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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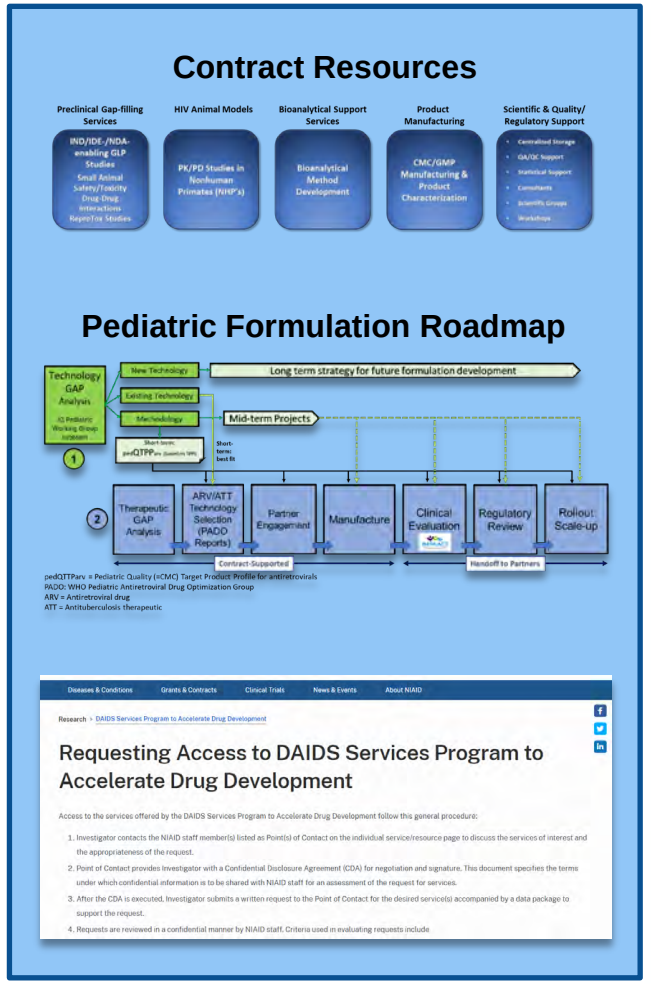
What are the Goals of This Presentation?

- 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?

- 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

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Multiple NIH Agencies are Interested in Development of Pediatric Formulations

NIH National Institute of Allergy and Infectious Diseases

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

NIH National Institute on Deafness and Other Communication Disorders

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.

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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**

*Anticipated award July 2023

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.

FDA Approval – July 2012

Truvada (FTC/TDF) pill

FDA Approval – December 2021

Cabotegravir injection

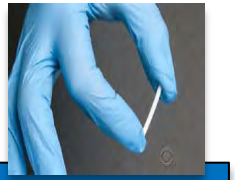
2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020

***Tenofovir gel**

*Development stopped due to adherence issues

Dapivirine IVR

SAHPRA Approval – March 2022
(South Africa)



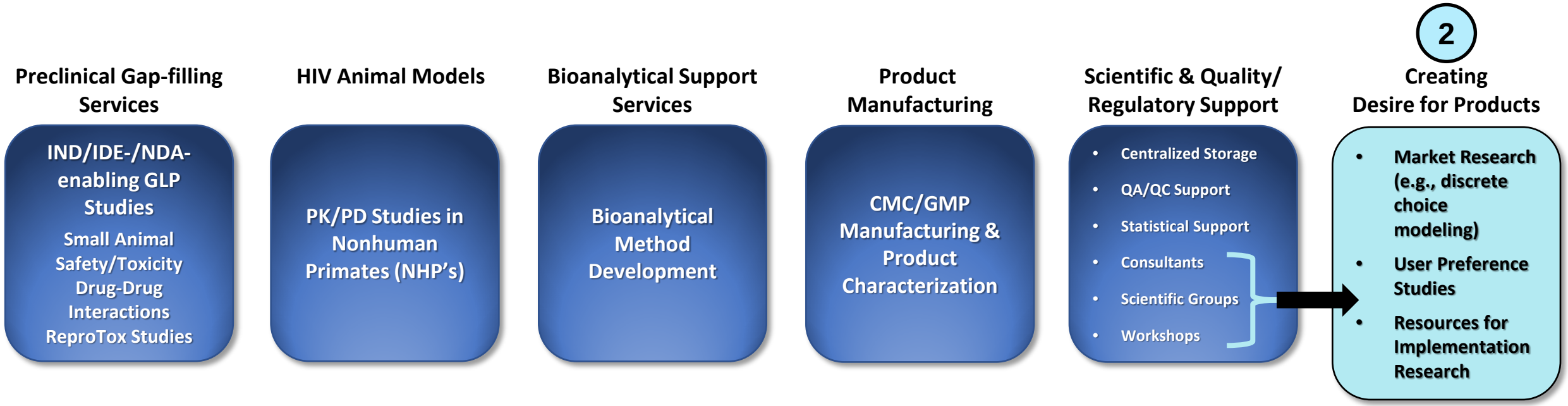
New Technologies – Injectable Depots & Implants

Topical/Coitally Dependent → **Systemic/Sustained Release**

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)

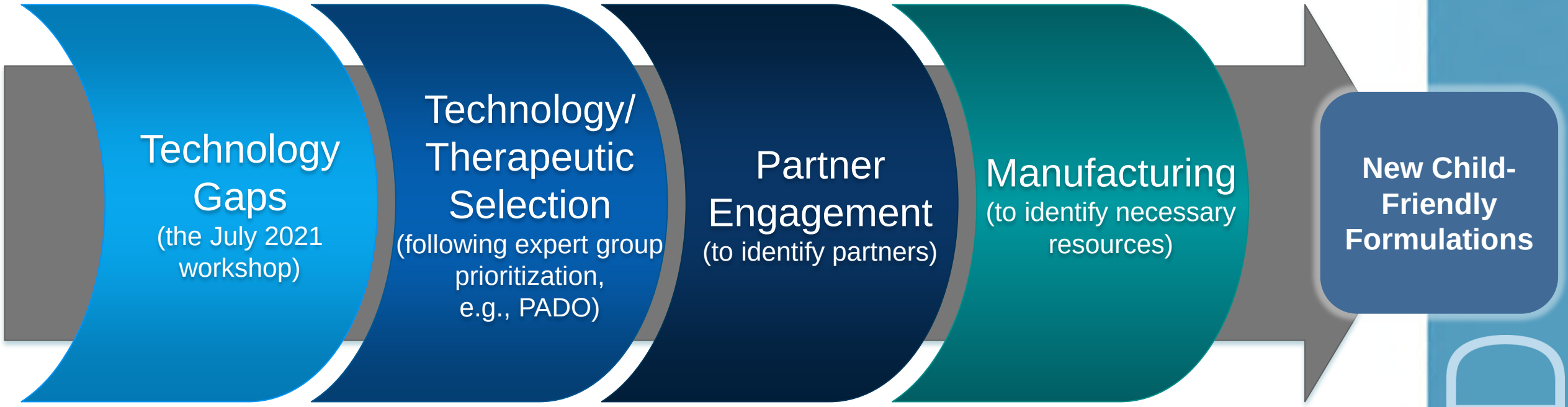


1. The resources available in these key task areas will allow expansion of the contract to support the range of preclinical activities that are necessary to develop age-appropriate formulations.

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

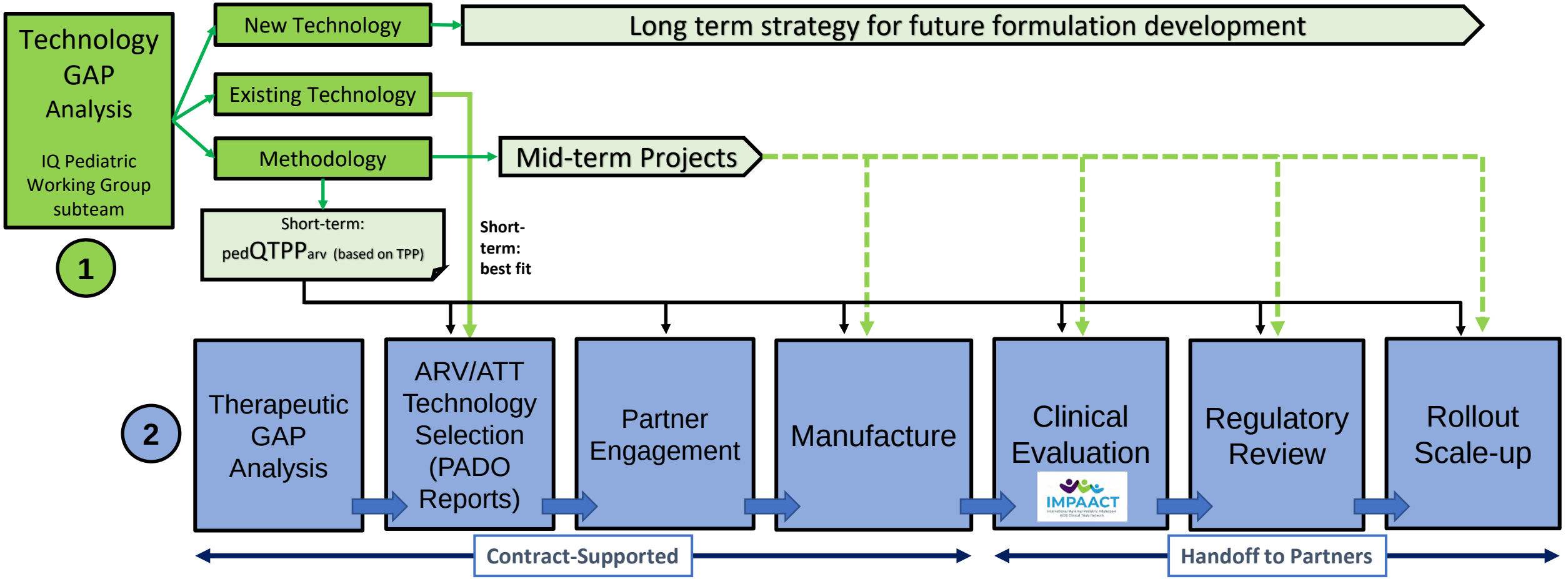
- Establish expertise to supplement NIAID programs in the development and optimization of age-appropriate drug formulations for infants, children, and adolescents (Drs. Dixit, Hoag, and Schaufelberger)
- Assist NIAID in planning contract activities to support development of age-appropriate formulations
- 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



- 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)

MTN microbicide trials network

ALLIANCE FOR MICROBICIDE DEVELOPMENT

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

CONRAD
Leaders in Reproductive Health and HIV Prevention

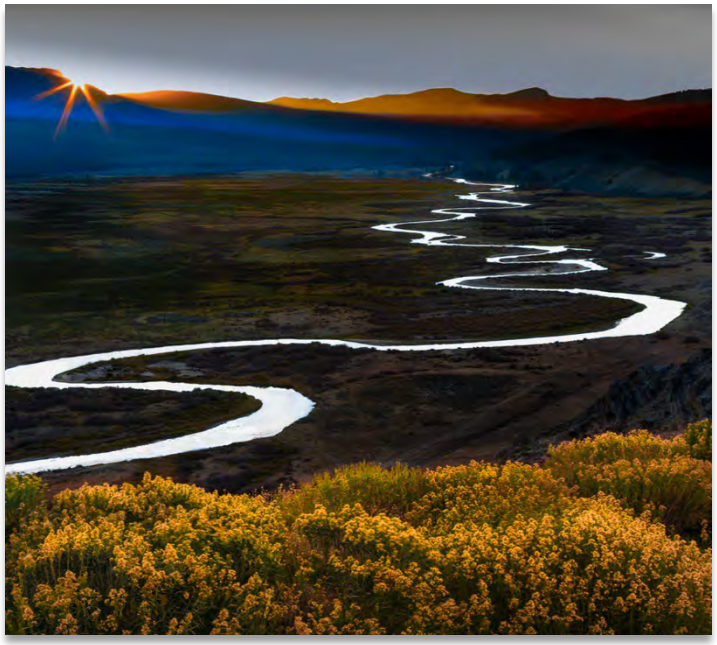
POPULATION COUNCIL
Ideas. Evidence. Impact.

ViiV Healthcare

USAID FROM THE AMERICAN PEOPLE

CDC

Leveraging Relationships



Identifying Opportunities

Future Partners
(HIV Prevention & Pediatric Formulations)

EUPFI

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

IQ INTERNATIONAL CONSORTIUM FOR INNOVATION & QUALITY IN PHARMACEUTICAL DEVELOPMENT

GAP·f Global Accelerator for Paediatric formulations
WHO Hosted Network

ViiV Healthcare

MERCK INVENTING FOR LIFE

Future Contract Expansion

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

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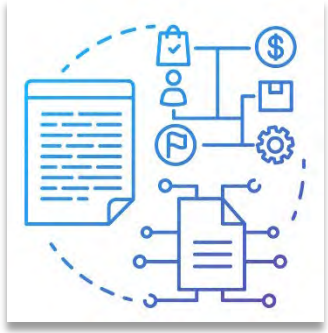
NIAID Funding Process for Accessing Pediatric Formulation Resources under the RAPPS Contract

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

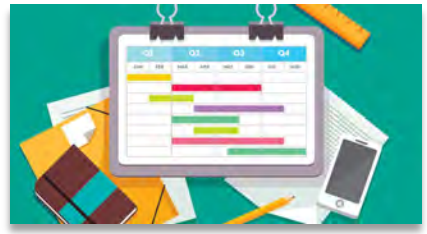
Request Support

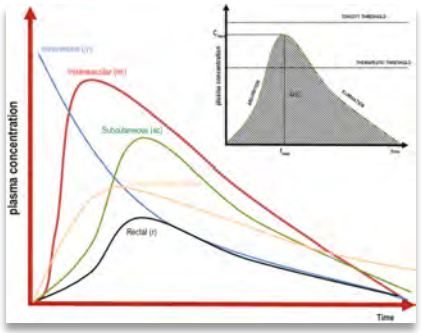
NIAID Program Review

- 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





*Opportunity to align product development activities with clinical evaluation of specific pediatric formulations through the NIAID clinical trials network (IMPAACT)

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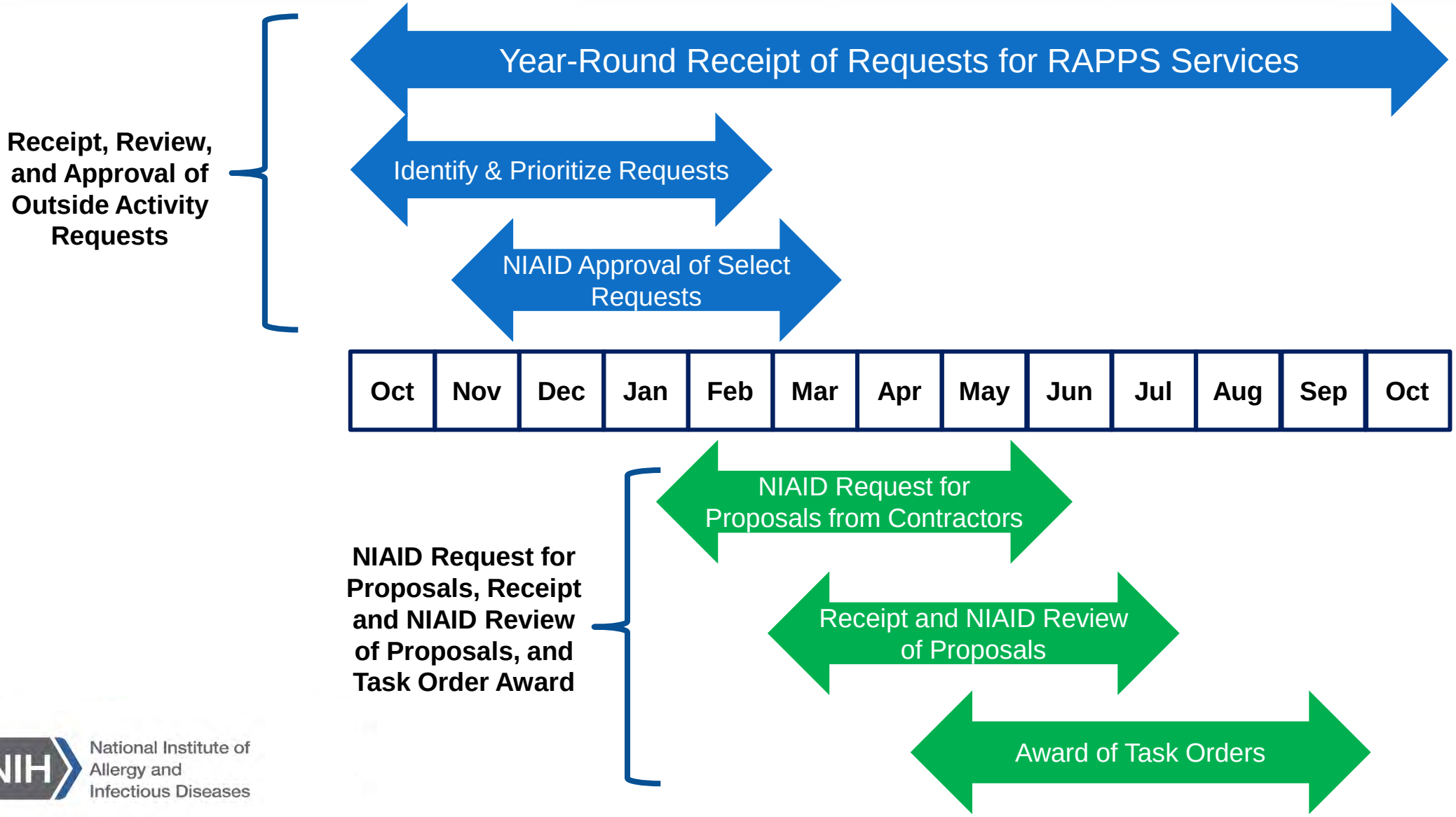
Timeline: Receipt, Review, Approval, and Award of Activities Under RAPPS Contract



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

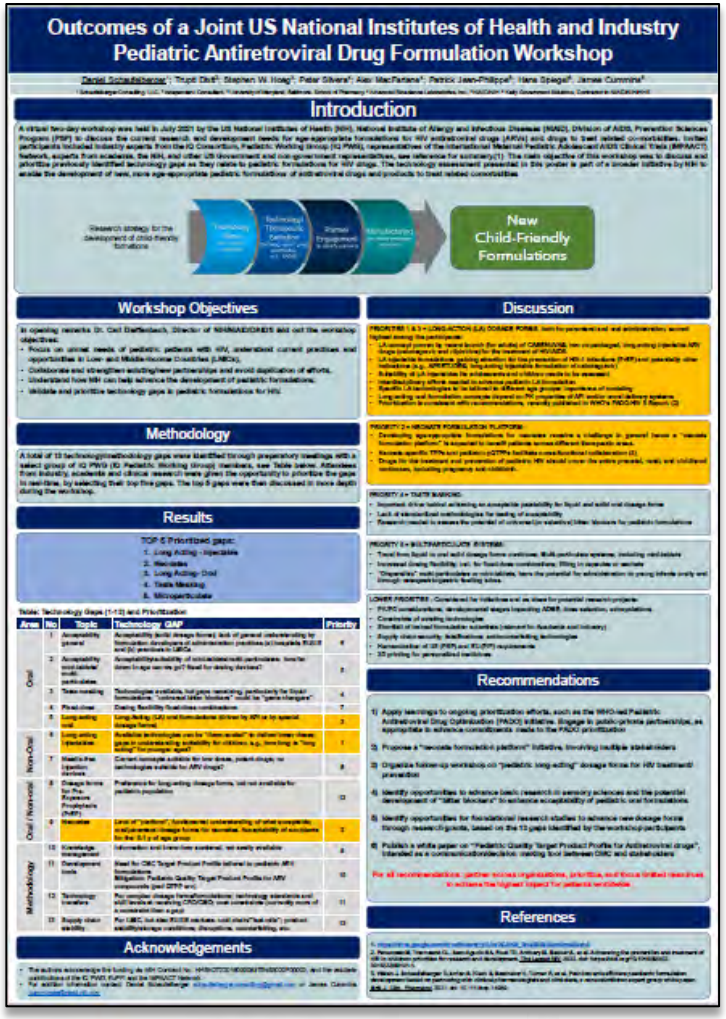
Website for requesting services under DAIDS contracts:

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

DAIDS Program Contact for more information:

James Cummins, Ph.D.
Email: cumminsje@nih.gov
Telephone: 240-292-4800

IQ Pediatric Working Group
Colleagues: Join the Effort!



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

Introduction

Workshop Objectives

Methodology

Results

Discussion

Recommendations

References

Acknowledgements

Specific Areas of Focus for Collaboration:

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

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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