Thieme

Paediatric Use of Herbal Medicinal Products: New Insights in RWD Generation – A Report on the RWD Workshop 2025 in Naples

Authors
Nico Symma[1], Andreas Hensel[2,5], Bernd Roether[3,5], Barbara Steinhoff[5], Rudolf Bauer[4,5]

Affiliations
1 Pharma Deutschland e. V., Bonn, Germany
2 Institute of Pharmaceutical Biology and Phytochemistry, University of Münster, Germany
3 Bionorica SE, Neumarkt, Germany
4 Institute of Pharmaceutical Sciences – Pharmacognosy, University of Graz, Austria
5 Foundation Plant for Health, Neumarkt, Germany

Keywords
children, phytotherapy, herbal medicinal products, real-world data, usage

received January 5, 2026
accepted after revision March 25, 2026
published online 2026

Bibliography
Planta Med 2026
DOI 10.1055/a-2845-2840
ISSN 0032-0943

Georg Thieme Verlag KG, Oswald-Hesse-Straße 50, 70469 Stuttgart, Germany

Correspondence
Em. Univ.-Prof. Dr. DDr. h. c. Rudolf Bauer
Institute of Pharmaceutical Sciences, University of Graz
Beethovenstraße 8, 8010 Graz, Austria
Phone: + 43 (0) 31 63 80 87 00, Fax: + 43 (0) 31 63 80 98 60
rudolf.bauer@uni-graz.at

ABSTRACT

Herbal medicinal products (HMPs) are widely used in European paediatric practice, but formal authorisations for their use in children remain limited. Following the 2024 workshop in Krakow, the Foundation Plants for Health (FPfH) organised a further workshop in Naples on 31 August 2025 as part of the 73rd International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA) to present updates of recent activities in the field of real-world data (RWD) and real-world evidence (RWE) for rationalising the usage of herbal medicines in children. Speakers presented concrete new data sources – private health insurance claims, patient reported outcome cohorts, and a social-media-based user survey – as well as modern methods in epidemiology. The workshop concluded that decision-relevant paediatric data on the use of HMPs can be generated efficiently by establishing new RWD data sources. For the subsequent next steps, it is necessary to engage with regulators to open usage of these data pools in regulatory practice.

Introduction

Across Europe, HMPs are widely used to treat common childhood conditions such as uncomplicated infections, e.g., the common cold, as well as cough, digestive complaints, or restlessness [1–3]. However, many EU herbal monographs limit the use of HMPs to patients aged 12 or 18 years and older, not because there is evidence of harm in younger children, but because of a lack of systematic paediatric data [2,3]. To find ways to reveal and document the real-world usage of HMPs in children, the Foundation Plants for Health (FPfH) has conducted a long-term project with a series of workshops and discussion groups with experts annually since 2022 [2–4]. In parallel, the FPfH is trying to examine how RWD can be established as a useful tool for documenting paediatric use of HMPs. One important pilot project is based on private health insurance data from Germany and was presented in this year's workshop, coupled with an extensive exchange on how to use epidemiologic methodology and other out-of-the-box approaches. The essential question is whether RWD can help to describe actual use, outcomes, and safety in a way that is practical for researchers and credible for regulators.

Current Status and Regulatory Context

Dr. Nico Symma, Pharma Deutschland e. V., reviewed the work of the foundation with respect to RWD within the past four years, especially pointing out the gap between real-life practice and the scope of application of authorised paediatric medicines. Randomised controlled trials in children are often difficult to conduct for ethical and logistical reasons. Therefore, RWD – drawn from observational studies, registries, pharmacy and dispensing data, and patient-generated information – become increasingly important. This has also been recognised by the European Medicines Agency (EMA), which tries to incorporate RWD into regulatory decision-making by establishing the DARWIN project [5]. Thus, the EMA's Committee on Herbal Medicinal Products (HMPC) also

ABBREVIATIONS

DARWIN	EMA's Data Analysis and Real-World Interrogation Network
EC	European Community
EMA	European Medicines Agency
FDA	Food and Drug Administration U. S.
FPfH	GA Foundation Plants for Health
HMP	Herbal medicinal products
HMPC	Committee on Herbal Medicinal Products
NIS	non-interventional studies
RCT	randomised controlled clinical studies
RWD	Real-world data
RWE	Real-world evidence

started working on this topic in the field of herbal medicinal products by introducing two pilot projects (*Pelargonii radix* and *Cannabis flos*) using the DARWIN infrastructure [6]. Furthermore, the HMPC recently published a draft "Reflection paper on data recommendations for herbal medicinal products and traditional herbal medicinal products used in children and adolescents", trying to provide basic recommendations for the establishment of EU herbal monographs with a paediatric indication by the HMPC [7]. However, the reflection paper grants RWD a supportive but not a central role and gives no concrete guidance on how to apply the new ICH E11A extrapolation framework to herbal products. Therefore, key obstacles persist, i.e., poor visibility of non-prescription medicines in large databases, inconsistent description of HMPs in the literature, and limited integration of HMPs across registries and the European Health Data Space, as well as uncertainty about regulatory acceptance of observational findings. Thus, enabling usage of RWD in HMPs by documenting their use in children is "a marathon, not a sprint".

Claims Data as a Long-View Sentinel

To overcome the above-mentioned challenges, Dr. Christian O. Jacke presented the results of a pilot project initiated by FPfH. The exploratory sentinel analysis of German Private Health Insurance (PHI) claims to assess whether RWD can document paediatric use of herbal antitussives (ATC R05CP01, thyme-containing products). The PHI frame covers ~ 8.7 million insured persons annually (≈ 10.5 % of the German population), with external validity of the study sample ranging from ~ 85 % to ~ 94 % versus the full PHI population in 2015–2023, supporting the robustness of the source frame. The sentinel approach used ATC codes for multiple thyme preparations and applied a resource-oriented data selection that accounts for deductibles and premium refunds influencing claims submission timing [8]. Descriptive analysis assesses utilisation patterns on the substance level by age, sex, and resource utilisation. For children and adolescents (< 18 years), 47 823 packages were identified over four years, with the highest absolute use in the 6- to 11-year band and broadly similar patterns by sex. Conversion from packages to persons yielded 13 628 paediatric users, with a raw administrative treatment prevalence of ~ 1.8 % in 2023 and a small male–female difference (1.9 vs. 1.8). Utilisation declined during the pandemic but has risen steadily since 2021, surpassing pre-pandemic levels by 2023; usage patterns in 0- to 5-year-olds differed slightly from those in older children (6 to 17 years). On average, exposure corresponded to ~ 1 package per person, with prescribed daily-dose-based estimates indicating predominantly short treatment durations. Co-medication was common: on average, ~ 6 additional medications per year, including cough/cold and nasal preparations, with age-related contributions (e.g., vaccines in 0–2 years). The analysis demonstrates that PHI claims can reveal age-, sex-, and time-resolved paediatric utilisation signals for herbal antitussives. However, lack of diagnostic details and outcome data precludes direct conclusions on effectiveness or safety. The study explored the feasibility and worth of the PHI claims data and points to the value of future linkage to diagnoses and clinical outcomes. It must be kept in mind that a bias can occur by using data from PHI, since the population insured by these companies may have a higher social economic status as the average of the population. However, private health insurance and many statutory health insurances reimburse the costs of herbal medicines prescribed for children by a doctor, which means that data are available that enable RWE generation.

Patient-Reported Outcomes for Acute Rhinosinusitis

Prof. Christian Apfelbacher, Institute of Social Medicine and Health Systems Research, Otto von Guericke University Magdeburg, introduced a health-services research program using virtual RWD to document routine management of acute rhinosinusitis (ARS), illustrated with the example of Sinupret extract. He first outlined the feasibility study ("SinAR"), which used online recruitment and a one-time questionnaire in adults and adolescents ≥ 16 years to capture demographics, disease history, over-the-counter medication use, and three patient-reported outcome measures (PROMs): the Major Symptom Score (MSSPAT), a numerical rating scale (NRS) for the overall bothersomeness of symptoms, and the Sino-Nasal Outcome Test-20 German Adapted Version (SNOT-20 GAV) for health-related quality of life. Completion rates were high (93.7 %, N = 2032 included participants), and the construct validity of PROMs was supported by plausible correlations among PROMs. Building on this, the ongoing virtual, prospective cohort ("SinARv") in Germany targets ≥ 5000 participants aged ≥ 12 years with daily self-documentation over 14 days. By 29 April 2025, the analysis set comprised 4992 participants (mean age 41.9 years; 70.8 % female; 21.5 % smokers). Baseline MSSPAT and SNOT-20 GAV were moderately correlated (Pearson r = 0.68). Over follow-up, symptom burden decreased while quality of life improved, with no evidence of sex-specific differences; smokers showed slightly higher symptom burden and lower quality of life throughout. Baseline PROMs resembled values reported in randomised trials of BNO 1016, suggesting that trial populations are broadly representative of real-world users. The work demonstrates that virtual cohorts can rapidly generate scalable, patient-centred RWD on ARS, and that the approach is adaptable to ado-

lescents and, with age-appropriate instruments and consent, to younger paediatric populations.

Causal Thinking for Observational Evidence

Dr. Fernando Urrutia-González, Dr. Willmar Schwabe, set out how modern causal-inference methods can raise the credibility of observational real-world evidence (RWE) for HMPs to a standard closer to randomised trials. Positioning description, prediction, and causality as distinct "tasks of data science", he argued that gaps between RWE and RCT findings often reflect design and analytic weaknesses and that "different methods–not different questions or data" can reconcile them. He then outlined a practical toolkit centred on target-trial emulation–specifying eligibility, treatment assignment, follow-up, and outcomes up front–together with explicit causal diagrams. Three pitfalls received particular focus: immortal time bias from misaligned cohort entry and exposure assignment; misuse of directed acyclic graphs, including inappropriate adjustment for mediators; and collider stratification, which can create spurious associations. Key take-aways were to align eligibility/assignment to avoid immortal time, to select minimally sufficient adjustment sets, and to avoid conditioning on colliders. He noted growing regulatory acceptance of these methods in guidance, concluding that HMP studies adopting disciplined emulation and transparent directed acyclic-graphs-guided adjustment are far more likely to be the basis of paediatric regulatory decisions.

Extrapolation and User Surveys

Dr. Olaf Kelber, Bayer Consumer Health and former member of the E11A Expert Working Group of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), outlined how the ICH E11A guideline on paediatric extrapolation [9] can be applied to herbal medicinal products by integrating all available evidence on disease similarity, pharmacology, dose–response, and safety to justify age extensions. Using a didactic case ("Drug X" for irritated throat), he showed that when adult and paediatric disease courses are sufficiently alike, ADME (adsorption, distribution, metabolism, excretion) is comparable, the therapeutic window is wide, and adverse reactions are rare and similar across ages, efficacy and safety in younger children can be inferred with limited additional data. He mentioned a pragmatic, age-staggered pathway [10] and conditional approval for adolescents supported by existing evidence, followed by iterative non-interventional studies to confirm safety and use patterns and to successively extend to younger age groups (e.g., 12–18 → 6–12 → ≥ 3 years). The approach of the ICH E11A guideline is based on structured knowledge-gap assessment and can be based also on RWD in children, e.g., by initiatives such as PhytoVIS, to strengthen the extrapolation concept and address remaining uncertainties [1]. Dr. Kelber concluded that paediatric extrapolation is feasible for herbal medicinal products and can help to reduce unnecessary clinical trials in children, but success depends on evidence integration also including fit-for-purpose RWD.

Discussion and Outlook

The final discussion returned to practical needs. First, herbal products must be included, identifiable, and precisely described in electronic data [11]. This requires consistent use of product-level identifiers in pharmacy systems, claims databases, registries, and electronic records so that usage of HMPs in children can be tracked. Second, multi-source study designs are likely to be the most informative. Claims and dispensing data can establish patterns of use, while patient-reported outcomes and clinical registries can provide effectiveness or clinical context and safety information. Third, dialogue with regulators is essential and must be intensified, individually for every single study and generally to further drive this concept forward. Participants agreed that these steps can help generate age-stratified evidence for HMPs without relying exclusively on randomised trials that are often hardly possible to conduct in children.

Conclusions and Outlook

The Naples 2025 workshop underscored both the urgency and the feasibility of building paediatric real-world evidence for herbal medicinal products. Insurance claims, patient-reported outcomes, and structured user surveys can document how these medicines are actually used by children and adolescents and can inform on dosing and safety. If accompanied by clear product identification and differentiation, careful causal design, and application of ICH E11A for extrapolation, such evidence can support more appropriate age- and especially children-specific recommendations in regulatory and clinical practice.

List of Speakers of the Workshop

- Prof. Dr. Christian Apfelbacher, Institute of Social Medicine and Health Systems Research, Otto von Guericke University Magdeburg, Germany
- Dr. Christian O. Jacke, Scientific Institute of Private Health Insurance (WIP), Germany
- Dr. Olaf Kelber, Steigerwald Arzneimittelwerk GmbH, Bayer Consumer Health, Germany
- Dr. Nico Symma, Pharma Deutschland e. V., Germany
- Dr. Fernando Urrutia-González, Dr. Willmar Schwabe GmbH & Co. KG, Germany

Acknowledgements

The authors are grateful to the contributors of the workshop entitled "Real-world data to document the use of herbal medicinal products in children: An update", held on 31 August 2025 in Naples, Italy.

Conflict of Interest

Rudolf Bauer and Andreas Hensel are professors for pharmacognosy at independent universities. Bernd Roether is working for a pharmaceutical company producing and selling herbal medicinal products. Nico Symma is working for Pharma Deutschland, a German pharmaceutical industry association.

References

[1] Nieber K, Raskopf E, Möller J, Kelber O, Fürst R, Shah-Hosseini K, Singh J, Kraft K, Mösgens R. Pharmaco-epidemiological research on herbal medicinal products in the paediatric population: data from the PhytoVIS study. Eur J Pediatr 2020; 179: 507–512. DOI: 10.1007/s00431-019–03532-3

[2] Symma N, Hensel A, Roether B, Steinhoff B, Bauer R. Real world data to document the use of herbal medicinal products in children – Report of a workshop in Krakow. Planta Med 2025; 91: 167–172. DOI: 10.1055/a-2523–3856

[3] Hensel A, Bauer R, Heinrich M, Hempel G, Kelber O, Kraft K, Lehmann B, Medà MM, Nieber K, Roether B, Rollinger JM, Wiebelitz R. Rationalising optimal dosing of phytotherapeutics for use in children: Current status – potential solutions – actions needed. Planta Med 2024; 90: 416–425. DOI: 10.1055/a-2294–5259

[4] Hensel A, Bauer R, Heinrich M, Kraft K. Consensus statement on the outcome of a workshop on paediatric phytotherapy: Rationalizing optimal dosing for use in children by real world data. Planta Med 2023; 89: 1442–1443

[5] Arlett P, Kjaer J, Broich K, Cooke E. Real-world evidence in EU medicines regulation: Enabling use and establishing value. Clin Pharmacol Ther 2022; 111: 21–23. DOI: 10.1002/cpt.2479.

[6] Vojinovic D, Hunt N. DARWIN EU® – Drug utilisation study on medicinal use of Pelargonii radix; D2.2.3 – Study Protocol for P3-C1-002; version V3.1; Darwin EU coordination centre. 2024. Accessed January 5, 2026 at: https://catalogues.ema.europa.eu/node/4051/administrative-details

[7] European Medicines Agency, Committee on Herbal Medicinal Products (HMPC). Draft reflection paper on data recommendations for herbal medicinal products and traditional herbal medicinal products used in children and adolescents. Amsterdam: EMA; 2025. Accessed January 5, 2026 at: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-reflection-paper-data-recommendations-herbal-medicinal-products-traditional-herbal-medicinal-products-used-children-adolescents_en.pdf

[8] Gothe H, Achstetter K, Begerow T, Goldhahn L, Hengel P, Jacke C, Köppen J, Kortmann M, Ramm P, Schaarschmidt J, Stallmann C. Versichertenbezogene ambulante Rechnungsdaten der privaten Krankenversicherung – Teil 1: Grundlagen und Voraussetzungen für die wissenschaftliche Nutzung. Gesundheitswesen 2025; 87: S208–S225. DOI: 10.1055/a-2637–3098

[9] International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). ICH guideline E11A on pediatric extrapolation. 2024 Aug 27. Accessed January 5, 2026 at: https://www.ema.europa.eu/en/ich-guideline-e11a-pediatric-extrapolation-scientific-guideline

[10] Kraft K. Position statement evidence generation in the paediatric population-Extrapolation. Phytomedicine 2017; 36: 126–127. DOI: 10.1016/j.phymed.2017.09.003

[11] Hölzle SS, Reineke T, Hoch S, Roether B, Francis M, Anquez-Traxler C, Symma N. Basic requirements and framework conditions of Real-World Data (RWD) on herbal medicinal products. Planta Med 2024; 90: 1056–1058. DOI: 10.1055/a-2409–3125