PART FOUR

Advancing International Pediatric Clinical Research

Facilitating Pediatric Medicines Development: Models of Global Cooperation

Part 1: 29 November 2022, 9:00-11:30 am ET

Part 2: 30 November 2022, 9:00-11:00 am ET

This series is supported by the FDA Scientific Conference Grant Program.

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

Disclaimer

PART FOUR

- The opinions expressed today are those of the speakers and are not intended to represent the position of Brigham and Women's Hospital, Harvard University, or any other organization, government, or entity.
- The MRCT Center is supported by voluntary contributions from foundations, corporations, international organizations, academic institutions and government entities (see www.MRCTCenter.org) and well as by grants.
- We are committed to autonomy in our research and to transparency in our relationships. The MRCT Center—and its directors—retain responsibility and final control of the content of any products, results and deliverables.
- I have no personal financial conflicts of interests to disclose.
- This webinar will be recorded and will be posted publicly on our YouTube channel.

Part One Recap

PART FOUR

- Presentations of 4 existing models of pediatric regulatory approval:
  - Pediatric Regulatory Cluster: Dr. Donna Snyder (US FDA)
  - Parallel Scientific Advice: Dr. Tahira Khan (AbbVie)
  - ACCELERATE Multi-Stakeholder Discussion Forum: Dr. Gilles Vassal (ACCELERATE)
  - Reliance Model: Dr. Marie Valentin (WHO)
- Panel Discussion: *Strengths and Opportunities of Existing Models of Global Cooperation*

Today's Agenda

- Presentation: *Moving Towards Greater Global Cooperation for Pediatric Medicines Development*
- Panel Discussion: Actions Towards Improving Existing Processes and Looking Toward the Future
- Wrap-up/moving ahead

Moving Towards Greater Global Cooperation for Pediatric Medicines Development

Christina Bucci-Rechtweg
Novartis Pharmaceuticals Corporation

Advancing International Pediatric Clinical Research

PART FOUR

Facilitating Pediatric Medicines Development: Models of Global Cooperation

30 November 2022

Christina Bucci-Rechtweg, MD

Global Head, Pediatric & Maternal Health Policy,
Novartis Pharmaceuticals Corporation

This series is supported by the FDA Scientific Conference Grant Program.

MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

Disclosure & Disclaimers

- Presenter's employing institution: Novartis Pharmaceuticals Corporation
- The views and opinions expressed in the following PowerPoint slides are those of the presenter and should not be attributed to her employing institution.
- These PowerPoint slides are the intellectual property of the presenter and are protected under the copyright laws of the United States of America. Used by permission. All rights reserved.
- All trademarks are the property of their respective owners.

Task & Outline of today's talk

PART FOUR

- Task
  - Consider the models of global cooperation presented on Day One and provide a blue sky view of how to evolve the pediatric medicines cooperation space
- Outline
  1. Reflection on Day One presentations
  2. The interplay of convergence pathways and existing gaps
  3. Opportunities: A blue sky vision

High-level messages from Day One

PART FOUR

- Existing pediatric development policies have enriched the innovative medicines development research space
- For certain molecules, authorization of pediatric uses continues to lag well behind adult authorization[1]
- Globally relevant and efficient pediatric medicines development requires global cooperation
  - In cluster calls, EMA and FDA have a high rate of convergence (~70%)[2]
- Reliance models can be used for any regulatory function[3]
- Models discussed on Day One of the workshop **each serve a useful purpose**, are **complementary** and **not mutually exclusive**
  - ✓ Pediatric Cluster; Parallel Scientific Advice; Multi-stakeholder Forums (ACCELERATE); Reliance

[1]Gilles Vassal, Gustave Roussy. Presentation on Day One.; [2]Donna Snyder, FDA. Presentation on Day One.;
[3]Marie Valentin, WHO. Presentation on Day One.
EMA = European Medicines Agency; FDA = U.S. Food & Drug Administration

Three archetypes of pediatric medicines development

PART FOUR

De novo pediatric medicines development

- For indications specific to or inclusive of pediatric conditions

Pediatric development on the *backbone* of adult innovation

- For same or similar indications, different indications by molecular mechanism of action, or age-specific formulations

X

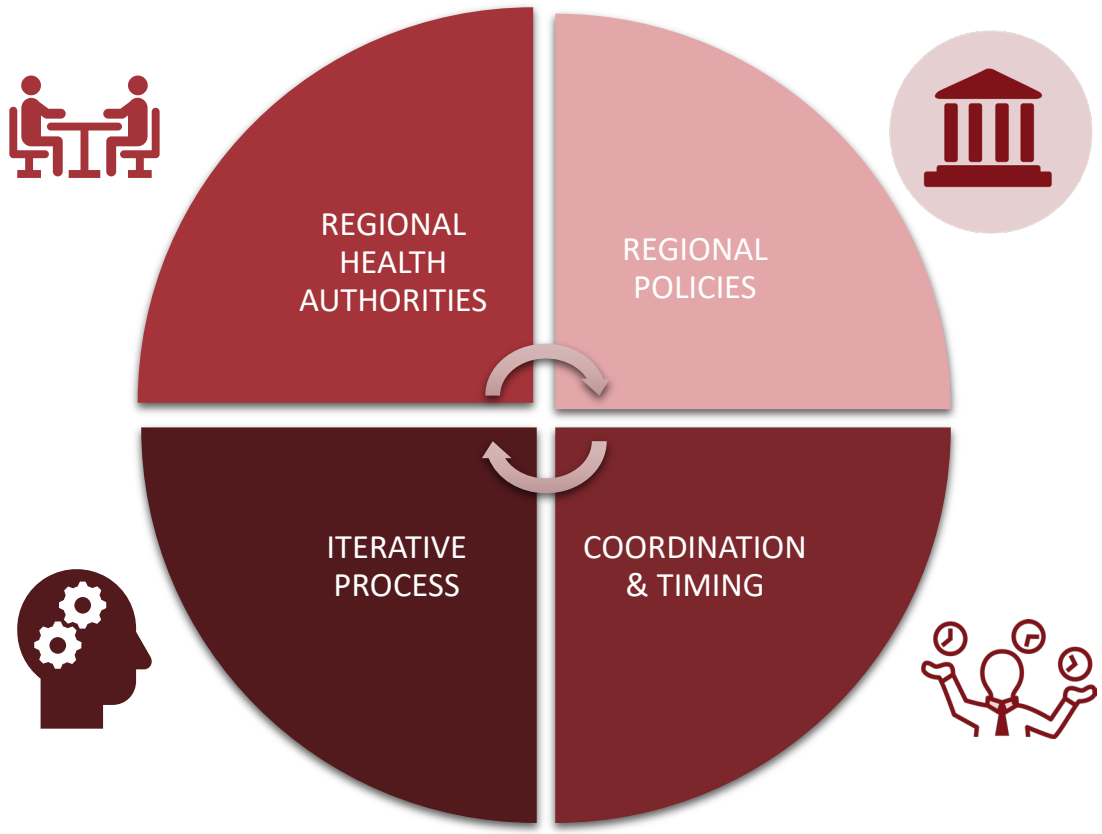
Re-purposing off-patent medicines

- Age-specific formulations, confirmation of age-specific dose or dose regimens

Agreeing a global pediatric plan suitable for regulatory decision-making (1)

PART FOUR

MULTI-STAKEHOLDER FORUMS

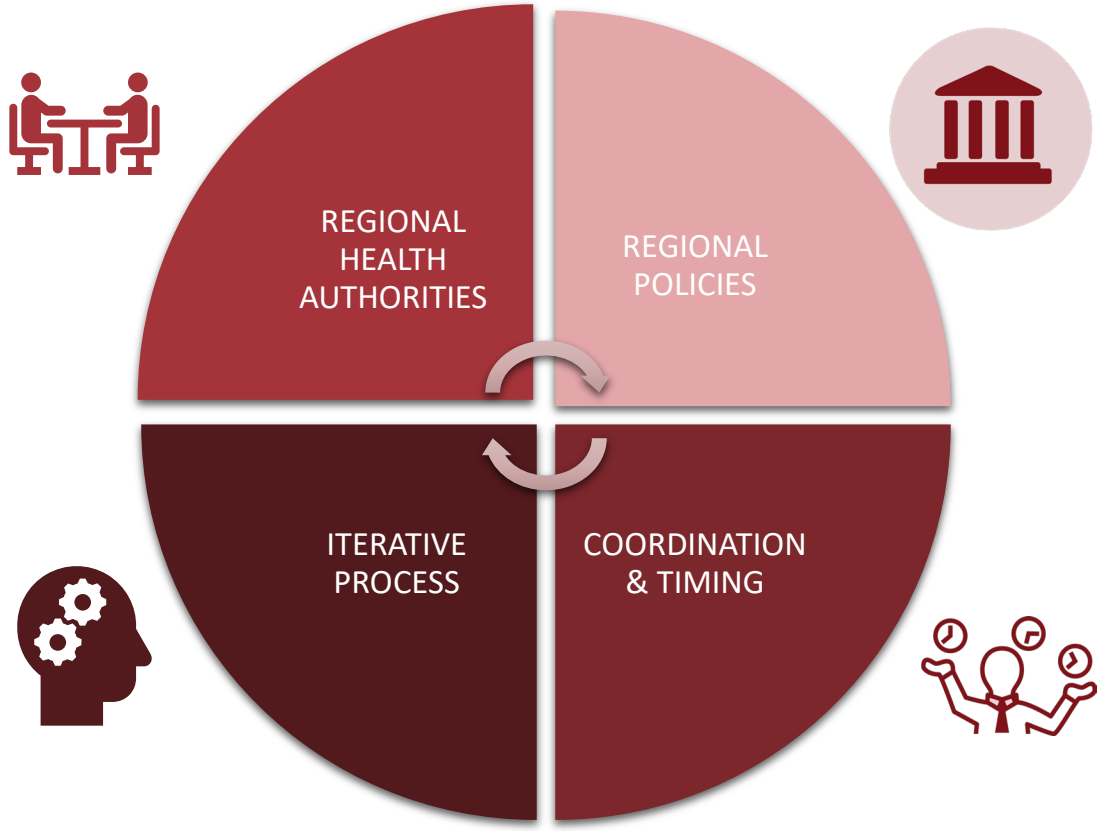


PAEDIATRIC MARKETING APPLICATION

Agreeing a global pediatric plan suitable for regulatory decision-making (1)

PART FOUR

MULTI-STAKEHOLDER FORUMS

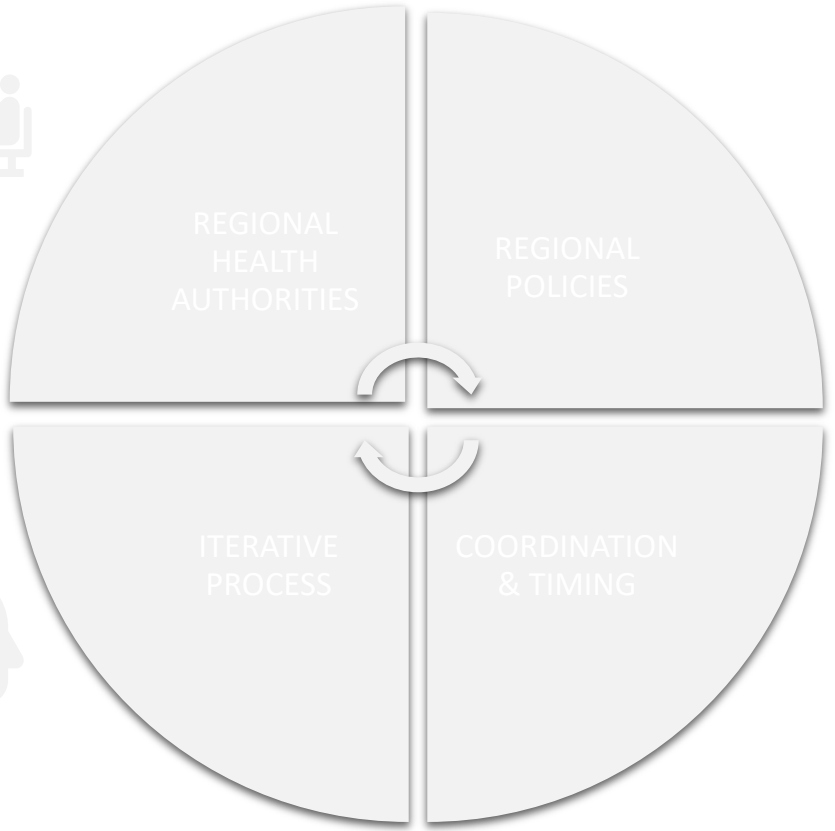


PAEDIATRIC MARKETING APPLICATION

Agreeing a global pediatric plan suitable for regulatory decision-making (1)

PART FOUR

MULTI-STAKEHOLDER FORUMS*



- ✓ Essential to incorporate academic/prescriber and patient/family perspectives
- ✓ Valuable in establishing development expectations grounded in best available scientific information
- ✓ Existing forums are pre-competitive by design
  - Limited to specific therapeutic spheres
  - Role for professional societies (as per adult development)
- ✓ Existing structures are suited to investigational projects in later stage development

*Examples include but are not limited to: ACCELERATE, Innovative Medicines Initiative (IMI) connect4children (c4c) strategy forums, Paediatric Rheumatology International Trials Organisation (PRINTO)

Agreeing a global pediatric plan suitable for regulatory decision-making (2)

PART FOUR

FDA

CDER,
CBER
(Division)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

SAWP
CHMP
PDCO

INFLUENCED BY:
PROFESSIONAL SOCIETIES & INTERNATIONAL BODIES (e.g. ICH)

NATIONAL COMPETENT AUTHORITIES*

AGES Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH

HSA Health Sciences Authority

ansm Agence nationale de sécurité du médicament et des produits de santé

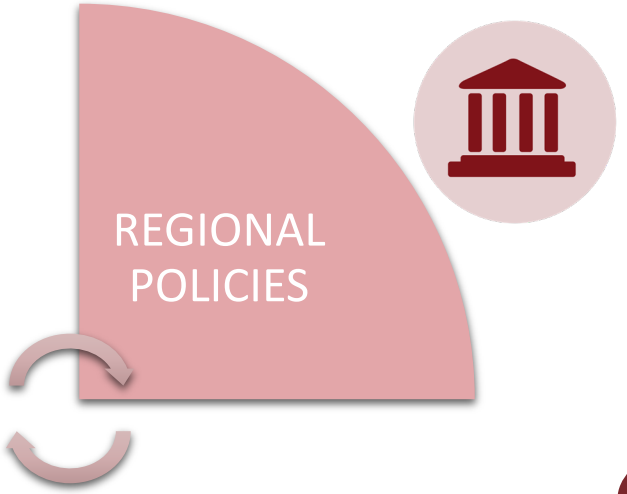
MHRA

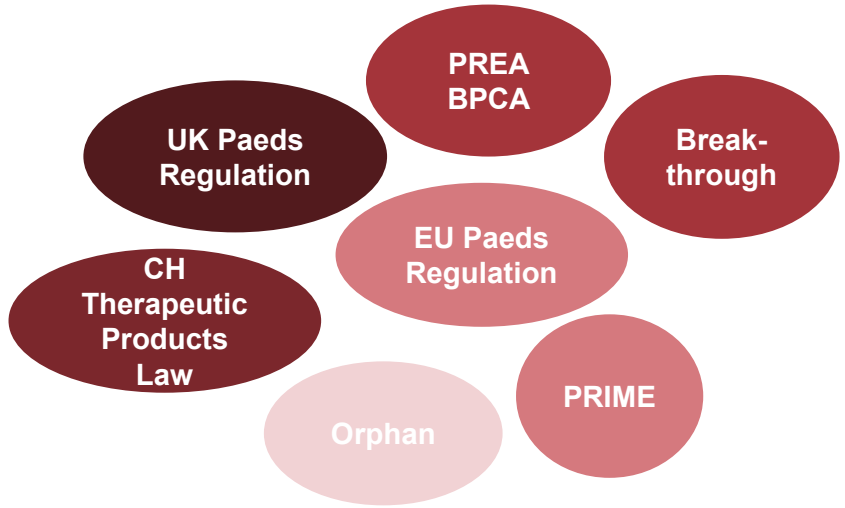
pmda 独立行政法人 医薬品医療機器総合機構 Pharmaceuticals and Medical Devices Agency

*Not an exhaustive list (intended to be illustrative only)
ICH = International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

Agreeing a global pediatric plan suitable for regulatory decision-making (3)

PART FOUR

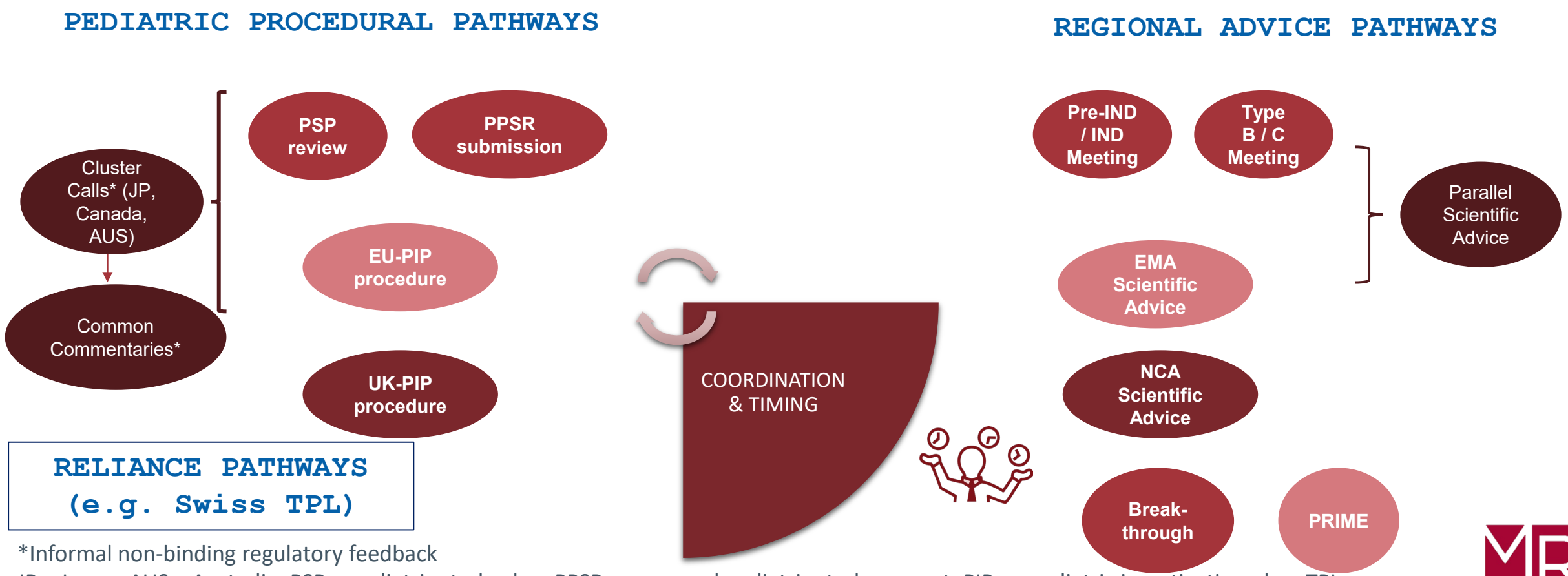




CH = Switzerland; UK = United Kingdom; EU = European Union; PREA = Pediatric Research Equity Act; BPCA = Best Pharmaceuticals for Children Act

Agreeing a global pediatric plan suitable for regulatory decision-making (4)

PART FOUR



*Informal non-binding regulatory feedback

JP = Japan; AUS = Australia; PSP = pediatric study plan; PPSR = proposed pediatric study request; PIP = paediatric investigation plan; TPL = Therapeutic Products Law; IND = investigational new drug; NCA = national competent authority

Agreeing a global pediatric plan suitable for regulatory decision-making (5)

PART FOUR

OPERATIONALIZE PLAN

GENERATE DATA

MODIFY or AMEND PLAN (if applicable)

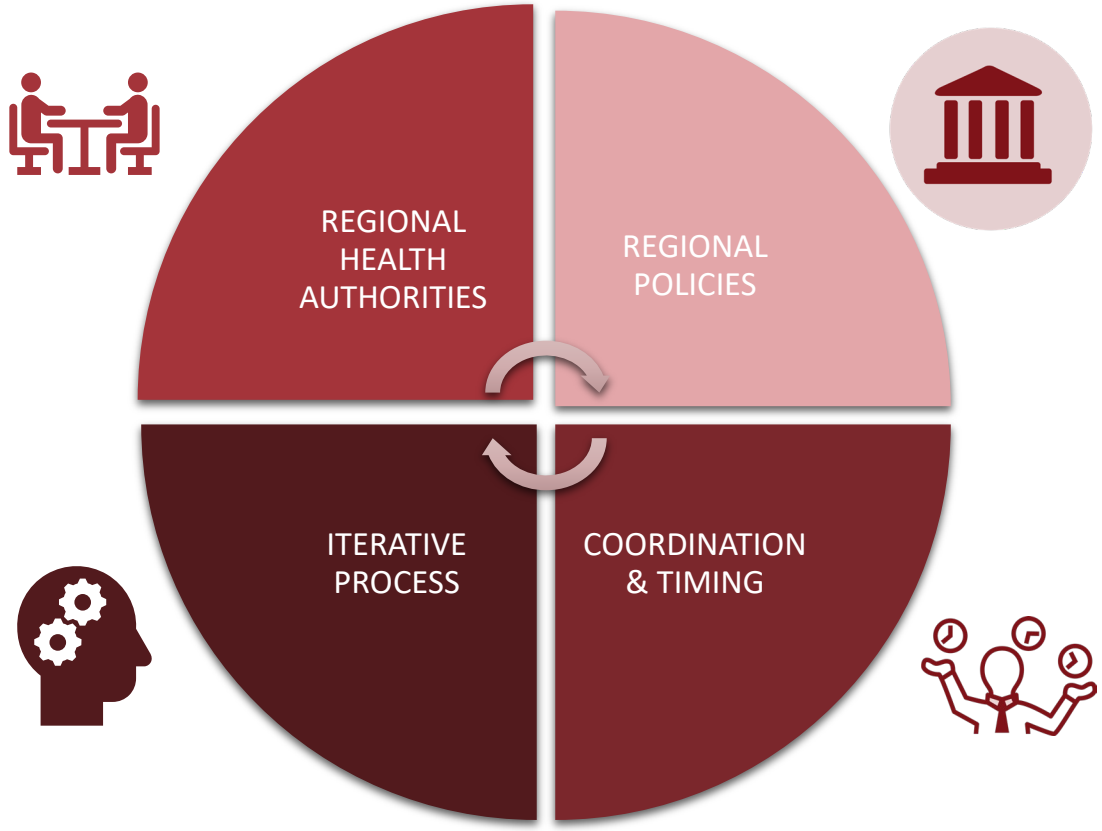
ANALYZE DATA

PAEDIATRIC MARKETING APPLICATION

Blue Sky Vision: Role for global cooperation in pediatric medicines development **planning** (1)

PART FOUR

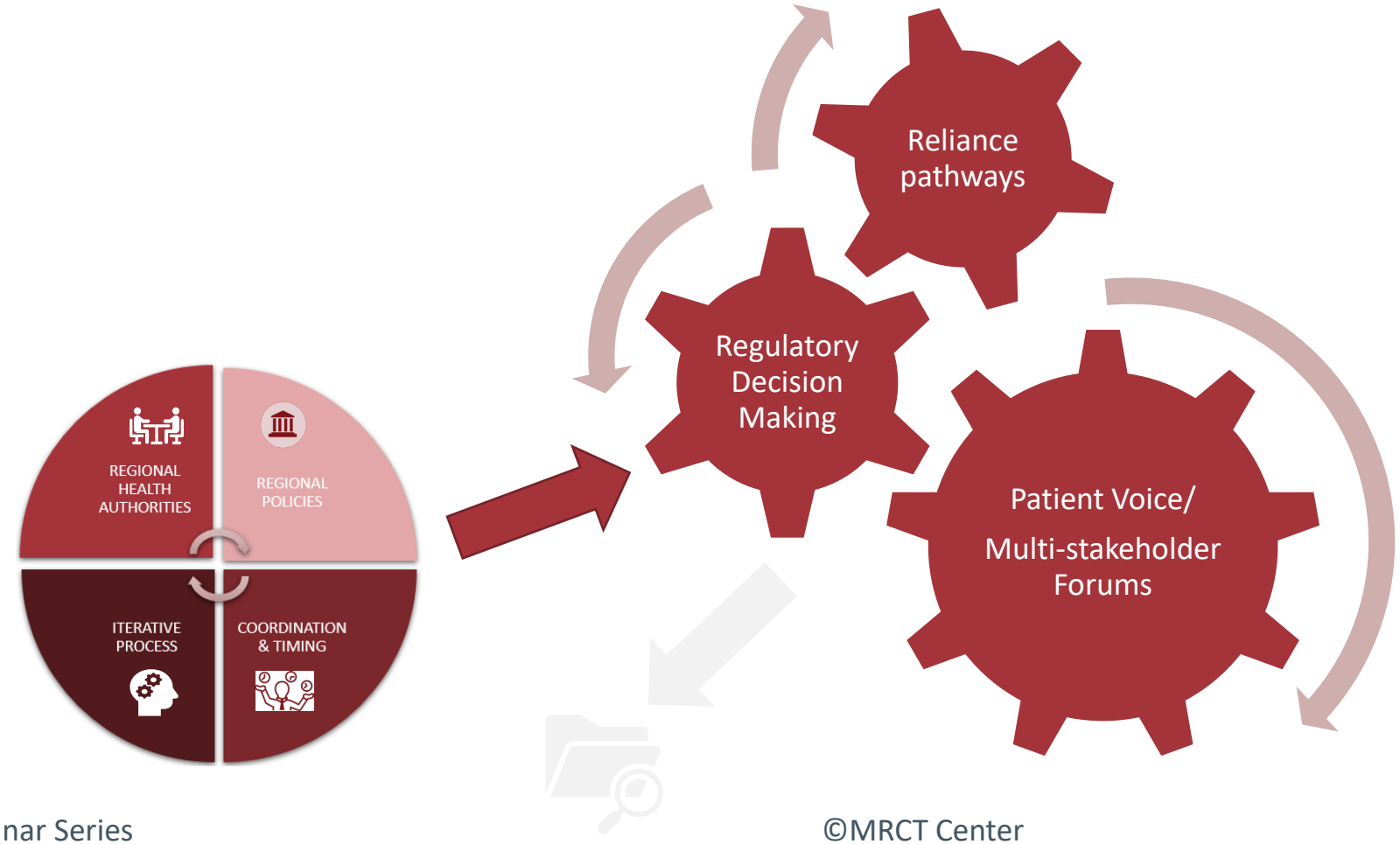
MULTI-STAKEHOLDER FORUMS



PAEDIATRIC MARKETING APPLICATION

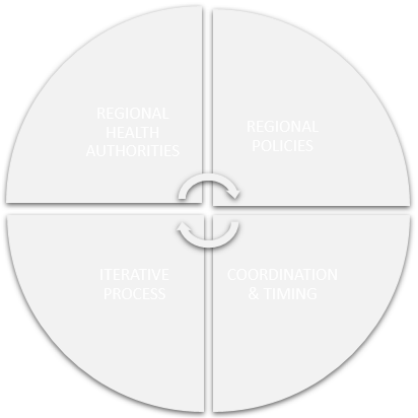
Blue Sky Vision: Role for global cooperation in pediatric medicines development **planning** (2)

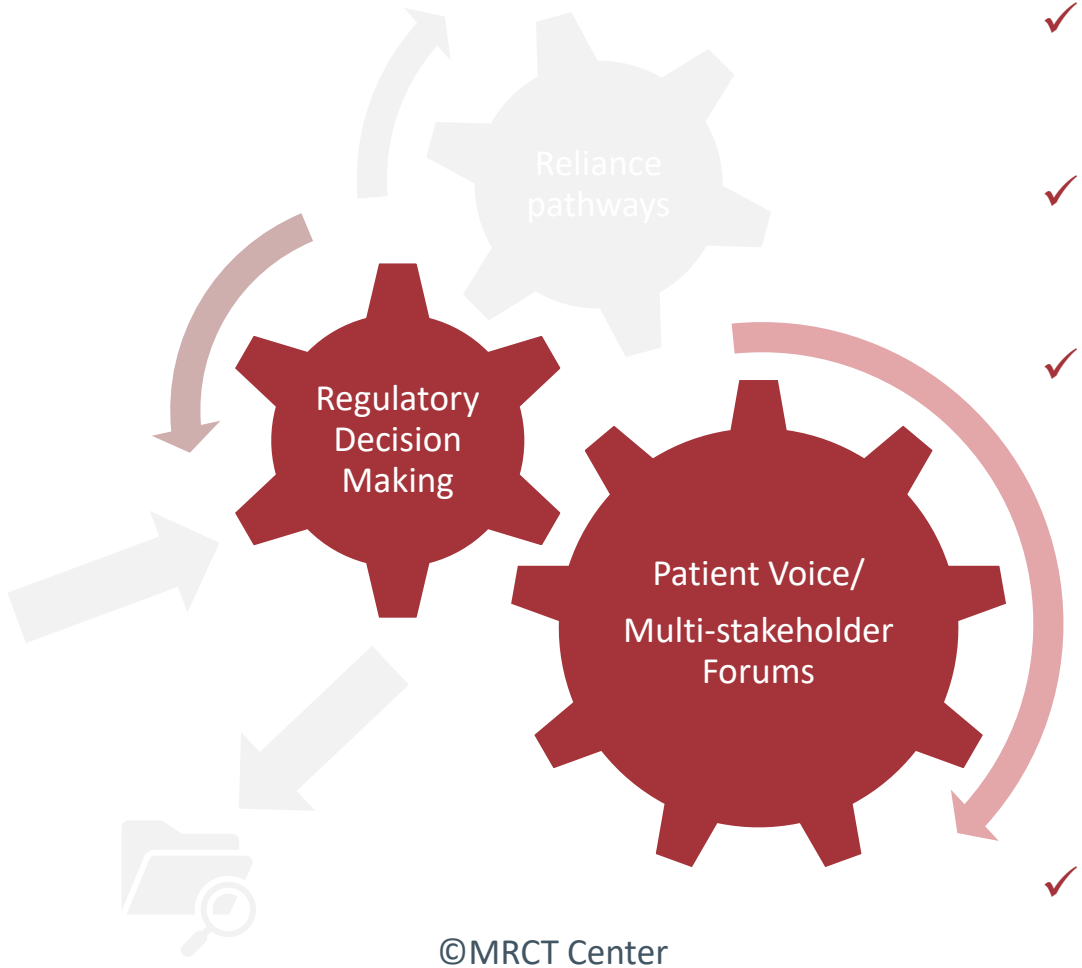
PART FOUR



Blue Sky Vision: Role for global cooperation in pediatric medicines development **planning** (3)

PART FOUR





Multistakeholder Forums

- ✓ Enhance inter-linkage to regulatory guidance (esp. when co-authored by regulators)
- ✓ Expansion to other therapeutic areas a/o competitive development spheres
- ✓ If intended to expand to early stage development, some structural modification is needed (consultancy agreements, confidentiality, published outputs clearly linked into relevant regulatory agency websites and/or incorporated into guidance)
- ✓ Role for professional societies

Blue Sky Vision: Role for global cooperation in pediatric medicines development **planning** (4)

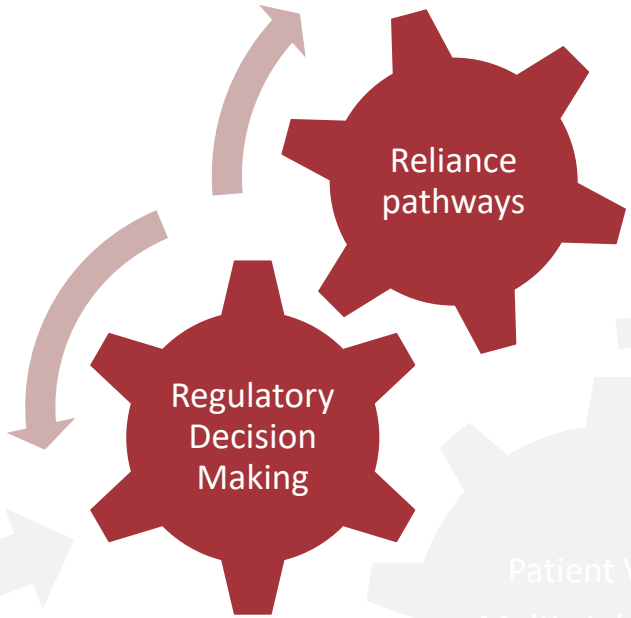
PART FOUR

Cluster

- ✓ Expansion to all regions where pediatric policies are implemented (including, MHRA and SwissMedic)
- ✓ If a Cluster leads to Common Commentary, agencies should review prior Scientific Advice Meeting Minutes to reduce risk for contradictory regulatory guidance

Parallel Scientific Advice

- ✓ A dedicated global pediatric scientific advice pathway is warranted for the 1/3 of pediatric plans where convergence on design elements cannot be achieved in Cluster



Reliance

- ✓ Given the "*high rate of convergence*" of Cluster conversations, 2/3 of pediatric plans may be suitable to a reliance procedure (i.e., to agree a pediatric plan)
- ✓ **Model 1** (existing): Switzerland - Reliance on US a/o EU decision on an agreed pediatric plans (at submission of marketing authorization)
- ✓ **Model 2**: Submission of a PIP or PSP through usual regional procedure. Cluster held to coincide within a region's procedure or agencies invited to listen as per *pediatric memorandum of understanding (or other)*. At completion of the procedure, other agencies have the option to adopt the reviewing agency's opinion for the plan.

Closing Remarks

PART FOUR

- Regional policies have given us over two decades of pediatric medicines development experience
- We have an opportunity to evolve
- Global cooperation offers opportunities for enhancement
  - Enhance the scientific credibility and value of plans
  - Facilitate broader global impact for children affected by disease
  - Reduce inefficiencies while conserving regulatory resource

"Coming together is a beginning. Keeping together is progress. Working together is success." – Henry Ford

THANK YOU

PART FOUR

- Contact information:

Christina Bucci-Rechtweg

Global Head, Pediatric & Maternal Health Policy

Novartis Pharmaceuticals Corporation

Christina.buccirechtweg@novartis.com

Panel Discussion: Actions Towards Improving Existing Processes and Looking Toward the Future

PART FOUR

Robert "Skip" Nelson
Johnson & Johnson

Christina Bucci-Rechtweg
Novartis Pharmaceuticals Corporation

Peter Adamson
Sanofi

Ralph Bax
European Medicines Agency

Alysha Croker
Health Canada

Dionna Green
U.S. Food and Drug Administration

Begonya Nafria Escalera
Hospital Sant Joan de Déu

Sumati Nambiar
Johnson & Johnson

Mark Turner
University of Liverpool

Closing Remarks and Thank you!

PART FOUR

- A huge thank you to all our speakers and panelists:

Peter Adamson
Elly Barry
Ralph Bax
Christina Bucci-Rechtweg
Alysha Croker
Begonya Nafria Escalera
Dionna Green
Dominik Karres
Tahira Khan
Franca Ligas
Sumati Nambiar
Skip Nelson
Greg Reaman
Donna Snyder
Mark Turner
Marie Valentin
Gilles Vassal

- And thank you to the dedicated planning committee!

Please follow the MRCT Center

PART FOUR

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of
BRIGHAM AND WOMEN'S HOSPITAL
and HARVARD

Thank you!