

# Best pharmaceuticals for children act [BPCA]

Overseeing a Pediatric Drug Development  
Program...even during times of crisis

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# Perdita...

- Has no financial disclosures
- Will not be discussing any proprietary information

# Drug Development



In general, pediatric drug development can be slow and patchy

- Primarily driven by adult drug development
- Problematic when the pediatric condition is different from the adult condition
- This model ultimately neglects neonates and rare pediatric conditions
- This model disintegrates during times of disaster/crisis

*Pediatric Drug Development: Challenges and Opportunities.* Spandoni, C. Current Therapeutic Research. Vol 90. 2019

# Considerations: Unique Challenges

## Did You Know



**Research in children is conducted only after taking special ethical and medical considerations into account.**



**Small patient populations make it challenging to recruit/enroll in clinical trials.**

*Pediatric cancers are especially rare, with about 11,000 children in the United States under the age of 14 expecting to be diagnosed with cancer in 2020.*

*Source: "Childhood Cancers," National Cancer Institute, January 28, 2019*



**Diseases in children are often biologically different than those in adults, requiring special assessments of medicine safety and efficacy.**



**Children respond differently to medicines than adults, requiring unique dosage and formulation considerations.**

<https://www.phrma.org/policy-issues/Research-and-Development/Pediatrics>

<u>Adults</u>	<u>Characteristic</u>	<u>Children</u>
Many	<b>Number of Trials</b>	Few (may only be one/ average 2.2 per compound)
Large (thousands)	<b>Population Available</b>	Small (hundreds)
May enroll large number	<b># Participants/Site</b>	Few enrolled
Not a major issue	<b>Ethical Consideration</b>	Determines feasibility of studies
Testing of volunteers part of drug development	<b>Available Population</b>	Healthy children cannot be used for testing
Feasible in large number	<b>Recruitment</b>	Pediatric patients difficult to recruit
Participation in study easier to arrange		Logistics of study participation requires coordination around family, school, and work schedules.
Less of a problem	<b>Intersubject Variability</b>	A major problem, particularly in infants ( <b>Ontogeny</b> )
Cost per patient less than in pediatrics		3 or 4 times the number of studies needed to cover developmental continuum

\*Experience is generally  
repetitious



*Implications of Unique challenges (can be magnified during times of disaster/crisis)*

- \***Drug Development Tools Missing**  
Delays in the availability of data to support usage
- \***Pharmacology (PK/PD) afterthought**  
Market failures  
Uncertainty of dosing, safety
- \***Science advances limited**

\*Failed Pediatric Drug Dev Trials. Momper et al. Clin Pharm Ther. 2015

# BPCA Legislative Overview\*

## BPCA Legislation

**FDA** (\*on-patent)

**NIH** (\*off-patent)

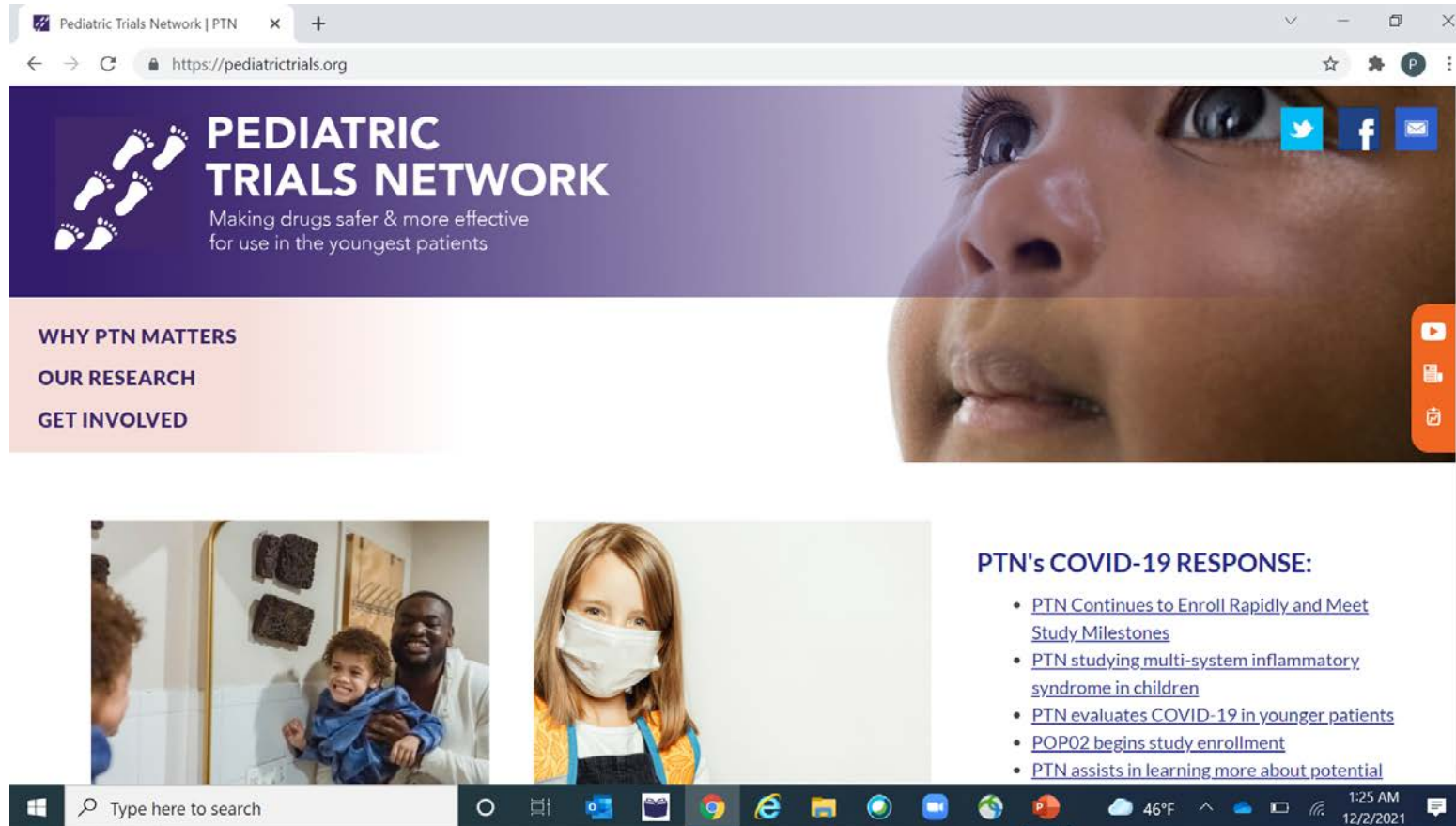
Pharmaceutical Companies'  
Drug Studies

Pediatrics Division Oversight

Prioritization/Dissemination  
Clinical Trials (Sponsor/Submit)  
Pharmacology Training  
Translational Research



# \*NIH BPCA Infrastructure



- Pediatric Trials Network ([www.pediatrictrials.org](http://www.pediatrictrials.org)) \_Duke Clinical Research Institute
- BPCA Data Coordinating Center \_EMMES Corporation
- Logistics Support Team, NIH, FDA (CDER PEDS)



# \*WHAT THE BPCA CLINICAL PROGRAM BRINGS TO THE TABLE\*...DOING TRIALS **BETTER**



## **Pharmacology expertise**

PK/PD modeling, simulation expertise  
Assay development and validation



## **Innovative research/trial design**

Novel trial designs including Standard of Care (SOC) and Opportunistic Trials  
Use of Master protocols



## **Trailblazing efforts in pediatric REGULATORY research**

Engagement and experience with MULTIPLE FDA review divisions (meetings for trial designs and trial results)  
Device trials



## **Cost efficiency**

SOC protocols  
Capitated payment system  
Central trial coordination  
Use of registries to support trial designs



## **Promoting Investigator Training**

T32 Training Program  
Junior Investigators involved in trials

# Disaster related priorities

- Collaborations
  - Pralidoxime (organophosphate poisoning—literature-based updates)
  - Hydroxycobalamine (cyanide assay dev in collab with NINDS)
- Dual-Purpose Studies
  - Midazolam
  - Doxycycline
- Personal Protective Equipment (PPE)

# \*Opportunistic Population Pharmacokinetics (PopPK)

- Empirical approach - measure drug levels in patients undergoing routine care
- Study many drugs within a single platform trial
- *With full pediatric extrapolation:* use data for pediatric label
- *With partial extrapolation:* design safer, efficient trials
- ‘Low hanging fruit’ approach, good BUT will only get us so far

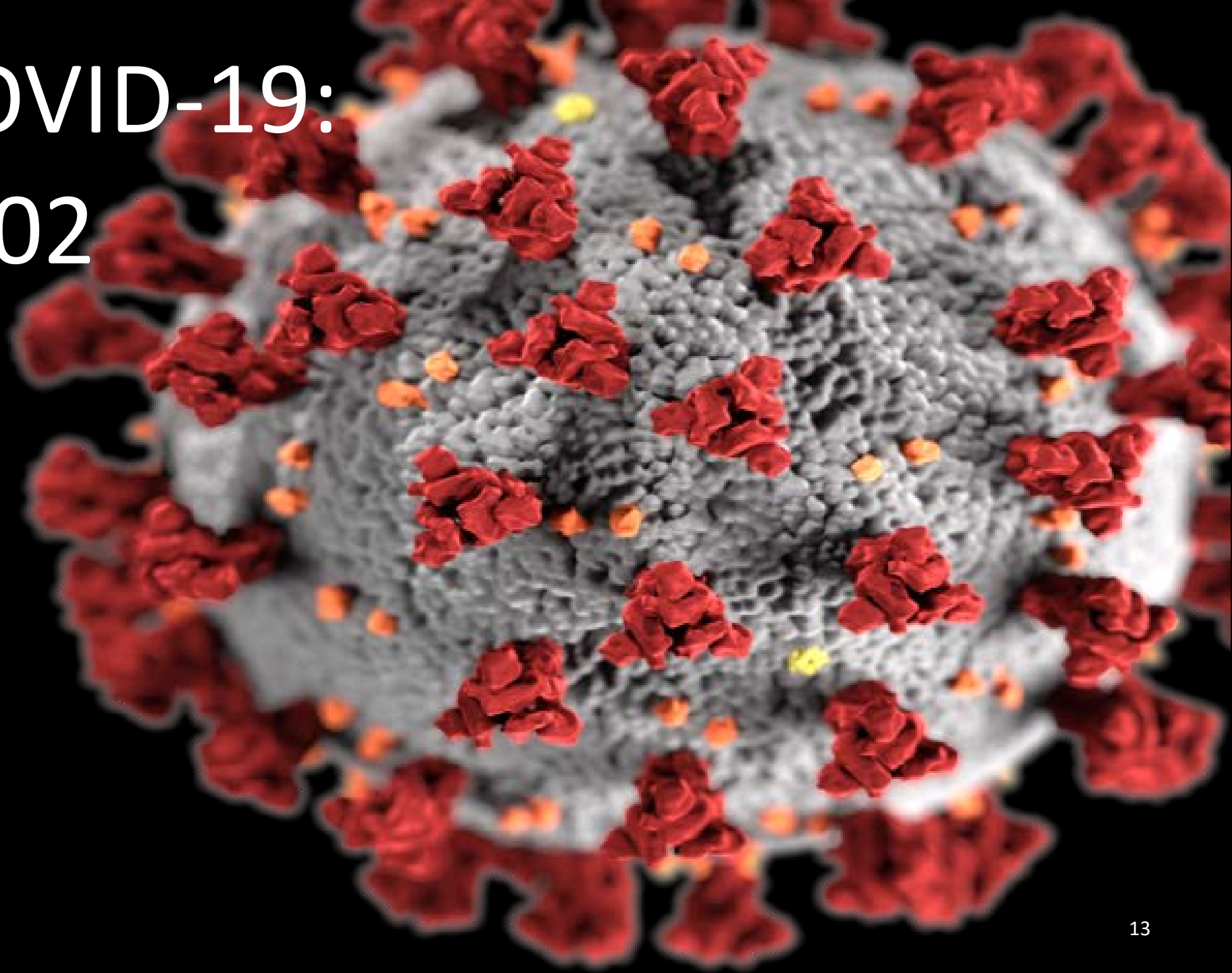
Pharmacokinetics of  
understudied drugs  
administered to children  
per standard of care  
(POPS)

Protocol Number:  
NICHD-2019-POPS02

NCT Number:  
NCT04278404

- 200+ molecules (cumulatively)
- >5000 enrolled patients (<21 years)
- ~100 study sites
- ~40 enrollments/month (PRE-COVID)
- Gives real world PK data
- Can also inform Phase 2/3 trials
- Provides a model for site capacity
  - IDEA States Network
  - INCLUDE Network collaboration
- Special populations (neonates, obese, extracorporeal membrane oxygenation, continuous renal replacement therapy)
- Adaptable to various populations, indications, and even pandemics

# PTN and COVID-19: POPS02



# 10 WAYS

## TO PIVOT WITH A VENGEANCE

Knowing the key drivers of change (and the potential need to pivot) will keep you on your toes so that you land on your feet!



1

### Stakeholders

Primary stakeholders include individuals with decision-making authority. But don't discount secondary stakeholders as they may be the influencers in the room that can make things happen for you.

2

### Playing Field

Make certain that you know an organization's rules—formal and informal—before deciding to break the rules. Responsible risktaking is smart and strategic.

3

### Communication

Accelerate your communication efforts via a relationship network. Extend your reach by leveraging mentors, your Career Advisory Board (CAB), and trusted team members.

4

### Org Dynamics

The dynamics of humans sharing spaces—four walls or virtual. Awareness of what's going on in the organization prepares you for taking advantage of unexpected opportunities and side-stepping potential setbacks.

5

### Known Risks

Known risks might not be obvious to you at first. Ask lots of questions and listen "between the lines" for potentially big changes coming down the pike that could impact you or your team.

### Word on the Street

Early change often makes itself known from the fringes or on the sidelines. Listen up at events and during meetings. Take notes and identify any potential risks or opportunities.

6

### Marketplace

Awareness of your community, the city where you live, regional and national trends, and what's going on globally. Don't get blindsided because you ignore what's happening around you.

7

### Intuition

Dance with the chaos and mystery of your intuition. Reach for the edges of your fears. Give yourself permission to trust your inner voice.

8

### Trust

Learning to trust yourself is as important as your team learning to trust you. Trusting the unknown and trusting your intuition are powerful sources of inner knowledge and creativity.

9

### Red Flags

Connect the dots—look for the big picture in the details. Build red flags into your project timeline wherever you determine or sense a disruptive element could surface to derail your plans.

10

Source

Seeding Change Online Course

Accelerated Career

<https://www.seedingchange.org/>

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## \*March 2020 the Ultimate PIVOT... COVID-19

- We have had several cases where we have had to adjust to new policies (e.g. central IRB), or conducting new trials with static funds (i.e., the BPCA funding).
- HOWEVER, we have never had to deal with a global pandemic in our lifetimes
  - Are we OK?
    - A central area was generated on the website for all COVID-19 communications.
  - Do we continue?
    - No restrictions on enrollments were placed by the study sponsors.
  - How do we continue?
    - Sites were instructed to follow local requirements and recommendations regarding support of ongoing studies.
  - How do we contribute to understanding this pandemic?

# POPS DATA and Timelines

- PK, safety and clinical data collection occurs for up to 90 days
- The SARS-CoV-2 appendices(P&Q) collect:
  - demographics, medical history, presenting symptoms
  - SARS-CoV-2 confirmatory testing, results of diagnostic tests to evaluate organ dysfunction (e.g., laboratory data and echocardiogram)
  - clinical assessments and outcomes (including safety)
  - Information collected if NOT treated
  - information on drugs used to treat SARS-CoV-2, information on safety of therapeutics, and blood samples for pharmacokinetics, biomarkers, and genotyping.
- In the **overall POPS study**, there are **~1000 enrolled, 46 sites**
- As of 10/29/21: There are **~578 Sars Co-V-2 + patients, 378** participants have been enrolled under 9 drugs of interest for COVID.
- We have enrolled **146 participants suspected to have MIS-C and 9 with Kawasaki's Disease.**
- \*October 2021, POPS became the first study in the CARING for Kids program to submit data to the ARING Data Platform



# Some of the changes we experienced, made, and continue to adopt

- During 2020, Several sites withdrew from the PTN, indicating financial and/or logistical impact of COVID-19 as a contributing factor
- Sites supported by DCC-EMMES/PTN by:
  - Supporting essential documents required for site activation and participate execution of ICFs to be executed using DCC provided **electronic signature tools**
  - Uptake and adapting to **remote monitoring**
  - Obtaining **IRB waivers from the requirement of written consent for applicable studies** e.g., minimal risk studies
  - Obtaining **IRB approvals for telephone scripts** for the introduction of the study, and conduct of the consenting “discussions” prior to obtaining consent
- **COMMUNICATE!**

# 2022 and beyond...

## Disasters happen, Prepare for the Pivot

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INFRASTRUCTURE (stable yet adaptable)

BUILD UPON YOUR STRENGTH



**EVEN IF YOU'RE ON THE**  
*right track*  
**YOU'LL GET RUN OVER IF YOU JUST**  
*sit there*

MOTHER TERESA

# How to get involved

- PTN on-line surveys and concept sheet for new study ideas
  - <https://pediatrictrials.org/for-health-care-professionals/>
- Participate in BPCA Announcements and Priority Reviews
  - <https://www.nichd.nih.gov/research/supported/bpca/activities>
- Access BPCA related-data on DASH
  - <https://dash.nichd.nih.gov/study/16018>
  - <https://dash.nichd.nih.gov/study/16020>
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# THANK YOU!



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