EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Reflections on the concept of a facilitation framework

EnprEMA annual meeting – 1 & 2 October 2024

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Common goal

Ensuring timely access to new safe and effective treatments in areas of high unmet medical need

Paediatric Drug Development Landscape

- **Paediatric drug development** primarily occurs in **the rare disease space**, is highly regulated, and is a **global enterprise**

- Growing **pipelines of innovative products** especially with new pharmaceutical legislation proposal (‘mode/mechanism of action’ developments):
  - How can we **identify and support completion of development** efforts in children for products that address existing **unmet medical needs**?
  - There is a **need to foster an innovative R&D environment** that **allows** for the **evolution of scientific knowledge** and considers changing evidence and unmet needs.

- **Regulatory decision making** on mandated paediatric developments **cannot occur in isolation** and requires acknowledgement of broader implications.

Solution?

A **framework**:

- that **facilitates science-focused feasibility discussions**
- to ensure mandated R&D efforts
  - target the most appropriate population with unmet needs and
  - generate robust evidence in a timely manner,
- while being mindful of patient resources across different development areas.

Article 95

European network

1. The Agency shall develop a European network of patient representatives, academics, medicines developers, investigators and centres with expertise in the performance of studies in the paediatric population.

2. The objectives of the European network shall be, inter alia, to discuss priorities in the clinical development of medicines for children, in particular in areas of unmet medical need, to coordinate studies relating to paediatric medicinal products, to build up the necessary scientific and administrative competences at European level, and to avoid unnecessary duplication of studies and testing in the paediatric population.

https://eur-lex.europa.eu/resource.html?uri=cellar:e3f40e76-e437-11ed-a05c-01aa75ed71a1.0001.02/DOC_1&format=PDF

Can a Multistakeholder Prioritization S Support Regulatory Decision Mak Review of Pediatric Oncology Stra Reflecting on Challenges and Opp this Concept

Dominik Karres[1,*], Giovanni Lesa[1], Franca Ligas[1], Pia Annunen[2,3], Maaike var Sara Galluzzo[3,7], Ralf Herold[8], Olga Kholma [illegible] Koen Norga[3,11,12,13]

Timely and successful drug development for rar consolidated efforts in the spirit of shared respc concept of multistakeholder Strategy Forum inv has been developed. In this study, we review the

Journal of Crohn's and Colitis, 2023, **17**, 249–258
https://doi.org/10.1093/ecco-jcc/jjac135
Advance access publication 21 September 202
Original Article

Paediatric Inflamn A Multi-Stakehold of Drugs for Child

Nicholas M. Croft,[a,*] Lissy [illegible] Frank M. Ruemmele,[e,f] Dan Tu Zuzanna Gołębiewska,[k] Floriane Laumond,[l] Maria Cavaller-Bellaubi,[m] Adam Elgreey,[n] Tara A. Altepeter,[o] Chrissi Pallidis,[p] Koen Norga,[q] Robert Nelson,[h] Wallace Crandall,[r] Gilles V

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European Journal of Cancer 177 (2022) 120–142
Available online at www.sciencedirect.c
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journal homepage: www.ejcancer.
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Review

3.5. Strategic recommendations

The high-level strategy for expediting new drug development for paediatric patients with IBD was proposed by meeting participants [Box 2].

Box 2. Next steps

1. A dedicated international multi-stakeholder core group should be set up to **coordinate actions required to accelerate access to new drugs** for children with IBD.
2. An international multi-stakeholder working group should further discuss **appropriate use of extrapolation from adult data in PIBD** in order to improve efficiency and feasibility of timely completion of studies.
3. A multi-stakeholder working group should explore how to **prioritize different classes of investigational drugs**.

European Journal of Cancer 146 (2021) 115–124
Available online at www.sciencedirect.com
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eview

romodomain and extra-terminal inhibitors—A onsensus prioritisation after the Paediatric Strategy orum for medicinal product development of epigenetic iodifiers in children—ACCELERATE

ndrew DJ. Pearson [a,*], Steven G. DuBois [b], Vickie Buenger [c], lark Kieran [d], Kimberly Stegmaier [b], Pratiti Bandopadhayay [b], elly Bennett [e], Franck Bourdeaut [f], Patrick A. Brown [g], Louis Chesler [h],

Blood 142 (2023) 6247–6249

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

A Potential Paradigm for the Robust and Systematic Prioritisation of Assets in Academic-Led, Multi-Industry Collaborative Trials in Rare Populations (Glo-BNHL)

Emma Seaford[1], Nicole Scobie[2], Lia Gore, MD[3,4], Sarah Alexander, MD[5], Auke Beishuizen, MD PhD[6], Birte Wistinghausen, MD[7], Veronique Minard-Colin, MD PhD[8], Catherine M. Bollard, MD[7], Karin Mellgren[9], Carl Allen[10], Anne Auperin[8], Victoria Buenger[11], Pamela R. Kearns, PhDFRCPC[12], Anna Lawson, BSc[12], Ellie Williams[13], Shanna Maycock, MSc[12], Zahra Ahmed[12], Mahnoor Muzaffar[12], Rhianna Parsons[12], Lucinda Billingham[12], Gladstone Austin Amos Burke, MB, PhD[14]

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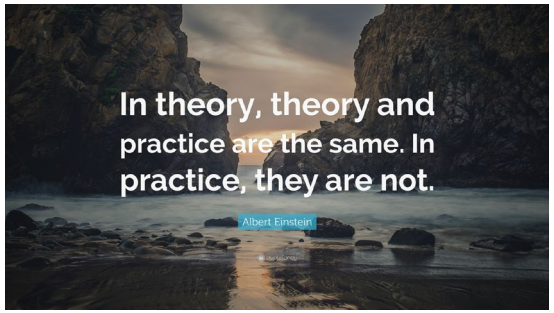
Role of Regulators

- Regulators have a **defined mandate** (based on regulation(s))
- **A life-cycle approach to evidence** underpins decisions making
- Acknowledgement **that choices* must be made** within the drug development ecosystem
- Driver for regulators is to **facilitate and support these choices** as part of this ecosystem

* https://www.tandfonline.com/doi/full/10.1080/21678707.2018.1491304

Regulatory support within the remit of regulation



Suitable **foundation in place** with **regulatory tools and processes** already **able to allow** such exercise to take place – enabling facilitation of scientific discussions, leading to regulatory submissions (as necessary), such that obligations can be fulfilled (or lifted as appropriate)

CD123 – November 2019	
Key Conclusions	Outcome Analysis
Pivekimab (ADC) North American + European trial	Development in AML deprioritized
Pivekimab frontline trial –primary refractory AML.	No
PIP Pivekimab prior to the opening of the trial	No PIPs for pivekimab
Flotetuzumab (CD123xCD3 bispecific antibody evaluation by PEP-CTN in the US	Development discontinued due to toxicity in favour of a second generation product
Lower age SAR443579, the bi-specific NK-cell engagei CD3-CD123 reduced to 12 years and patients are enrolled in Europe	
CD123 is a very high priority target	
PedAL/EUPAL Strongly endorsed	

BET inhibitors – July 2020		
Key Conclusions		Outcome Analysis
Trials for NUT carcinoma should include children, adolescents and adults	✓	3 trials opened 2/3 with inclusion age <18 years
Not scientifically justified or feasible undertake simultaneously early clinical trials of all pan-BET inhibitors	✓	Only Trials opened AFTER the meeting for NUT carcinoma + additional arm with CC90010 (BMS trial)
Further clinical development postponed until results BMS-986158	✓	Trial still recruiting - No other trials opened except NUT carcinoma
	✓	Further pre-clinical investigation
	✗	Not as yet

Menin – June 2022		
Key Conclusions		Outcome Analysis
Ziftomenib and SNDX-5613 (revumenib) -promising - warrant clinical evaluation	✓	2 Paediatric trials ziftomenib ALL – open, AML and ALL – development 3 new paediatric trials for SNDX-5613
Menin inhibitors move **rapidly into front-line** - infant leukaemia, greatest unmet clinical need	✗	No frontline studies yet – company very willing and in discussions
Limited paediatric population, simultaneous completed **development 6 inhibitors infeasible** - Trials of 3 products open/about to open - 4th impossible -Benefit of other companies to **"wait and see"**	✓	Trials for 2 inhibitors open and opening a third trial is delayed
Mechanism of action currently available menin inhibitors appears to be very similar except Biomea warrants further development & clinical evaluation	✓	BMF-219 - 4 adult trials - no pediatric trials yet
Company's **discussions with Pedal/EuPAL and** formalise discussions with **regulators** ASAP -submit simultaneously a PIP and iPSP	✗	No PIP


European Journal of Cancer 177 (2022) 25–29

Available online at www.sciencedirect.com

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Original Research

European regulatory strategy for supporting childhood cancer therapy developments

Dominik Karres [a,*], Giovanni Lesa [a], Franca Ligas [a], Sylvie Benchetrit [b,c], Sara Galluzzo [d,e], Karen Van Malderen [f,c], Jaroslav Sterba [g,c], Maaike van Dartel [h,c], Marleen Renard [i,f,c], Peter Sisovsky [j,c], Siri Wang [k,c], Koen Norga [l]

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No implementation into regulatory process

Can we operationalise prioritisation across developers with identified R&D priorities being implemented into regulatory process in a consolidated way?

A **framework**:

- that **facilitates science-focused feasibility discussions**
- to ensure mandated R&D efforts
- target the most appropriate population with unmet needs and
- generate robust evidence in a timely manner,
- while being mindful of patient resources across different development areas.

→ Enabling innovation

Facilitation rather than prioritisation

Key Issues in Developing a Facilitation Framework

- Clarity in **definitions and subsequent challenges**, including facilitating **late** vs. **early** development and unintended consequences (e.g., halo effect impacting adult development).
- Ensuring a **safe space** for discussions.
  - Need for **regulatory oversight, including outcome sharing**
  - Discussions under **confidentiality agreements** (CDA) with transparency in terms of **Conflict of Interest** (CoI)
  - Utilizing existing infrastructure (e.g., academic networks like ITCC).
- **Clear scientific focus** with pre-agreed scientific questions targeting a population, not a product.
- **Connecting outcomes to regulatory processes** (PIP/MOD; SA, etc.).
- Academia should appreciate that it is the drug developer's choice to take up any recommendations.

Framework proposal facilitating content discussions between developers and experts in '**safe space**'

Scientific population based focus – discussions on **pre agreed questions**

Framework proposal – supported by regulators – observing meeting

Broad academia representation with relevant expertise, transparent CoI

Discussions under CDA

using existing (academic) infrastructures (eg ITCC)

Individual discussion with **company** developing: **Product A**

Individual discussion with **company** developing: **Product B**

Individual discussion with **company** developing: **Product C**

Recommendations

EMA supporting connecting outcome(s) to regulatory process as appropriate

Potential for regulatory implementation

Conclusions

- **'Why' remains key** – if all stakeholders see their individual benefits - 'how' then follows; particularly in context of the new pharmaceutical legislation proposal
- **Challenges** and **unintended consequences** need to be **recognized** and acted upon
- **Needs 'safe space'** – regulatory initiation and oversight, ensuring clear scientific population focus
- Need to be **clear** about what **defines success**
- Is it always needed – no.
  - If used, it would need to be iterative process – once framework discussions triggered – need to come back together when new evidence (milestones) come to light
- **Expectation management key**

Any questions?

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