SWISS PED DOSE

Nationale pädiatrische Arzneimitteldosierungen
Posologies pédiatriques nationales
Posologie pediatriche nazionali
National pediatric drug doses

patientensicherheit schweiz
sécurité des patients suisse
sicurezza dei pazienti svizzera

Aktionswoche Patient:innensicherheit 2025

**Webinar: When Standard Dosing Fails – Pediatric Insights, Broader Implications**

# Efficacy and safety in drug dosing for children

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# Children are not small adults

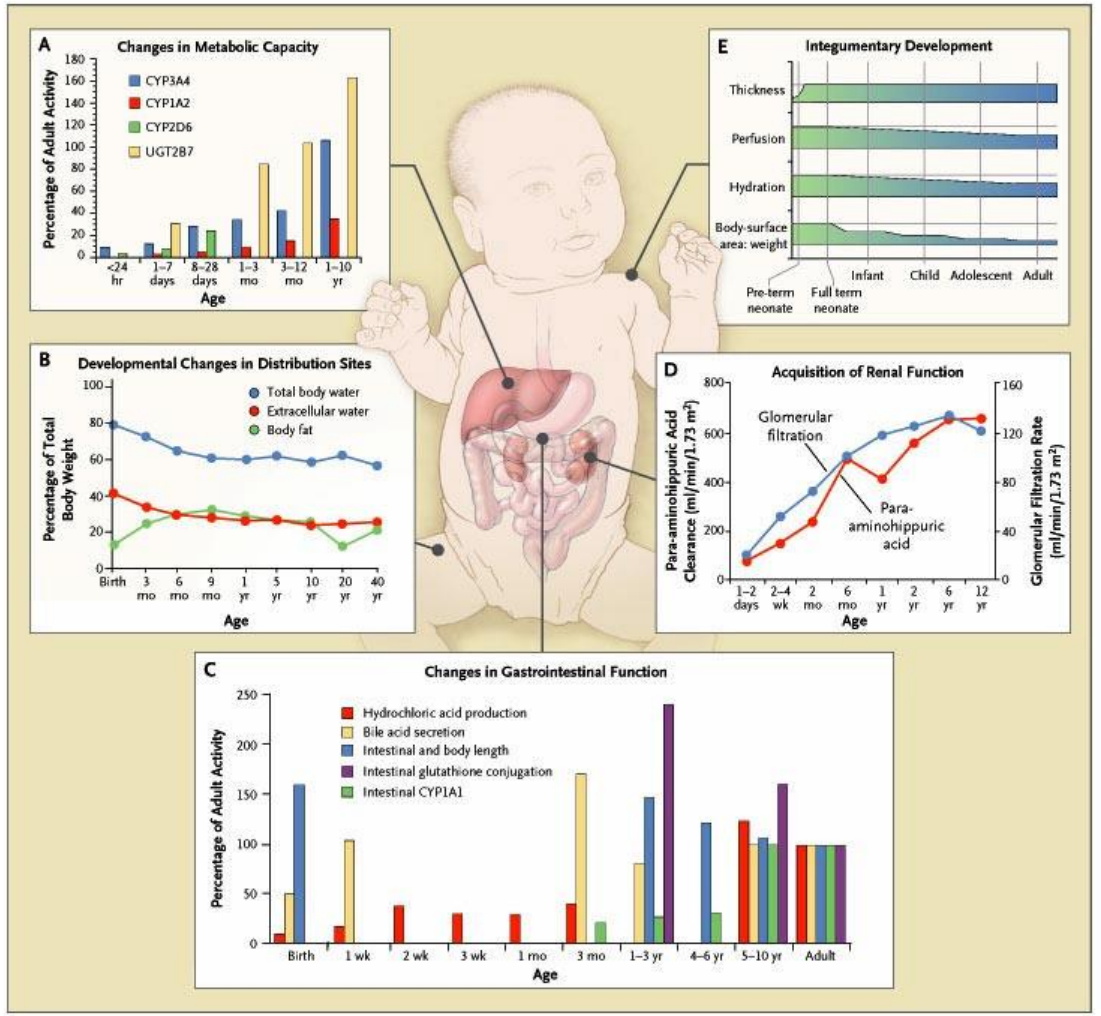
# Developmental pharmacology

**Absorption** Gastric pH in neonates.
Shorter intestinal transit times in infants

**Distribution**
Higher amount of body water in infants

**Metabolism**
Delayed maturation of drug-metabolising enzyme activity. Increase in plasma clearance for liver metabolised drugs

**Excretion** immature glomerualr filtration rate and tubular secretion in the 1st year of life.




Kearns GL et al. Developmental pharmacology--drug disposition, action, and therapy in infants and children. N Engl J Med. 2003;349:1157-67. doi: 10.1056/NEJMra035092.

# Drug prescribing in children

**Children are not small adults → Impact on pharmacokinetics**

- Absorption, distribution, metabolism, and excretion differ depending on age group and from adults

**Drug dosage finding** for children

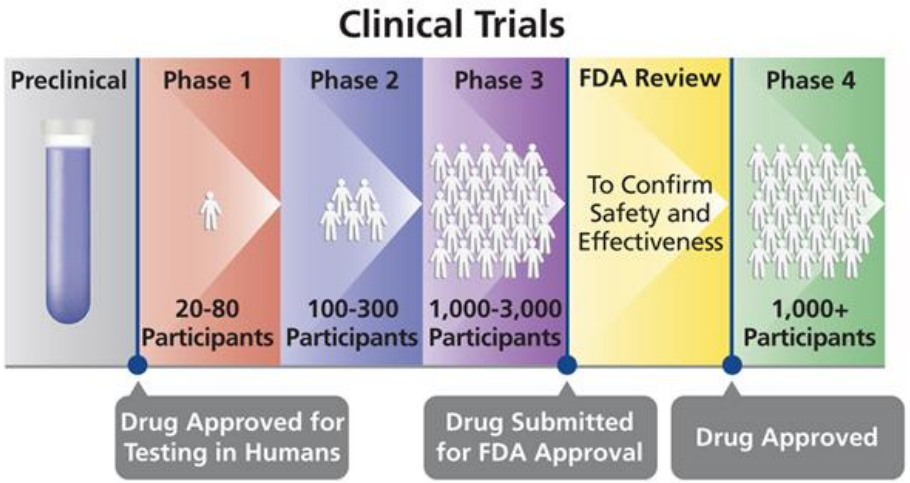
- Define *efficacy* per age group:
  dose per kg body weight may be too low (infant) or too high (teenager)
- Check *indication*: identical as in adults, particular pediatric indications with particular dosage
- Consider *toxicity* per age group (A, D, M, E see above)
- Provide *galenic forms* per age group (absorption, ability to provide the exact dose, child's ability to swallow)

**= critical prerequisites for age-based drug dosage recommendations for children**

# Drug prescribing in children

Drug dosage *finding* and dosage *recommendations* for children have to address:

- Heterogeneous age groups:
  studies difficult to conduct and complex
  (for each age group, blood sampling, ethics)
- Galenic forms: often not studied (if adult studies only)
  (availability? bioavailability, stability?)
- Small market: thus often lacking data




➔ Most drugs are not studied by company in children
➔ Often no label by licensing authority

***But these children need and benefit from treatment***

# Children as «therapeutic orphans» in a study from a Swiss pediatric university hospital based on the «label»

| | 0–28 days | 1–23 months | 2–11 years | 12–18 years | Total |
|---|---|---|---|---|---|
| No of patients, n | 11 | 20 | 24 | 5 | 60 |
| No of prescriptions, median (range) | 6.0 (3–20) | 8.0 (2–18) | 7.5 (3–13) | 9 (4–12) | 7.5 (2–20) |
| No of prescriptions, n (%) | 94 (100) | 166 (100) | 182 (100) | 41 (100) | 483 (100) |
| Following the terms of the marketing authorisation, n (%) | 50 (53) | 80 (48) | 97 (53) | 20 (49) | 247 (51) |
| Total Unlicensed and off-label, n (%) | 44 (47) | 86 (52) | 85 (47) | 21 (51) | 236 (49) |
| Unlicensed, n (%) | 18 (19) | 55 (33) | 36 (20) | 5 (12) | 114 (24) |
| Pharmacy preparations, n (%) | 9 (10) | 42 (25) | 27 (15) | 4 (10) | 82 (17) |
| Medicines prepared for Swiss hospitals*, n (%) | 4 (4) | 6 (4) | 9 (5) | 1 (2) | 20 (4) |
| Foreign medicines, n (%) | 5 (5) | 7 (4) | 0 (0) | 0 (0) | 12 (2) |
| Off-label, n (%) | 26 (28) | 31 (19) | 49 (27) | 16 (39) | 122 (25) |
| No paediatric information, n (%) | 13 (14) | 14 (8) | 26 (14) | 13 (32) | 66 (14) |
| Age, n (%) | 6 (6) | 10 (6) | 6 (3) | 0 (0) | 22 (5) |
| Indication & contra-indication, n (%) | 0 (0) | 1 (1) | 4 (2) | 1 (2) | 6 (1) |
| Dose & frequency, n (%) | 6 (6) | 3 (2) | 11 (6) | 2 (5) | 22 (5) |
| Route of administration, n (%) | 1 (1) | 3 (2) | 2 (1) | 0 (0) | 6 (1) |

* by authorized manufacturers

Di Paolo et al. Unlicensed and off-label drug use in a Swiss paediatric university hospital. Swiss Med Wkly. 2006

# Off-label use

**Prescribing a medication for a condition not described in the label approved by Swissmedic.**

Label:
- Authorized by national authority and process
- i.e. positive assessment based on scientific evidence for efficacy and safety provided by company

No label.
- possible unanticipated risks?
- responsibility of the prescribing physician only?
  → Patient has to be informed
  → Health insurance coverage is not guaranteed

# Unlicensed use

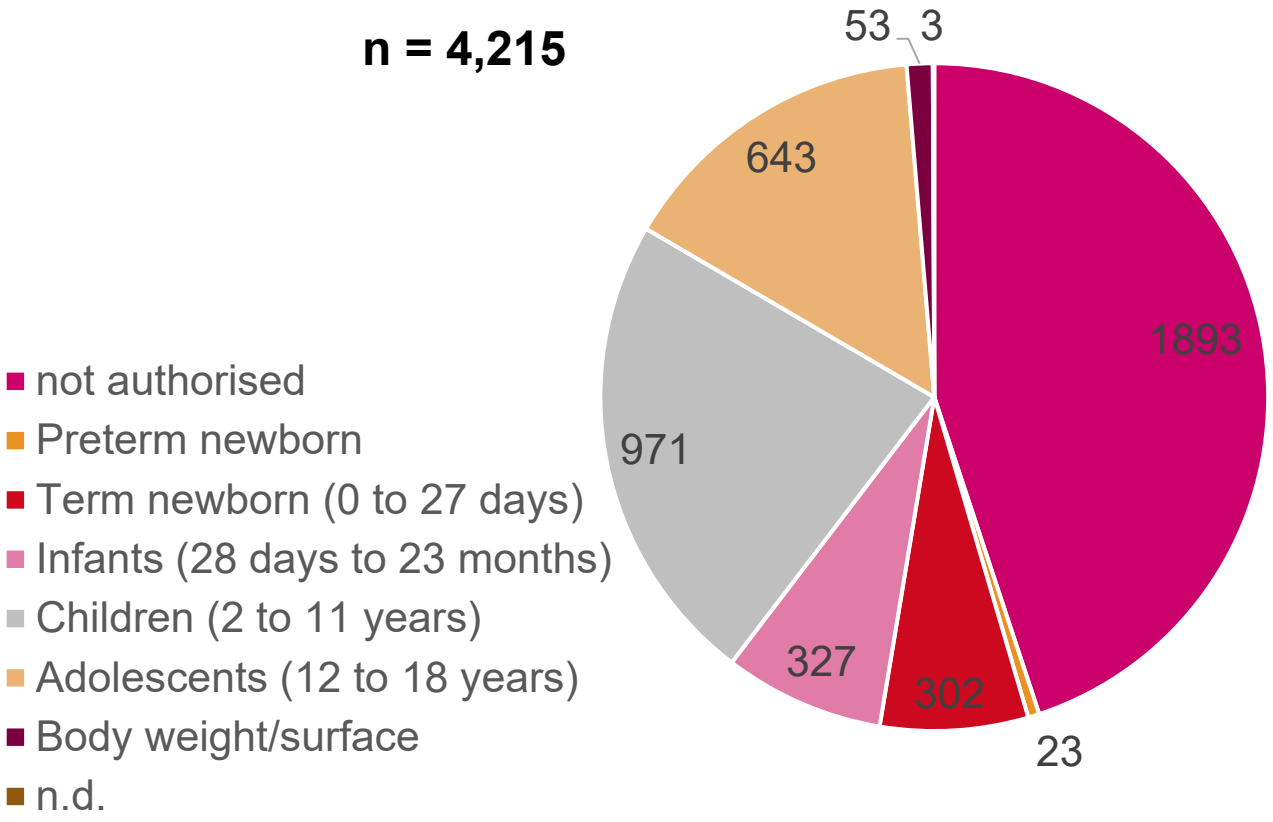
Galenic formulations often inadequate for children. Special dose strengths of capsules or oral liquid formulations are to be produced by hospital pharmacies.

Indication:
juvenile arthritis


# Licensed / label use in Switzerland

**55.1% of brand-named drugs are authorised and**
**44.9% are not authorised for use in children.**

**n = 4,215**




- 45% of drugs on Swiss market are *not authorised* for use in children.
- minority of SmPCs contain clear indication or contraindication for use in children.
- Evidence-based paediatric data present in only 1/3 of Swiss SmPCs.

## WHAT DOES THIS MEAN

⇒ In absence of information in SmPCs about children
professionals prescribing drugs for children ***need to consult other sources providing evidence- and expert-based off-label dosing recommendations***

Tilen R et al. Arch Dis Child. 2024;109:586-591.
doi: 10.1136/archdischild-2023-325611.

# Drug prescriptions in Children: mostly without license / label

Despite regulations and incentives for pediatric drug research (last 20 years) for authorities and pharmaceutical companies to add pediatric guidance to the prescribing labels:

**< 50 percent** of medication labels have any guidance for providers on a drug's use in children

.. at an academic medical center, that rate might be as high as 60-80 % for medications used among hospitalized patients.

¼ approved, ¼ unlicensed, 50% off-label due to age, dose, indication, route

.. no "substantial evidence" from "adequate and well-controlled investigations" upon which the licensing authority can determine regarding that drug's safety and effectiveness in children. …. it does not mean prohibited or experimental….

American Academy of Pediatrics

AAP Policy statement updated 2020. Frattarelli DA et al. Off-label use of drugs in children. Pediatrics. 2014;133:563-7.

Boston Children's Hospital

General Pediatrics | Off-label Drug Prescriptions | Boston Children's Hospital accessed September 10, 2025

# Children deserve medicines + dosages adapted to their needs

## Looking beyond the label for prescription guidance

*Dosage recommendations needed:*
*effective treatment / toxicity, updated evidence-based, available in emergency:* ***patient safety issue***

Without a pediatric label providers must rely on their best judgment and the best evidence.

Sources for evidence for providers:

- Peer-reviewed literature
- Consensus statements, (AAP) policies and practice guidelines
- Information from organizations such as the Cochrane Collaboration and UpToDate

"Providers should rely on their own and their colleagues' expertise, as well as on any expert opinions and trial data they can access”

**<u>Goal</u>: independent expert consensus-based dosage recommendations**
**→ to increase efficacy and prevent toxicity of drug prescription and administration in children**

# Heilmittelgesetz / Loi sur les produits thérapeutiques (2018)

**Art. 67*a*[1] Provision of information about the use of medicinal products in certain population groups**

[1] In order to improve safety in the use of medicinal products in paediatrics, the Federal Council may allow for the collection, harmonisation, evaluation and publication of data relating to the prescription, supply and use of medicinal products.

[2] The Confederation may arrange for a database to be established and operated by third parties for this purpose. This database may not contain personal data.

SWISSPEDDOSE

**Swiss Database for Dosing Medicinal Products in Pediatrics** (SwissPedDose) aims to increase the safety of the use of drugs in children

Medical professionals in pediatrics have access to dosage recommendations developed in a standardised harmonisation process throughout Switzerland

## Association

The SwissPedDose association operates the national database and is responsible for coordinating the harmonisation. The founding members of the association are the 8 largest children's clinics in Switzerland (Category A children's hospitals), GSASA and pädiatrie schweiz.

**More ...**

## Task

The Swiss Federal Office of Public Health (FOPH) has commissioned the SwissPedDose association to operate the database. The legal basis for the creation of the national database was established by Article 67a of the Therapeutic Products Act (TPA).

**More ...**

## Harmonisation process

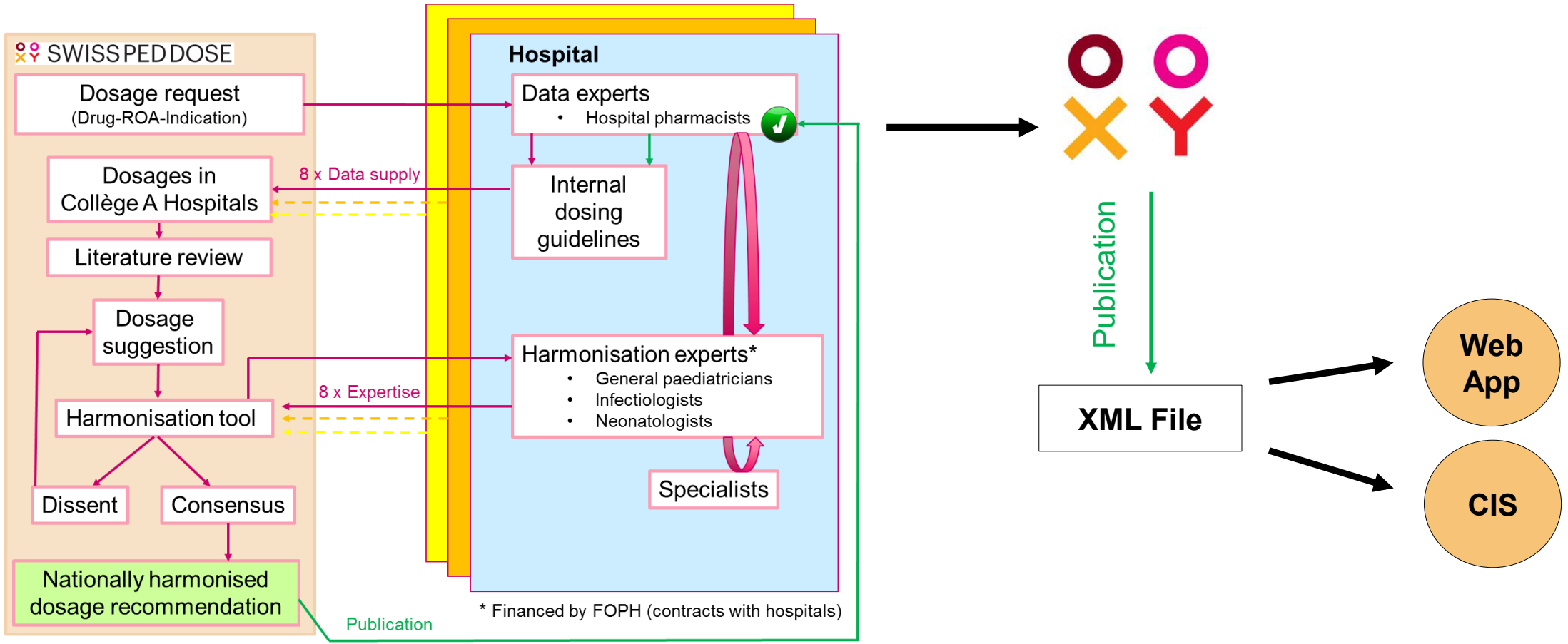
The dosage harmonisation process is based on a standardised process. The Category A children's hospitals in Switzerland are key players in this process. They provide the basic data, evaluate and jointly decide on dosage recommendations.

pädiatrie schweiz · GSASA · CHUV · HUG · INSELSPITAL · UKBB

KSA Kinderspital Aarau · luzerner kantonsspital · OSTSCHWEIZER KINDERSPITAL · UNIVERSITÄTS-KINDERSPITAL ZÜRICH · Swiss Society of Neonatology

# Harmonisation of dosage recommendations for children

- By SwissPedDose and its 8 children's hospitals
- Finding national expert consensus in a **unique harmonisation process**
- using an **online tool to discuss cases (individual dose recommendations)**




Tilen et al. Development of the Swiss Database for dosing medicinal products in pediatrics. Eur J Pediatr 2022

# Ibuprofen – Algifor Junior

## *(Information for professionals)*

***Galenische Form und Wirkstoffmenge pro Einheit***

1 Dosis zu 5 ml Suspension enthält 100 mg Ibuprofen.

***Indikationen/Anwendungsmöglichkeiten***

Rheumatische Erkrankungen (juvenile rheumatische Arthritis) bei Kindern über 2 Jahren.

Fieberhafte Krankheitsbilder bei Infektionskrankheiten.

Schmerzzustände wie z.B. nach Verletzungen sowie postoperativ (z.B. nach Zahnextraktionen, kleineren chir

***Dosierung/Anwendung***

Die übliche tägliche Dosierung beträgt 20 bis 30 mg Ibuprofen pro kg Körpergewicht, aufgeteilt in 3–4 Dosen.

Abstand zwischen 2 Einnahmen: 6 bis 8 Stunden.

### *Kontraindikationen:*

Säuglinge < 6 Monate und Kinder < 5 kg Gewicht

### Concerns for age < 6 months

- Adverse gastrointestinal effects
- Risk of renal failure
- Increased risk of necrotizing fasciitis
- Reye's Syndrome

Evidence from literature:

### 1. Efficacy & safety

(***Ziesenitz V, Paediatr Drugs. 2017; 19:277***)

- Assessment of safety and efficacy in infants (11 studies, 39293 patients, > 207 children < 6 months)
- Conclusion: short-term use (< 3 days) relief of fever/ pain: safe >3 months, body weight > 5-6 kg
- Recommended dose: 5-10 mg/kg 3-4x daily, max. 30-40 mg/kg/day)

### 2. AE of ibuprofen in infants

***(Walsh et al, PLoS One. 2018;13:e0199493)***

Infants (n: 31560) < 6 vs. 6-12 months of age

- GI and renal AEs not higher in infants < 6 months

Infants < 6 months of age

- AEs increased in infants < 6 months with ibuprofen compared with those with paracetamol alone

### 3. **Proposition in tool,** discussion among experts

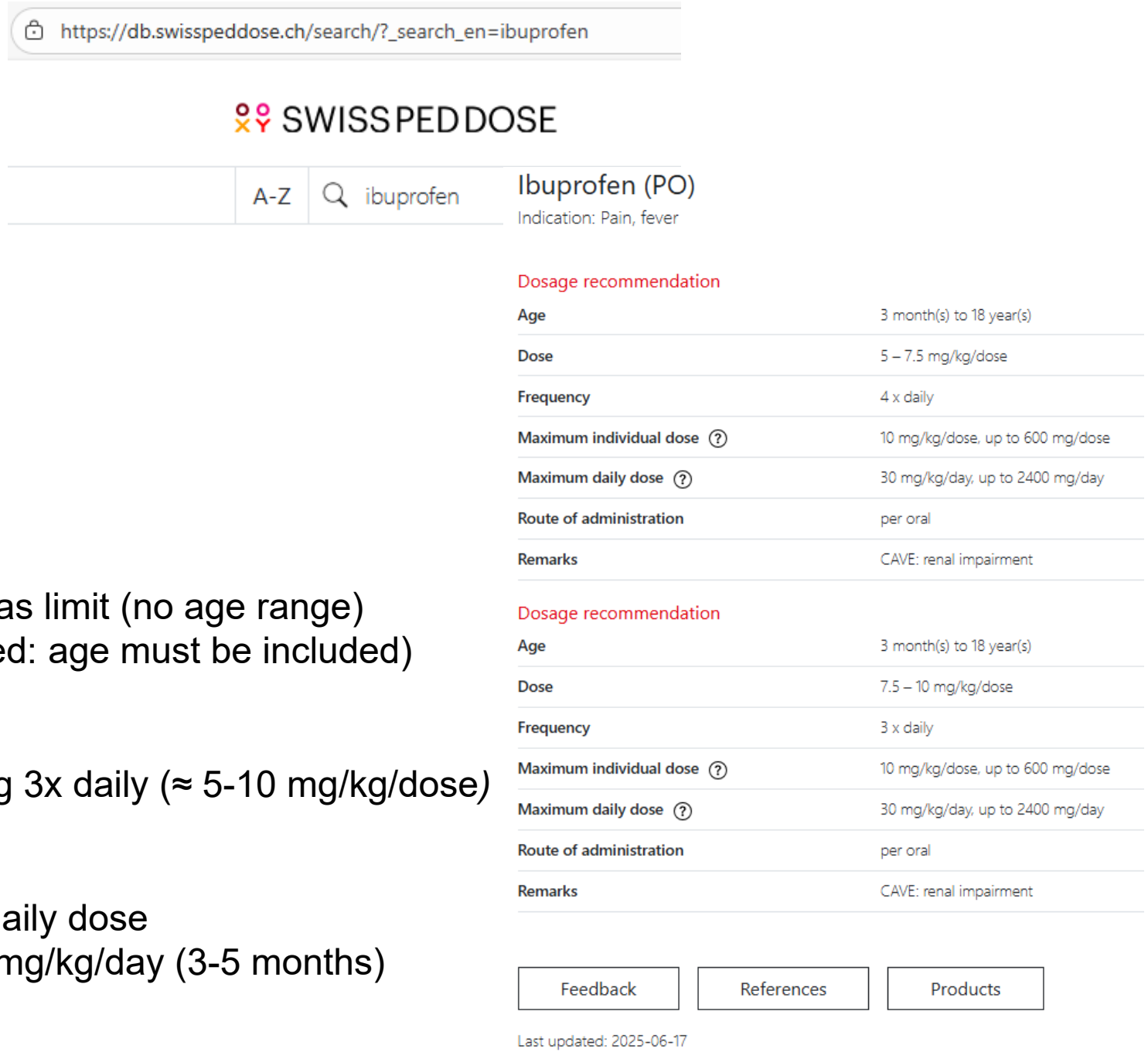
→ *harmonisation successful*, all documented in tool

# Ibuprofen:
# Recommendation

- No concerns for use in
  children 3 to 6 months of age

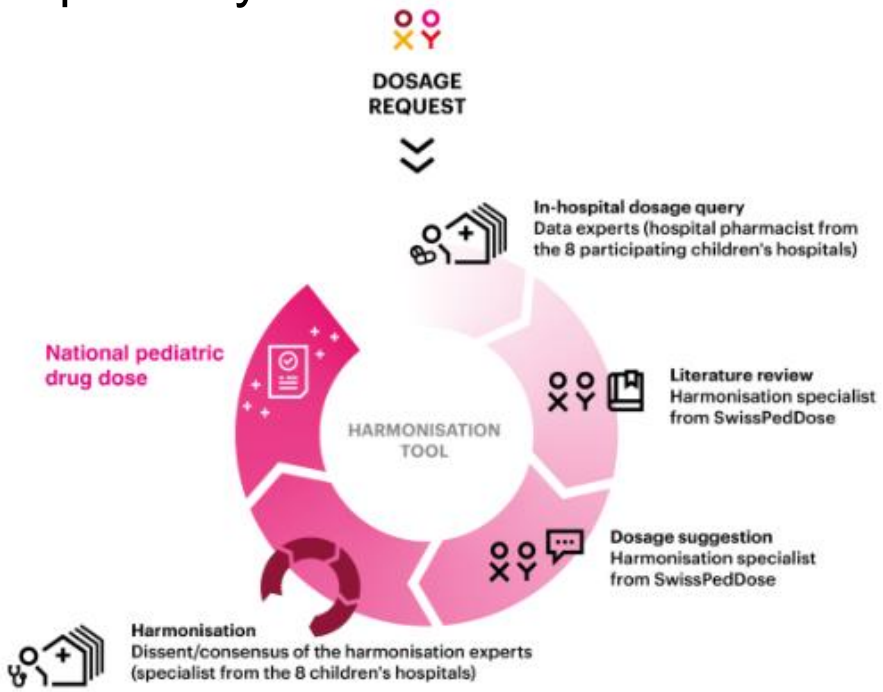
- EMA Assessment: proposal 5 kg as limit (no age range)
  -> not implemented (regul. required: age must be included)

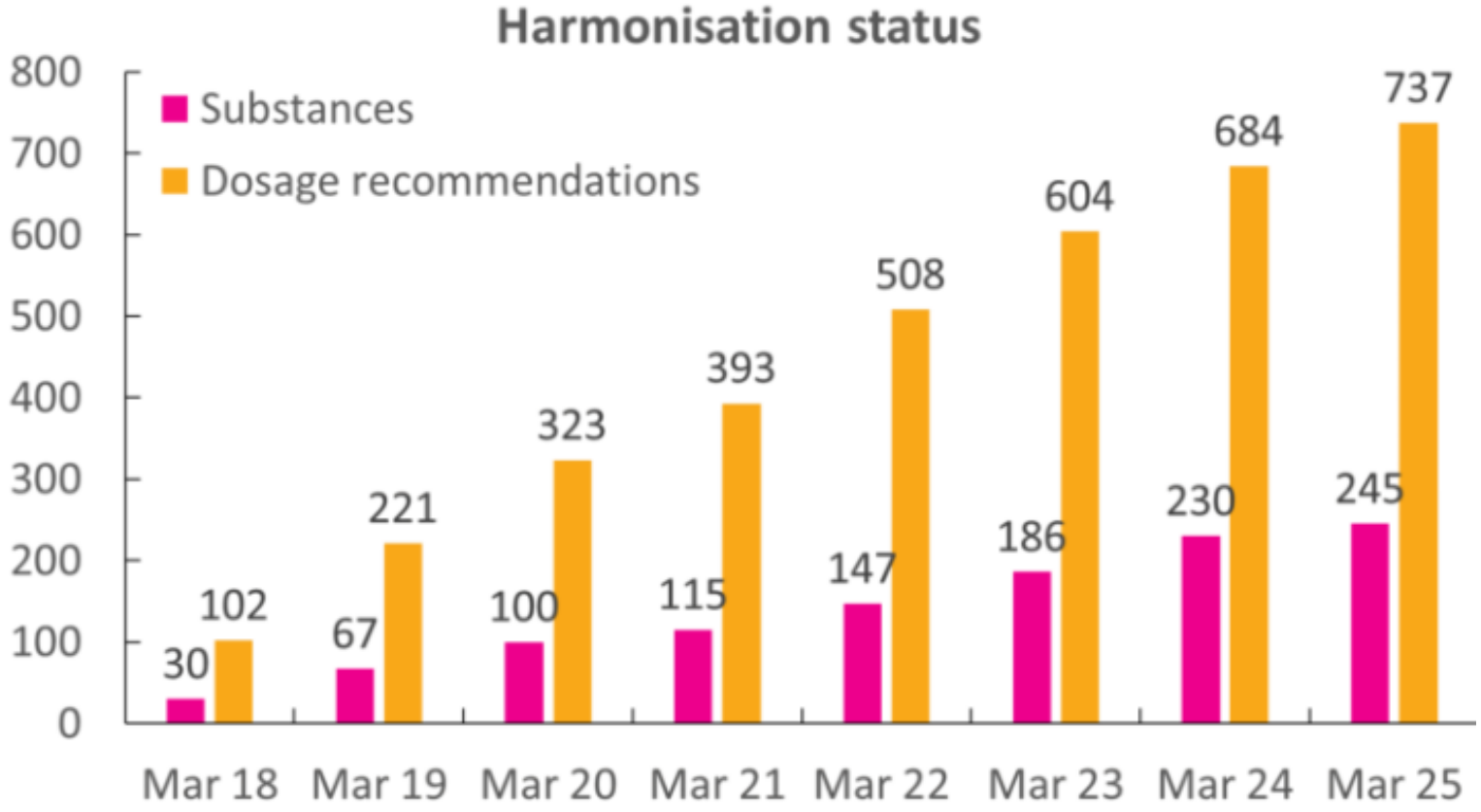
- Licensed in UK (Nurofen)
  infants 3-6 months & >5 kg: 50 mg 3x daily (≈ 5-10 mg/kg/dose)
- BNFc:
  5 mg/kg 3-4x/day (1-2 months),
  50 mg/dose 3x a day, maximum daily dose
  to be given in 3-4x; maximum 30 mg/kg/day (3-5 months)



# Harmonisation process and Harmonisation status

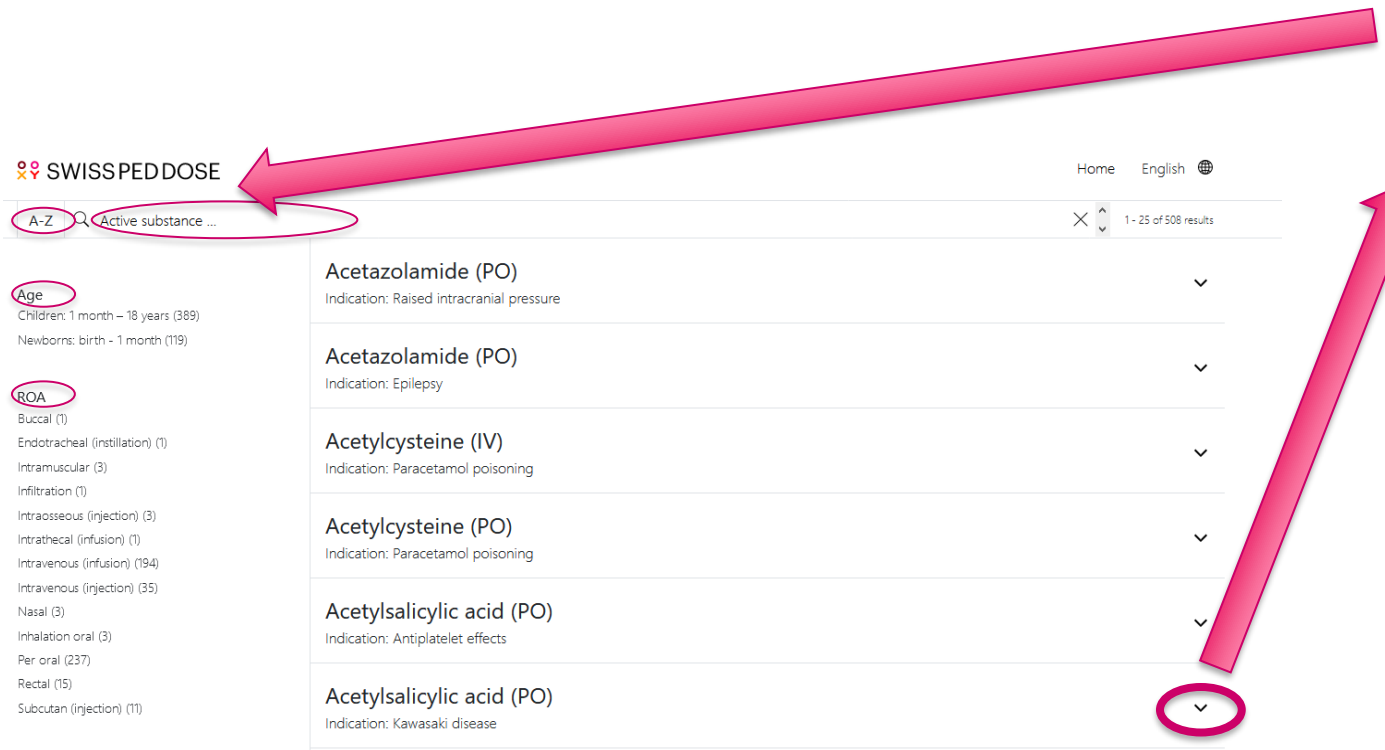
Documented harmonization process based on current scientific literature and expert consensus with regular update cycles

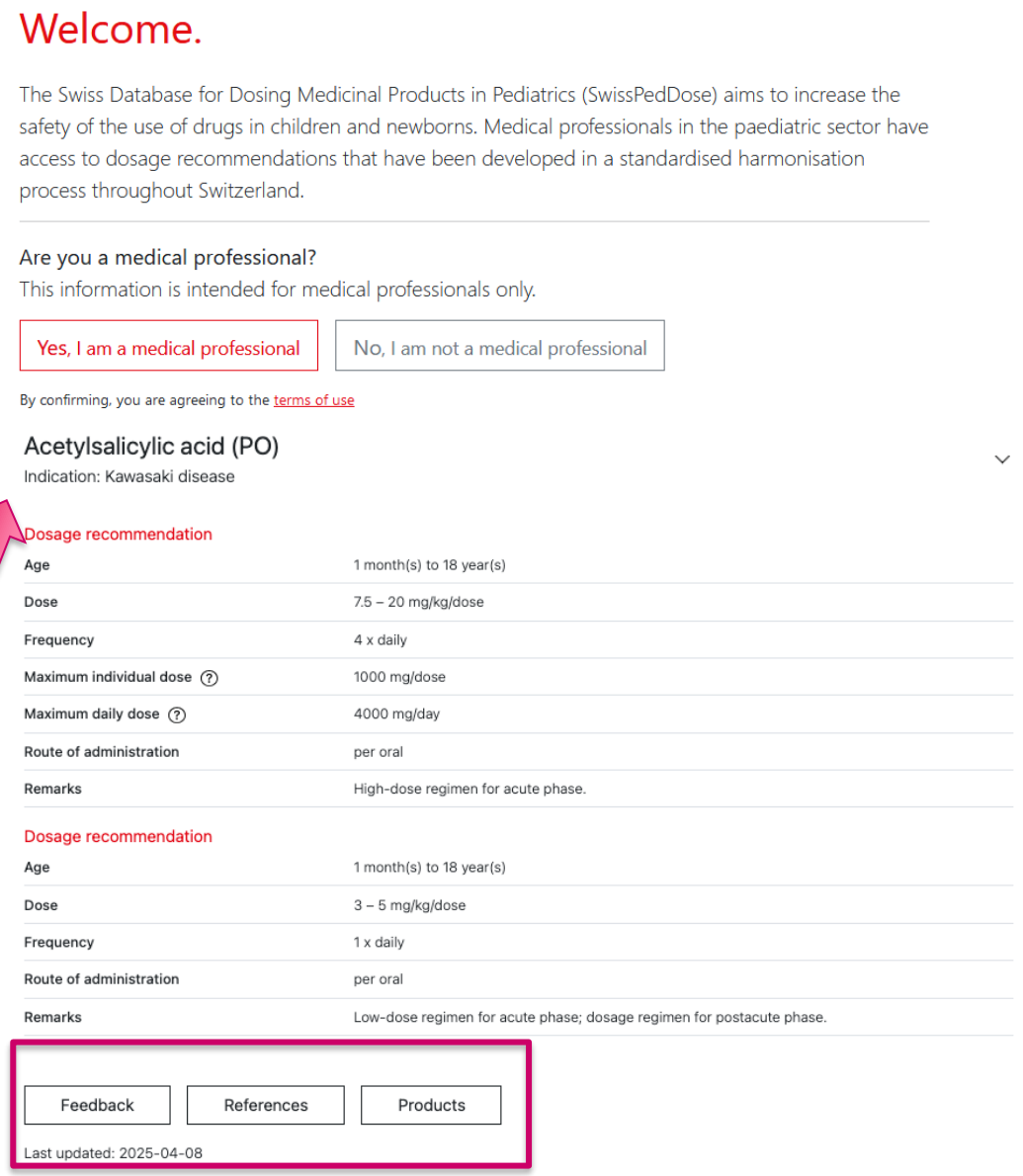


# Database

https://db.swisspeddose.ch/de/



# Access to SwissPedDose dosage recommendations

For institutions: free software integration file (XML) after each update

For all medical professionals (self identification):

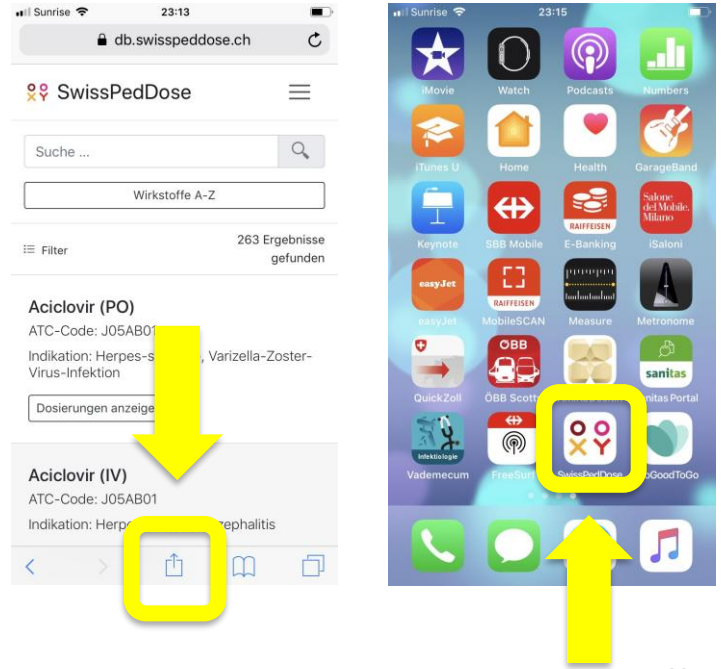
**db.swisspeddose.ch**

**Free availability of dosage recommendations for children for all medical professionals**

- based on evidence,
- independent national expert consensus
- customized to Switzerland

**QR code**

**Favicon for homescreen**



# Access to SwissPedDose dosage recommendations

For institutions: free software integration file (XML) after each update

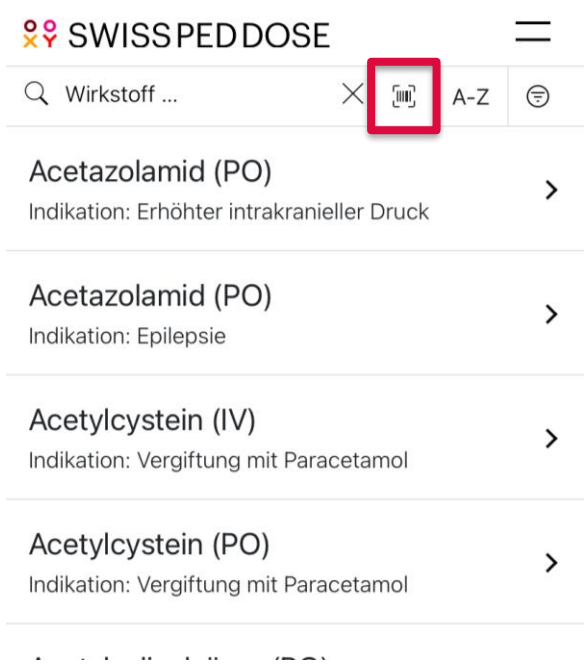
For all medical professionals (self identification):

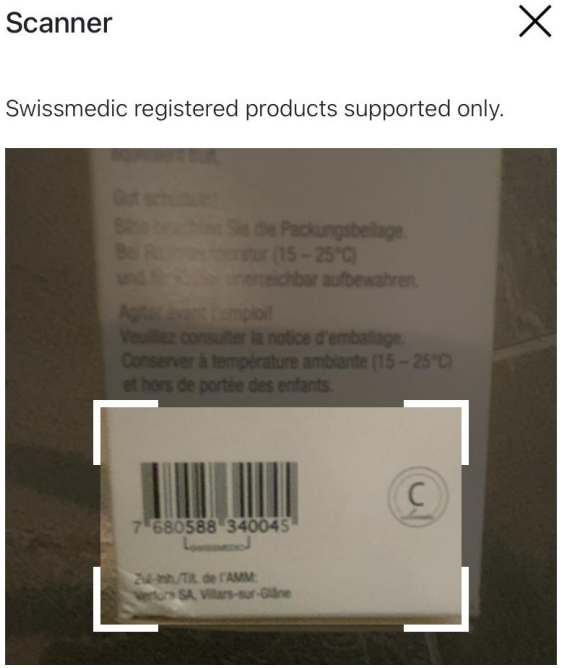
## db.swisspeddose.ch

### Integration in HCI solution (compendium)


### Scanner: db.swisspeddose.ch, mobile version

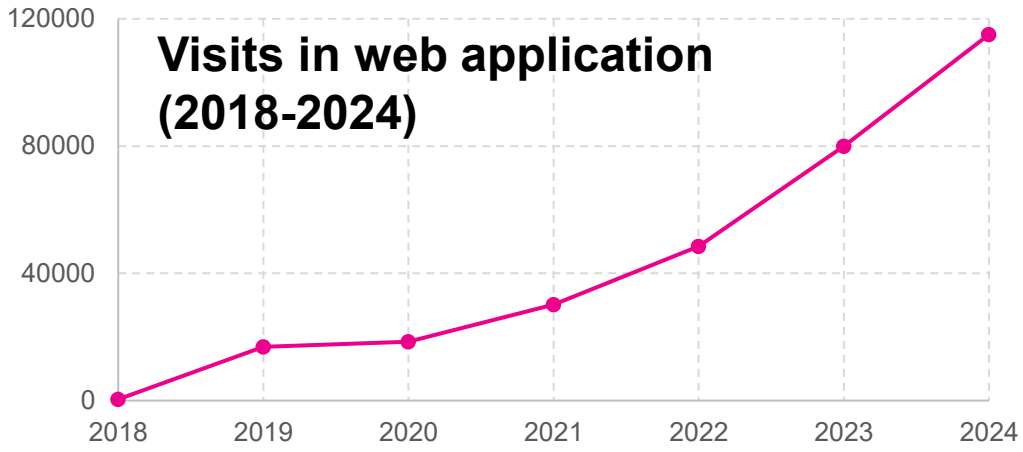
link via Swissmedic authorization number in GTIN



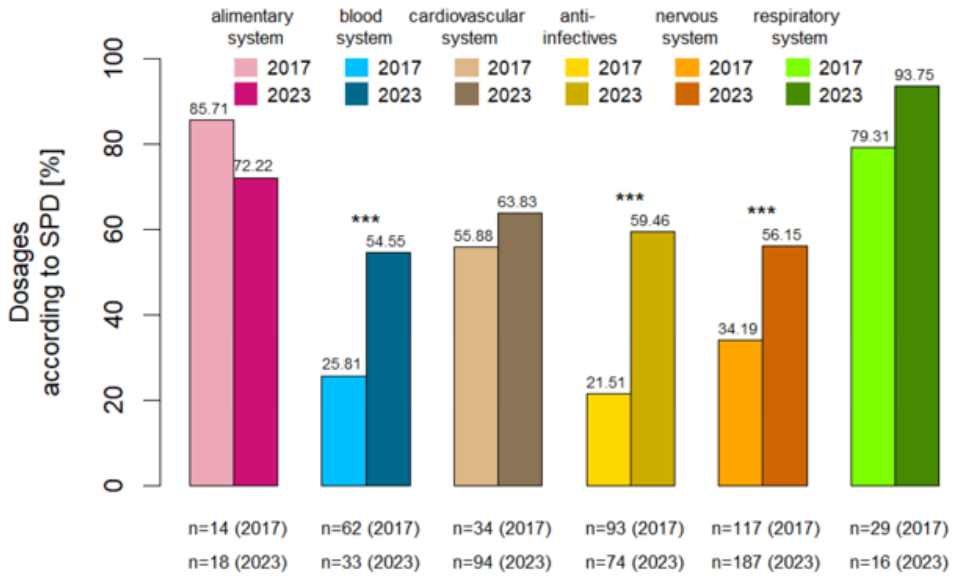
# Swisspeddose dosage recommendations: Implementation and use

**Database visitors via website increase steadily**
From 17’000 (2018) to 115’000 (2024),
this in addition to many hospitals and institutions receiving the regularly updated full xml file.




**Implemented in all 8 Swiss A children clinics**

**Evaluation in hospitals beyond the 8 A-clinics:**
increasing use = implementation of SPD dosage recommendations in every day practice in hospitals:
+ 500 prescriptions 2023 since introduction 2017




**Awareness of Swisspeddose in pharmacies:**
Survey of retail pharmacies (n=107) 2021:

- Do you know Swisspeddose? 79%
- Do you use/check Swisspeddose? 64%

Masterthesis J. Schleiss, 2024

# Swisspeddose: where we are

Swisspeddose is an interprofessional association with essential support by a **college A clinics** in Switzerland and **pädiatrie schweiz** providing drug dosing recommendations for children

**Until end of 2025 financed through FOPH** (since 2018) based on HMG 67a,
Stakeholders action ongoing for future financing, in the mean time:

**Bridging financing for 2026 and 2027 with minimal budget of CHF 80'000/y**
to keep the database up to date and available any time

**Revenue Streams:** it is essential to the purpose that **harmonization by independent experts** is maintained for a **database with dosage recommendations for children accessible** at no cost in Switzerland: minimal operating budget of CHF 200'000/year

Swisspeddose enables that dosage recommendations (**https://db.swisspeddose.ch**/)
- are continuously available to all healthcare professionals also 2026, then in its own database
- are kept up to date and the database is developed at a minimal level

Swisspeddose does everything to continue and is looking for and evaluating funding opportunities

# Efficacy and safety in drug dosing for children

**Children are not small adults → impact on pharmacokinetics**
- absorption, distribution, metabolism, and excretion develops with age

**Drug dosage finding** for children is along age
- to reach and optimize *efficacy* and minimize *toxicity* to be offered in respective *galenic forms*

**Looking beyond the label for prescription guidance**
- in absence of label (lack of studies) and absence of information in SmPCs
- drug prescribers for children need sources for evidence- and expert-based recommendations

**Swisspeddose provides dosage recommendations for children to medical professionals**
- evidence and independent national expert consensus-based
- interprofessional, highly accepted, regularly updated and easily available, *so far*

This is a significant contribution to improve medication safety in children

**Children deserve medicines - and dosages - adapted to their needs**