5. Anderson BJ, Allegaert K, Van Den Anker JN, Cossey V, Holford NHG. (2006). Vancomycin pharmacokinetics in preterm neonates and the prediction of adult clearance. *Br J Clin Pharmacol*; **63**(1):75–84.
6. Germovsek E, Osborne L, Gunaratnam F, Lounis SA, Busquets FB, Sinha AK. (2019). Development and external evaluation of a population pharmacokinetic model for continuous and intermittent administration of vancomycin in neonates and infants using prospectively collected data. *J Antimicrob Chemother*, 1–9.

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P100

A PRACTICAL FRAMEWORK FOR THE ASSESSMENT OF RISKS AND BENEFITS OF OFF-LABEL PRESCRIBING IN PAEDIATRICS (ARBOP-P)

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Background Guidelines for off-label prescribing are emerging.^{1–6} However, these guidelines do not provide practical guidance to assess the risk benefit balance and select the right paediatric dose. We, therefore, aimed to develop a practical framework to guide paediatric healthcare professionals to assess the risks and benefits of off-label use.

Methods We have reviewed available literature on the suggested criteria for appropriate off-label use and evaluated these criteria for relevance in paediatrics. For guidance on dose-selection we searched for regulatory guidance on paediatric drug development. Next, the literature was searched for strategies that can be applied to assess the risks and benefits of off-label use. Based on literature findings a framework was proposed to provide practical guidance to physicians for off-label prescribing. Finally, the framework was applied to a case.

Results The following conditions for appropriate off-label use were identified based on available literature: 1. *Medical need for off-label use*. 2. *Off-label use is based on ‘high quality evidence’*. As ‘high quality evidence’ in paediatrics is often lacking, we propose to replace the need for high quality evidence by a positive risk-benefit assessment based on available evidence. 3. *Parents and patients are informed*. This is not feasible for every single drug prescribed off-label, we propose a graded approach. 4. *The outcomes of off-label use are followed up*.

The PROACT-URL framework⁷ for decision-making as well as the FDA paediatric decision tree⁸ seem helpful tools to guide decisions in real-life practice.

Conclusion We identified important aspects and tools to develop a framework (ARBOP-P) to guide healthcare professionals on how to systematically assess and balance the benefits and risks for off-label use, including dose selection, to ultimately optimize efficacy and safety of paediatric off-label prescribing.

REFERENCES

1. Frattarelli DA, Galinkin JL, Green TP, et al. Off-label use of drugs in children. *Pediatrics* 2014;**133**:563–7 Online.
2. Dooms M, Killick J. Off-label use of medicines: The need for good practice guidelines. *Int J Risk Saf Med*. 2017;**29**:17–23 Online.

3. Gazarian M, Kelly M, McPhee JR, Gaudins LV, Ward RL, Campbell TJ. Off-label use of medicines: consensus recommendations for evaluating appropriateness. *Med J Aust* 2006;**185**:544–8 Online.
4. Largent EA, Miller FG, Pearson SD. Going off-label without venturing off-course: evidence and ethical off-label prescribing. *Arch Intern Med* 2009;**169**:1745–7 Online.
5. Ansani N, Sirio C, Smitherman T, et al. Designing a strategy to promote safe, innovative off-label use of medications. *Am J Med Qual* 2006;**21**:255–61 Online.
6. Weda M, Hoeber J, Vervloet M, et al. Study on the off-label use of medicinal products in the European Union.: www.ec.europa.com 2017.
7. Hammond J, Keeney R, Raiffa H. Smart Choices: A practical guide to making better decisions. Boston, MA.: Harvard Business School Press.; 2002.
8. Dunne J, Rodriguez WJ, Murphy MD, et al. Extrapolation of adult data and other data in pediatric drug-development programs. *Pediatrics*. 2011;**128**:e1242–9 Online.

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P101

EXTENDING THE DUTCH PAEDIATRIC FORMULARY ACROSS EUROPE: SUCCESSFUL DEVELOPMENT OF COUNTRY SPECIFIC, PARALLEL, PAEDIATRIC DRUG FORMULARIES

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Backgrounds As many drugs in paediatrics are used of off-label, prescribers across Europe face a lack of evidence-based dosing guidelines. The Dutch Paediatric Formulary (DPF) was developed to provide dosing guidelines based on best available evidence from registration data, investigator-initiated research, clinical experience and consensus (1). The DPF has recently joined forces with Germany, Norway and Austria aiming to develop multi-language, parallel, paediatric drug formularies based on the DPF.

Methods

The DPF database and ICT framework were extended to a duplicate database for Germany. The dosing guidelines were translated to German and reviewed for fit with German practice. Relevant drugs and dosing recommendations were selected and country-specific information was added to address country-specific needs. Work-sharing on content development was studied in a small pilot.

Results The German Pediatric Formulary (www.kinderformularem.de) was launched on 1 October 2018 within a German paediatric medication safety project (KiDSafe). At that time 119 of 769 drugs were reviewed and published in the German formulary. The dosing recommendations of the DPF show a good fit with German practice; i.e. adaptations were needed in less than 10% of the cases caused by differences in licensing status, national guidelines or availability of formulations. There were no differences in interpretation of evidence. Nine drugs - highly relevant for German practice, but not listed in the DPF, were added to the German formulary based on SmPC. The content