GAP·f
Global Accelerator for Paediatric formulations
WHO Hosted Network

World Health Organization

Towards closing the gap in access to child-friendly formulations of essential medicines

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Suggested citation. Towards closing the gap in access to child-friendly formulations of essential medicines. Geneva: World Health Organization; 2025. https://doi.org/10.2471/B09623. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at https://iris.who.int/.

Cover image: © WHO / Zakarya Safari

Design and layout by 400 Communications Limited.

Contents

Acknowledgements

The body of work summarized in this technical report was led by the WHO Essential Medicines Secretariat with contribution from the Global Accelerator for Paediatric Formulations Secretariat in the WHO Science Division. Asma Hafiz and Tiziana Masini led the writing of this report with input from Bernadette Cappello and Martina Penazzato. WHO thanks Tiziana Masini, Rehab Rayan and Jenny Walsh (WHO consultants) for conducting a thorough assessment of all formulations included in the project and Global Accelerator for Paediatric Formulations partners, including the Penta Foundation, St George's, University of London and the Clinton Health Access Initiative for their contribution to the overall project. WHO would also like to acknowledge Emelyne Gres (Penta Foundation) for her support with the summary assessments included in the annexes.

This report is based on a project funded by the Gates Foundation. The findings and conclusions contained within are those of the authors and do not necessarily reflect positions or policies of the Gates Foundation.

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Acronyms

EML	WHO Model List of Essential Medicines
EMLc	WHO Model List of Essential Medicines for Children
GAP-f	Global Accelerator for Paediatric Formulations
PADO	paediatric drug optimization
PQPPAT	paediatric quality product profile assessment tool

Background

Ensuring that all children have access to safe, effective and age-appropriate medicines is a global health imperative. The vision is that paediatric formulations exist for a much wider range of diseases and conditions and that these formulations are widely available and accessible to children everywhere – including those in the most resource-constrained settings. Realizing this vision requires coordinated action by researchers, regulators, industry, global funders and global health partners to overcome longstanding barriers in paediatric drug development and delivery.

Although regulatory incentives and increased investment from researchers and public–private partnerships have sought to advance paediatric formulation development *(1–3)*, a critical gap persists: the global availability of age-appropriate medicines for children remains limited, especially in low- and middle-income countries *(4, 5)*. Globally, only one third of countries include paediatric formulations in national essential medicines lists, and when that happens, the number of formulations considered is too little to cover all children's needs *(6)*. Too often, adult formulations are adapted for paediatric use – commonly by splitting or crushing tablets – practices that can alter drug exposure, produce inaccurate dosing and increase the risk of suboptimal outcomes or adverse events *(7, 8)*. Such modifications also make treatment more complex, reduce tolerability and acceptability and compromise long-term adherence – sometimes preventing children from accessing essential medicines altogether *(9)*.

To address these challenges, WHO established the Global Accelerator for Paediatric Formulations (GAP-f) *(10)* in 2020, building on the political commitment of the 2016 World Health Assembly resolution *(11)* that emphasized the need for innovation and access to quality, safe, effective and affordable medicines for children across the product life cycle. Hosted within the WHO Science Division and guided by a dedicated strategy, GAP-f functions as a WHO-led network and catalyst for coordination across stakeholders – including regulators, industry, procurement agencies, funders and implementers. Its goal is to accelerate the development, uptake and availability of missing paediatric formulations by streamlining efforts and addressing formulation gaps across a broad spectrum of therapeutic areas.

A cornerstone of this effort within WHO is the Model List of Essential Medicines for Children (EMLc) *(12)*, first published in 2007 and updated biennially – most recently in September 2025 *(13)*. The EMLc is a globally recognized, evidence-informed reference that identifies medicines required to meet the priority health-care needs of children up to 12 years of age. By guiding the development and revision of national essential medicines lists and formularies, it enables countries to ensure that medicines that offer the best health value are accessible, affordable, of assured quality and available in child-appropriate formulations within functioning health systems.

Scope and objectives of this project

Over four years, under the framework of GAP-f, WHO comprehensively reviewed formulations of medicines listed on the EMLc to inform the 2023 and 2025 updates of the EMLc.

The project included the following activities and sub-activities:

assessing the perceived needs and gaps in age-appropriate formulations among health-care workers around the world *(14)*;

reviewing the current market landscape for age-appropriate formulations based on multiple data sources available *(15)*;

evaluating age-appropriateness in the context of therapeutic utility for children to identify potential modifications to the EMLc and paediatric formulation gaps *(16, 17)*:

- designing and testing a dedicated paediatric quality product profile assessment tool (PQPPAT) to support systematic assessment of age-appropriateness of formulations of medicines in the context of their therapeutic utility;
- systematically evaluating medicines and indications only included in the WHO Model List of Essential Medicines (EML) to be considered for inclusion in the EMLc because of their therapeutic utility for children;
- identifying formulations to propose to be added to or deleted from the EMLc based on their age-appropriateness and market availability; and
- identifying paediatric formulation gaps for essential medicines to inform future research and development and address unmet paediatric formulation needs.

The needs and gaps perceived by health-care workers

Two online surveys were conducted to capture the perspectives of frontline health-care professionals (physicians, pharmacists and nurses) on the availability and use of paediatric medicines. Respondents highlighted challenges such as acceptability from a child's perspective, ease of use for caregivers, reliance on extemporaneous preparations, frequent off-label use, concerns about pharmacokinetics, dosing and safety, the need for accelerated development of paediatric formulations, lack of child-appropriate formulations and barriers to access.

These surveys provided valuable insight into critical gaps in paediatric medicines. A total of 455 professionals across multiple regions participated, identifying 290 medicines as missing (either entirely or in age-appropriate formulations) and 387 as problematic. The most frequently reported gaps included oral liquids, tablets and injectables. Ciprofloxacin, phenobarbital and omeprazole were cited among the most needed but unavailable medicines, while lopinavir + ritonavir and amoxicillin + clavulanic acid were frequently mentioned as difficult to administer because of poor acceptability, usability or stability. Broader issues included widespread off-label use, dependence on improvised formulations and dosing complexities *(14)*.

The current market landscape for child-friendly formulations

Data from global wholesale pharmacy sales, procurement databases and household and health facility surveys were collected and analysed to identify child-appropriate formulations likely to be prescribed to children and assess the usage patterns for these formulations for EMLc-listed medicines. Descriptive analysis was performed, including the frequencies and percentage for each therapeutic class. The initial analysis was carried out to assess the overall prescribing patterns of EMLc medicines. These data sources were considered valid proxies for prescribing behavior, as they reflect real-world availability, access, and utilization trends across diverse settings. Following the initial analysis, the percentages of child-appropriate formulation used by formulation types were calculated, of which the percentages of dispersible tablets and other formulation types (such as syrup or powder) were analysed. The analysis was presented by country and WHO region.

Review of the age-appropriateness of medicines listed in the existing WHO EMLc

Designing and testing a dedicated PQPPAT

To facilitate the review of the age-appropriateness of formulations for children in the EMLc, WHO designed and applied an assessment tool *(18)*.

The development and application of a quality target product profile tool is well recognized within pharmaceutical development. Such tools form the basis of the design of a drug product and consider various product attributes including, for example, the route of administration, dosage form, dose strength, container closure and product attributes that affect pharmacokinetic properties and the quality of the drug product *(19)*. The use of a paediatric-focused tool that includes additional attributes of key relevance to children has been recommended to facilitate the development of new age-appropriate formulations *(20)*. These tools are usually used prospectively in designing new pharmaceutical products. To retrospectively evaluate existing formulations on the EMLc, in 2020 WHO conceptualized, developed and tested the validity and use of a new paediatric-focused tool that also included attributes focusing on the needs of low- and middle-income countries (Box 1).

Box 1. About the PQPPAT

- **Identification of attributes:** child-centric attributes were collated from regulatory guidelines and literature, with additional consideration of challenges relevant to low- and middle-income countries such as high humidity, temperature extremes, and limited storage and transport facilities *(24, 25)*.The targets for each attribute were defined using regulatory guidance, balancing paediatric needs and realities in low- and middle-income countries (Annex 1).
- **Qualitative scoring system:** a simple qualitative scoring system was developed to assess dosage forms against predefined attribute targets with the result of each attribute for each formulation being compared to the target and rated as follows:
  - low risk of not being age-appropriate (meets the target)
  - moderate risk of not being age-appropriate (partly meets the target)
  - high risk of not being age-appropriate (does not meet the target).

  This approach enabled consistent, transparent evaluation of the age-appropriateness of formulations listed in the EMLc.
- **Application of the tool:** Summaries of product characteristics or product labelling for products approved by a regulatory agency were used as the primary information source, extracting details such as indicated age range, dosage, administration instructions, excipients, packaging, shelf life and storage conditions. For formulations having more than one product licence available, an overview of the results for each attribute was recorded. These data were entered into the tool, compared against attribute targets and scored.

Systematically evaluating medicines and indications only included in the WHO Model List of Essential Medicines (EML) to be considered for inclusion in the EMLc because of their therapeutic utility for children

Medicines listed on the 2019 EML but not included in the EMLc were identified by compiling age-specific lists from the electronic EML covering neonates, children (aged one month to 12 years, adolescents and adults). These lists were cross-checked against both the electronic EML and the PDF version of the EMLc to ensure accuracy. The data were then filtered to confirm which medicines and indications were absent from the EMLc. Medicines considered therapeutically irrelevant for children, such as contraceptives, uterotonics and medicines for parkinsonism, were excluded from the analysis.

The remaining medicines were reviewed and assessed for their potential suitability for inclusion in the EMLc using regulatory information from the United States Food and Drug Administration and the United Kingdom Medicines and Healthcare products Regulatory Agency and, when necessary, from the European Medicines Agency and Australian Therapeutics Goods Administration. Additional evidence sources, including disease prevalence among children and the European Medicines Agency paediatric needs lists, were used to assess relevance.

Medicines were categorized according to their licensing status for paediatric use, distinguishing between those approved for children above or below 12 years of age and those with uncertain use for children. The findings were then compared against the updated 2021 EMLc to determine whether the identified medicines or their therapeutic equivalents had subsequently been included.

In total, 214 medicines were identified for detailed review. Of these, 31 medicines listed on the 2019 WHO EML were considered potential candidates for addition to the EMLc. Subsequent comparison with the 2021 EMLc showed that 18 of these medicines had already been incorporated, and the remaining 13 medicines were flagged for consideration in future updates. An additional 23 medicines or indications were identified as having potential therapeutic utility for children, warranting further evaluation.

The results of this review were shared with WHO technical focal points and subject-matter experts to support the identification of medicines and indications that should be evaluated for inclusion in subsequent EMLc updates.

Identifying formulations to propose for adding to or deleting from the EMLc based on their age-appropriateness and market availability

The application of the PQPPAT supported the identification of formulations of essential medicines that could be proposed for potential addition given their age-appropriateness and the identification of formulations to be proposed for deletion because they were not appropriate or not available. When possible, assessments were shared and discussed with relevant content experts within and outside WHO for their input and feedback. Fig. 1 provides an example of an assessment conducted using the WHO-developed tool. An overview of the assessments conducted for all medicines listed on the EMLc is available here.

Fig. 1. Example of assessment: amoxicillin

	Solid oral dosage form	Powder for oral liquid	Powder for injection
	(250 mg; 500 mg (as trihydrate))	(125 mg/5 mL; 250 mg/5 mL (as trihydrate))	(250 mg; 500 mg; 1 g (as sodium) in vial)
Target population	🟡	🟢	🟢
Dose and dose flexibility	🟡	🟢	🟢
Patient acceptability (0 to <6 years)	🔴	🟢	🟡
Patient acceptability (6–12 years)	🟢	🟢	🟡
Excipient safety	🟢	🔴	🟢
Administration considerations	🟢	🟡	🟡
Stability, storage conditions and primary packaging material	🟡	🟡	🟡
Registration status	🟢	🟢	🟢

Red: does not meet the target; orange: partly meets the target; green: meets the target.

Draft reports of preliminary findings were presented and discussed during two WHO-convened virtual consultations with international paediatric experts and other stakeholders in November 2022 and December 2024. The reports were then revised to incorporate the feedback received from these consultations and formed the basis of applications submitted to the Expert Committee on Selection and Use of Essential Medicines in 2023 and 2025, respectively. In accordance with the standard procedures for applications to the Expert Committee, these applications were published on the WHO website for public comment *(16, 17)*. The proposals made for changes to the EMLc were endorsed by the Expert Committee *(21, 22)*. Box 2 provides examples of some of the changes implemented.

Identifying paediatric formulation gaps for essential medicines to inform future research and development

The application of the tool based on the methods described above also served to highlight areas with gaps in age-appropriate formulations of essential medicines for children, which informed additional research and development activities to fill priority unmet formulation needs for children. The identified gaps were also discussed and refined during virtual consultations with international paediatric experts and stakeholders.

In particular, several of the gaps identified through this work informed subsequent paediatric drug optimization (PADO) *(23)* exercises, which were convened with a broad range of stakeholders – including researchers, clinicians, implementing partners, market-shaping entities and funders. These exercises facilitated structured discussions on unmet needs and gaps to identify key priority products for development. Establishing such priorities is a critical first step toward enabling a targeted research and development approach, helping to direct the efforts and resources of researchers and manufacturers towards the most urgently needed, age-appropriate dosage forms for children.

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Box 2. Example of the changes implemented

Amoxicillin was included in the 2021 EMLc as powder for injection, powder for oral liquid and solid oral dosage form. Solid oral dosage forms (such as hard gelatine capsules and unscored tablets) did not meet the target for acceptability for younger children who are unable to swallow solid dosage forms and only partly met the targets for dose flexibility, since they are not suitable for children requiring doses below 250 mg (weighing less than 6 kg), and stability, since capsules may require protection from moisture. The powder for oral liquid did not meet the target for excipient safety due to the presence of preservatives, flavourings and sweeteners and partly met the targets for stability (once reconstituted, it requires storage at 2–8°C with a short in-use shelf life (7–14 days)) and administration considerations since it requires reconstitution and has the potential for dosing errors if the measuring device is used incorrectly (Fig 1). Amoxicillin 250-mg and 500-mg dispersible tablets were identified in the market through sales and procurement datasets reviewed as part of the project and are also listed in the United Nations Children's Fund (UNICEF) supply catalogue. Once dispersed in water, these formulations are acceptable across the paediatric age range, and administering half of a scored 250-mg dispersible tablet enables accurate dosing for children weighing less than 6 kg. Dispersible tablets were considered more likely to contain fewer excipients of concern (such as preservatives) and have a smaller bulk footprint than powders for oral liquid. They also eliminate the need for a measuring device at the point of administration. They were therefore proposed for addition and included in the 2023 EMLc.

Cefalexin was listed on the 2021 EMLc (6.2.1 access antibiotics) as powder for oral liquid and solid oral dosage forms. However, 125 mg and 250 mg dispersible tablets were identified in some markets. Since dispersible tablets are more acceptable to younger children and have a lower bulk footprint than powders for oral liquids and since a measuring device would not be required for administration, the addition of this dosage form was proposed and implemented in the 2023 WHO EMLc.

Morphine was included in the 2023 EMLc (2.2 opioid analgesics) in several dosage forms, including slow-release tablets and granules (10 mg to 200 mg). To avoid challenges related to the procurement of specific strengths, it was proposed to replace the strength range with specific strength formulations corresponding to the dose strengths commonly prescribed for children younger than 12 years of age: 20 mg, 30 mg, 60 mg and 100 mg. The 200 mg strength, considered too high to support dosing for children, was proposed for removal from the EMLc while being retained in the EML because of its utility for adults.

Key outcomes

The review of the age-appropriateness of formulations on the EMLc resulted in substantial updates – including additions, removals and other modifications – all of which were adopted and reflected in the 2023 and 2025 editions of the list. This foundational work ensures that the EMLc remains the most up-to-date global reference for countries and procurement agencies, supporting the alignment of internationally and nationally procured formulations with the latest available options for children.

This extensive work also enabled the identification of 79 medicines with gaps in age-appropriate formulations, providing a clear basis for WHO and partners to address these gaps through PADO exercises and related follow-up activities (Fig. 2).

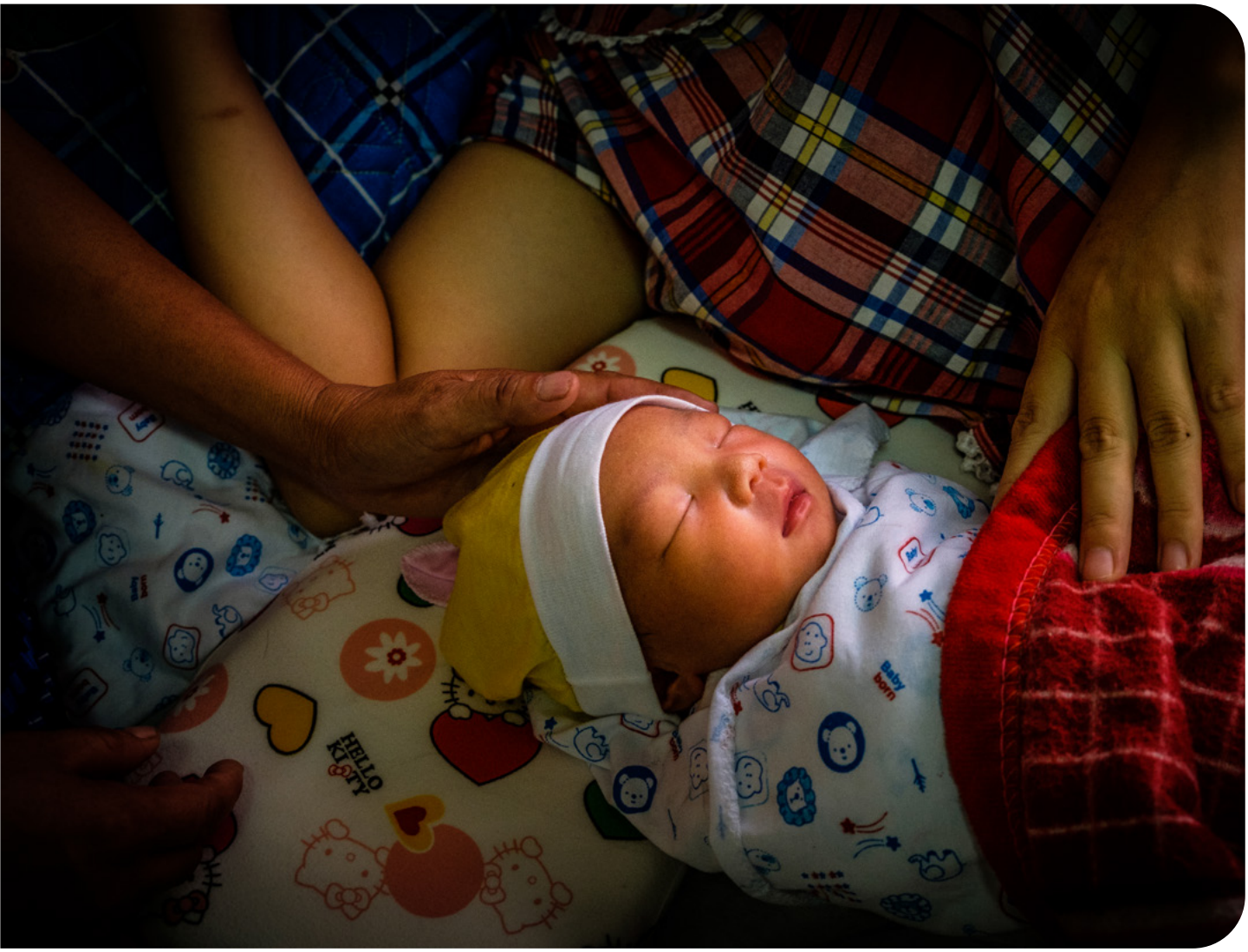

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Fig. 2. Overview of medicines reviewed and proposed changes to the EMLc

In a snapshot

290
Medicines reviewed[a]

499
Dosage forms reviewed[b]

4769
Formulations reviewed[c]

Zooming in

- *Ensure that national lists of essential medicines are updated in accordance with the latest available options designed appropriately for children and to avoid promoting the procurement and use of formulations that are no longer available in quality-assured fashion or appropriate for paediatric use.*
- *Streamline procurement and supply and avoid confusion by procurement entities*

200
Medicines with an EMLc proposal

92
Formulations proposed for removal

- Not found in stringent regulatory authority or WHO-listed authority markets
- Not relevant for administering the indicated dose for children younger than 12 years
- More age-appropriate formulations available (considered for addition)

163
Formulations proposed for addition[d]

- Found in stringent regulatory authority or WHO-listed authority markets and with added value compared with listed formulations in terms of acceptability, dose flexibility or other characteristics

85
Formulations for which other changes were proposed

- Replace strength ranges with specific strengths
- Add the information on the presence of a functional scoring line
- Align relevant footnotes and details with the latest WHO guidelines for use

- *Clearly defined formulation characteristics are critical to inform appropriate and accurate procurement decisions*

79
Medicines with a GAP-f proposal

- Identification of medicines for which a gap in age-appropriate formulations exists

a. Medicines appearing in more than one section were counted as separate entries. This approach was adopted because the assessment was indication-specific: although certain attributes (such as excipients) were consistent across indications, other critical attributes (such as dose flexibility, formulation requirements or age-appropriateness) varied depending on the clinical context.

b. This refers to the different dosage forms listed for the same medicine, such as tablets, capsules, dispersible tablets and solution for injection.

c. This refers to all the strengths of the dosage forms of the medicines reviewed (such as tablets 50 mg, 100 mg and 200 mg).

d. This includes both new strengths of existing dosage forms and new dosage forms.

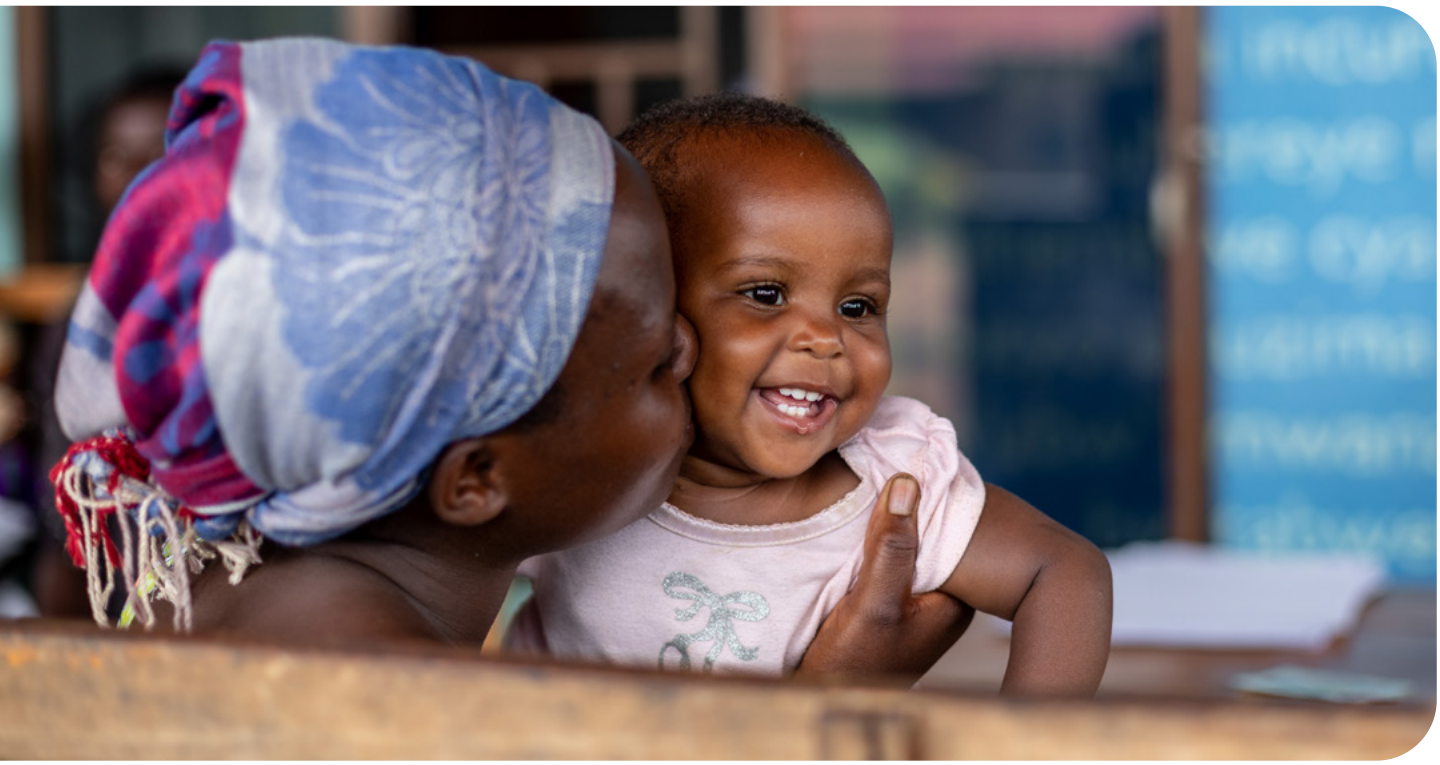
Informing PADO

This project provided a critical foundation for identifying gaps in the availability of age-appropriate formulations across multiple disease areas and for guiding the development of priority medicines for children. Building on the comprehensive review of formulations included in the EMLc, PADO *(23)* exercises were conducted for antibiotics *(26)*, childhood cancer *(27)*, neglected tropical diseases *(28)* (including schistosomiasis, human African trypanosomiasis, visceral leishmaniasis, onchocerciasis and scabies), epilepsy and malaria.

These exercises brought together a broad range of stakeholders to identify key formulation gaps, define priority products and outline preferred product characteristics for research and development. PADO processes apply core drug-optimization principles, considering existing access and market challenges while maintaining a long-term view that aligns paediatric innovation with advances in adult research and development. Priority-setting has therefore been central to GAP-f since its inception – enabling a targeted and efficient research and development approach. By establishing a clear portfolio of the most needed paediatric formulations, GAP-f has helped to direct resources toward optimal dosage forms that address the most urgent therapeutic gaps for children.

PADO is strategically linked to other WHO drug-optimization and normative functions, including clinical guideline development, adult drug priority-setting exercises, prequalification and updates to the EML and EMLc. This ensures coherence across the product life cycle and facilitates timely integration of new evidence and innovations into WHO recommendations.

The outcome of the work on the age-appropriateness of essential medicines for children has not stopped at PADO exercises. The evaluation undertaken based on the dedicated qualitative assessment tool has set the basis for developing target product profiles for priority medicines, outlining the shortcomings of existing available formulations and providing a solid basis for the specifications that enable manufacturers to develop and market age-appropriate formulations – as demonstrated by recent target product profiles developed for antibiotics (Box 3) and childhood cancer (Box 4).



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Box 3. Antibiotics

In 2023, WHO launched the first-ever list of priority paediatric formulations for antibiotics *(26)* so that more targeted research and development efforts can address the specific needs of infants and children with bacterial infections. The PADO priority list for antibiotics includes three legacy antibiotics that already have an indication for children but for which an optimal formulation is missing, including azithromycin and nitrofurantoin. In May 2024, WHO, with support from GAP-f partners, convened a technical consultation designed to develop target product profiles for these two antibiotics *(29)*. The key characteristics of existing formulations for azithromycin and nitrofurantoin were carefully examined, including the lack of dispersible tablets and the poor palatability of marketed liquid formulations, which also contain excipients of concern, emphasizing the importance of developing better formulations for children. The group emerged with a clear set of characteristics for two new formulations to be developed:

- nitrofurantoin orodispersible multiparticulates (minitablets or sprinkles), 5 mg per unit dose, preferred; dispersible tablets, 5 mg,10 mg (scored) as an alternative; and
- azithromycin orodispersible multiparticulates (minitablets or sprinkles), 50 mg per unit dose or scored dispersible tablet 100 mg, as preferred; dispersible tablets, 50 mg as an alternative.

In March 2025, both were subsequently included in a new dedicated expression of interest list *(30)* that formally invites manufacturers to submit for WHO prequalification better paediatric formulations for these two critical antibiotics.

Box 4. Childhood cancer

In early 2024, WHO launched the first-ever list of priority paediatric formulations for cancer medicines so that more targeted research and development efforts could be made to address the specific needs of children with cancer. The first PADO exercise targeted a review of oral formulations relevant to the Global Initiative for Childhood Cancer starting with those in the EMLc. After examining the formulation gaps the EMLc evaluation had identified, the PADO group gave priority to six cancer medicines for which an optimal formulation is missing: five medicines already included in the EMLc – cyclophosphamide, etoposide, mercaptopurine, methotrexate and procarbazine plus temozolomide – still to be reviewed for inclusion. These medicines were subsequently discussed in December 2024 when a dedicated group of experts was gathered virtually to identify specific optimal and minimum profiles for each of the six prioritized medicines. These target product profiles, developed based on the gaps identified for the five medicines in the EMLc based on the PQPPAT assessment as well as additional evaluation specific to the chemical characteristic of each compound (especially if cytotoxic), now provide a clear vision for the novel formulations on which manufacturers should focus their work. WHO is currently developing an expression of interest for childhood cancer that will formally invite manufacturers to develop and apply for WHO prequalification for optimal formulations.

Next steps for GAP-f: our shared path forward

To accelerate progress towards universal access to child-appropriate medicines, a set of priority actions has been identified. These actions focus on strengthening the uptake of the updated EMLc, supporting national adoption and/or adaptation, addressing research and development gaps and reinforcing advocacy and political commitment. Together, they provide a pathway to ensure that all children benefit from safe, effective and affordable medicines tailored to their needs.

Adopt the use of the PQPPAT in all future EMLc applications: use the WHO PQPPAT *(19)* to guide novel applications and to increasingly set standards for the age-appropriateness of formulations intended for children.

Strengthen EMLc uptake: support countries in integrating updated EMLc recommendations into national essential medicines lists, procurement and treatment guidelines as required by local epidemiology.

Pilot and scale an ecosystem approach: pilot a framework of analysis and action in Asia and expand to other regions to promote a paediatric ecosystem approach aligning essential medicines packages with local epidemiology and access pathways.

Address research and development and formulation gaps: guide research priorities and support partnerships to accelerate the development of child-friendly formulations where none exist, promoting investment and exploring efficiency to accelerate timelines.

Enhance advocacy and political commitment: work with civil society, regional networks and global health stakeholders to keep paediatric medicines high on the policy agenda as an essential contributor to Sustainable Development Goal target 3.8 on universal health coverage and equitable access to essential medicines for all.

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Annex 1. Paediatric quality target product profile attributes and targets

Attribute	Target	Comments
Target population (age)	Entire age range 0 to ≤12 years	The target population is for WHO EMLc. The product should ideally be suitable from birth, although the patient population age will depend on the medicine and indication. The drug product may be restricted to a paediatric age subset. If no age or weight limits are listed, it is assumed the product is intended for 0 to ≤12 years.
Dose and dose flexibility	Defined paediatric dose range and dose increments	The product concentration and strength and format should enable correct and flexible dosing according to the patient age, weight or body surface area. Dose banding may be possible.
Acceptability to patients	Acceptable for the proposed patient population	The dosage form must be suitable for use in the proposed paediatric population. Different dosage forms may be required for different age groups. Depends on many factors, including the route of administration, dosage form and patient and caregiver characteristics, including age, disease and ability.
Excipient safety	Excipients with an acceptable safety profile for the proposed patient population	Excipient benefit versus risk should be considered if product excipients are listed (such as on the label). If excipient details are unavailable, the potential excipient risks associated with the dosage form should be considered (such as preservatives, sweeteners, surfactants and co-solvents in liquids).

Attribute	Target	Comments
Administration considerations	The required doses can be easily and accurately administered, with minimal preparation	Evaluate according to setting (such as at home versus a health-care facility) and the characteristics of the individual administering the product. The administration device (if required) should be readily available and appropriate for the intended use. Multiple dilutions should be avoided. Guidance on compatible administration vehicles or diluents and storage time (if required) should be available. The proposed dosing vehicles should be readily available. The accuracy of splitting scored tablets (if relevant) should be considered.
Stability, storage conditions and primary packaging material	Stable for two years minimum under long-term storage conditions (as defined by the International Council for Harmonisation). Packaging should be suitable for hospital and/or home use, easy to use and unambiguous.	Global climatic conditions should be considered, including for in-use stability if applicable. Refrigerated (2–8°C) and freezer storage is less favourable. • The primary packaging should ideally be lightweight, portable and with child-resistant closure. • If specific information on the pack and shelf life is unavailable, potential pack options and stability according to the dosage form and formulation type should be considered.
Registration status	Positive opinion or approved by a stringent regulatory authority	Regulatory status and potential registration strategy (if required) should be considered. Prior approval can facilitate further or subsequent licence approvals and WHO prequalification.

Annex 2. Paediatric quality target product profile tool scoring criteria

Attribute	Considerations for scoring		
	High risk and issues; does not meet target **Score = 1**	**Moderate risk and issues; partly meets target** **Score = 2**	**Low risk and no issues; meets target** **Score = 3**
Target population (age) (0 to ≤12 years)[a]	Not suitable for all or most children younger than 12 years.	Suitable for most of the paediatric population for which the active pharmaceutical ingredient is indicated.	Suitable from birth. Suitable for the age range indicated for the active pharmaceutical ingredient.
Dose and dose flexibility[b]	Lack of or poor dose flexibility. Not able to administer the required doses without manipulation.	Some limited dose flexibility, such as limited dose strengths available. Not able to administer the required doses to some patients.	High dose flexibility. Able to easily measure and administer the required doses to all patients.
Acceptability to patients 0–5 years old[c]	Unacceptable for this age range, such as high volumes of oral liquids or large quantities of multiparticulates (mini) tablets per dose. Anticipated to have strongly aversive taste, painful injection etc.	Some concerns about acceptability in this age range, such as poor palatability, frequent dosing and formulation unsuitable for some patients.	Acceptable for this age range.
Excipient safety[d]	Contains several excipients of potential or known concerns.	Contains one or two excipients of potential concern.	Contains excipients that generally have an acceptable safety profile.

Attribute	Considerations for scoring		
	High risk and issues; does not meet target **Score = 1**	**Moderate risk and issues; partly meets target** **Score = 2**	**Low risk and no issues; meets target** **Score = 3**
Administration considerations[e]	Complex manipulation required, such as reconstitution with a fixed volume of vehicle (home use), multiple dilutions (health-care personnel and home use). Complex administration device or procedure (health-care personnel and home use).	Some manipulation required (such as food mixing) or measurement of dose required (home use) Some manipulation required (such as food mixing or reconstitution with a fixed volume of vehicle) or measurement of dose required (health-care personnel use).	No manipulation or measurement required (home use) No manipulation required, easy to measure and administer required doses (health-care personnel use).
Stability, storage conditions, primary packaging material[f]	Requires freezer or refrigerated storage. Less than 18 months of shelf life. Bulky or heavy packaging. Complex packaging design.	May be stored at room temperature[g] but the constituted product requires refrigerated storage. Requires protection from moisture. Less than two years of shelf life.	May be stored at room temperature.[g] Minimum two years of shelf life. Light packaging with low bulk footprint. Simple packaging design.
Registration status	Not approved by any regulatory authorities and no approval anticipated.	Approved by a regulatory authority with maturity level 3 and above.[h] Approval by a stringent regulatory authority anticipated.	Approved by at least one stringent regulatory authority.

a. The lowest indicated or recommended age should be considered. The minimum age may be older than from birth. For example, if the condition is only prevalent or possible to diagnose from three years of age, the minimum target age is three years.

b. The strength or concentration should enable the required doses to be accurately and easily administered. Tablet splitting may be permitted if supported by the product licence. Dose banding may be possible.

c. Score according to age group. Numerous factors involved – an overall score should be applied. Excipient considerations should be excluded and scored separately. Frequent dosing is mitigated by short-term use.

d. Excipient safety depends on the route of administration. Neonates and infants are more vulnerable to excipient adverse effects than older children.

e. Need to consider the setting, the availability of the device (if required), the complexity of the process, the potential for misdosing or dosing errors.

f. If the shelf life is not listed on the label, consider the dosage form or formulation type, handling, required storage conditions and packaging type.

g. Defined here as 20–25°C (USP <659> Packaging and Storage Requirements defines controlled room temperature as 20–25°C).

h. Maturity level 3 is defined as "stable, well-functioning and integrated regulatory systems"; maturity level 4 is defined as "regulatory systems operating at advanced level of performance and continuous improvement".

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