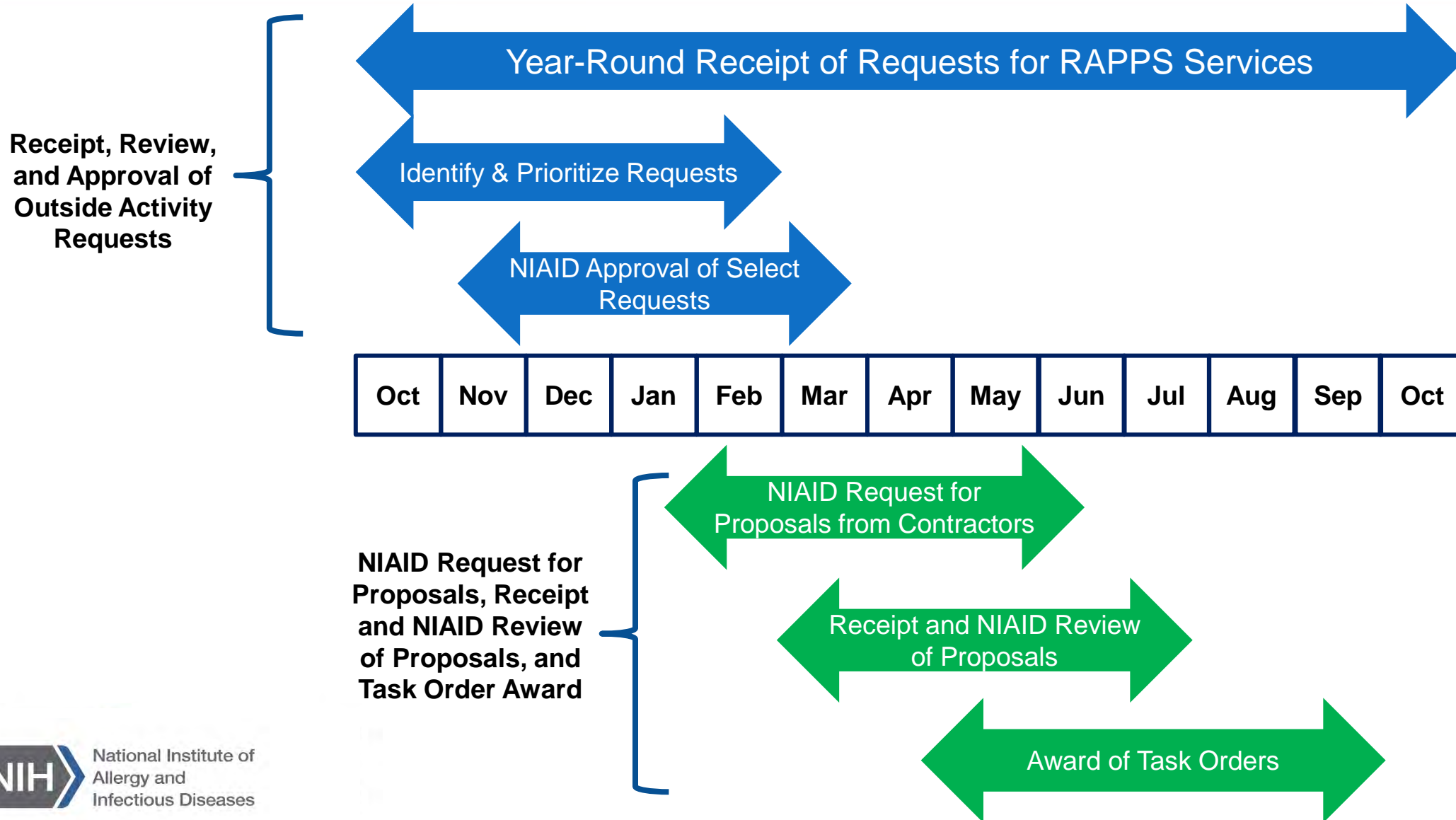
- Assess specific requests and alignment to Program research priorities
- May include requests for specific high priority needs from Program
- Consider available resources
- Prioritize activities for each fiscal year (2023-2030)\*

Select Projects Funded

## Initiative Activity with NIH Contractors



# Timeline: Receipt, Review, Approval, and Award of Activities Under RAPPS Contract



# How Do You Learn More about These Resources?

Details on the new contract:

<https://www.niaid.nih.gov/grants-contracts/pediatrics-and-hiv-prevention-science-rfp>

Website for requesting services under DAIDS contracts:

<https://www.niaid.nih.gov/research/requesting-access-daids-services-program>

DAIDS Program Contact for more information:

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# IQ Pediatric Working Group Colleagues: Join the Effort!

**Outcomes of a Joint US National Institutes of Health and Industry Pediatric Antiretroviral Drug Formulation Workshop**

*David Schifano, PhD; David D'Arcy; Stephen W. Hoag; Peter O'Brien; Alan MacFarlane; Patrick Liao-Phillips; Hans Spiegel; James Cummins*

**Introduction**

A virtual two-day workshop was held in July 2021 by the US National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS, Prevention Services Program (DAP) to discuss the current research and development needs for age-appropriate formulations for HIV antiretroviral drugs (ARV) and drugs to treat related comorbidities. Invited participants included industry experts from the IQ Consortium, Pediatric Working Group (PWG), representatives of the International Pediatric Advanced AIDS Clinical Trials (IPACT), Network, experts from academia, the NIH, and other US Government and non-government representatives, see reference for summary (1). The main objective of this workshop was to discuss and identify previously identified technology gaps in their status for pediatric formulations for HIV drugs. The technology assessment presented in this paper is part of a broader initiative by NIAID to advance the development of new, more age-appropriate pediatric formulations of antiretroviral drugs and products to treat related comorbidities.

**Workshop Objectives**

In speaking remarks Dr. Carl D'Arcy, Director of NIAID/DAIDS, discussed the workshop objectives:

- Focus on unmet needs of pediatric patients with HIV, understand current practices and opportunities in Low- and Middle-income Countries (LMICs).
- Collaborate and strengthen relationships between and avoid duplication of efforts.
- Understand how NIH can best advance the development of pediatric formulations.
- Identify and prioritize technology gaps in pediatric formulations for HIV.

**Methodology**

A total of 13 technology gaps were identified for high preparatory meetings with a select group of 12 PWG (2) pediatric working group members, see Table below. Advances from industry, academia and clinical research were given the opportunity to prioritize the gaps in and out, by reaching out to the gaps. The top 5 gaps were then discussed in more depth during the workshop.

**Results**

**TOP 5 Prioritized gaps:**

1. Long Acting - Injections
2. Taste Masking
3. Long Acting - Oral
4. Taste Masking
5. Microencapsulation

**Table: Technology Gaps (1-13) and Prioritization**

Area	No.	Topic	Technology GAP	Priority
Overall	1	Acceptability (taste)	Acceptability (taste) design forms and general understanding to formulation development of antiretroviral products for children (18-24) and (30-34) in LMICs.	4
	2	Acceptability (oral solution)	Acceptability (oral solution) antiretroviral products, limited data in age groups 2-7 for ready delivery.	5
	3	Microencapsulation	Microencapsulation, full range, including pediatric for oral formulations, "universal bitter blockers" used in "taste changers".	4
	4	Long Acting - Injections	Long Acting (LA) and formulation design for HIV in LMICs.	3
	5	Long Acting - Oral	Acceptability (oral solution) antiretroviral products, limited data in age groups 2-7 for ready delivery.	5
	6	Taste Masking	Acceptability (taste) design forms and general understanding to formulation development of antiretroviral products for children (18-24) and (30-34) in LMICs.	4
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**Recommendations**

1. Apply learnings to ongoing prioritization efforts, such as the WHO-led Pediatric Antiretroviral Drug Optimization (PAO) efforts. Engage in public-private partnerships, as appropriate in advance commitments made to the PAO prioritization.
2. Propose a "universal formulation platform" initiative, involving leading global leaders.
3. Organize follow-up workshop on "pediatric long-acting" dosage forms for HIV treatment/prevention.
4. Identify opportunities to advance basic research on sensory sciences and the potential development of "taste blockers" to enhance acceptability of pediatric oral formulations.
5. Identify opportunities for translational research studies to advance new dosage forms through research grants, based on the 13 gaps identified by the workshop participants in the 13 top 5 gaps.
6. Publish a white paper on "Pediatric Quality Targeted Profile for Antiretroviral drugs", identified as a consensus/industry/academic working list between DAP, and academic leaders.

*For all recommendations, further research opportunities, in LMICs, will focus on LMIC research to advance the highest impact for pediatric patients.*

**References**

1. Schifano D, D'Arcy D, Hoag S, et al. Pediatric Antiretroviral Drug Formulation Workshop: Summary Report. *Journal of Clinical Pharmacy and Therapeutics*. 2021;46(5):545-554.

2. Pediatric Working Group (PWG) members: [List of members]

**Specific Areas of Focus for Collaboration:**

- Long-acting formulations
- Neonate formulation platform
- Research in taste-masking / universal bitter blockers



IQ DPLG Pediatric Working Group

NIAID



# ACKNOWLEDGMENTS



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# Glossary of Terms



IND: Investigational New Drug Application

IDE: Investigational Device Exemption

NDA: New Drug Application

ARV = Antiretroviral drug

ATT = Antituberculosis therapeutic

CMC: Chemistry Manufacturing Controls

GLP: Good Laboratory Practices

GMP: Good Manufacturing Practices

QA/QC: Quality Assurance/Quality Control

NIAID: National Institute of Allergy and Infectious Diseases

NIH: U.S. National Institutes of Health

PADO: WHO Pediatric Antiretroviral Drug Optimization

RAPPS: Resources to Advance Pediatrics and HIV Prevention Science

pedQTPParv = Pediatric Quality Target Product Profile for antiretrovirals

SAHPRA: South African Health Products Regulatory Authority