work sharing was piloted by the development of a new monograph and the periodic revision of a monograph complying to the Dutch standard operating procedure by Germany. This pilot has shown the feasibility of work-sharing in developing and updating drug monographs.

**Conclusion** The Dutch framework has successfully been extended to the German situation. Work-sharing on the development of closing recommendations is feasible. Similar extension to Norwegian and Austrian nation-wide formularies has started.

**REFERENCES**


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**Abstracts**

**P102 ALTERNATIVE SPlicing OF THE SLC01B1 TRANSPORTER IN PAEDIATRIC LIVER**

1BD van Groen*, 1C Bl, 1R Gagdik, 1V Stagg, 1D Tiliboel, 1,3SN de Wildt, 1JS Leeder.

1Erasmus MC – Sophia Children’s Hospital, Rotterdam, The Netherlands; 2Children’s Mercy Hospital, Kansas City, MO, USA; 4Radboudumc, Nijmegen, The Netherlands

**Background** Alternative mRNA transcripts occur in >90% of human genes and may be triggered by developmental signals. The hepatic transporter OATP1B1 (gene name SLC01B1) traffics substrates across the hepatic membrane, and shows age-related changes in protein expression. We aimed to predict novel isoforms of OATP1B1 by studying alternative splicing of SLC01B1 in human paediatric post-mortem liver tissue, and the relationship of their mRNA expression with age.

Methods mRNA expression of SLC01B1 transcripts was determined using RNA sequencing (HiSAT2/StringTie). Novel mRNA transcripts were considered of relevance when (1) the expression was >5% of the annotated isoform, (2) it was a SLC01B7 and SLC01B1 hybrid transcript, or (3) when the expression was associated with age. The software packages ORF-finder, TMpred and TOPO2 were used to predict the protein sequence and structure of the novel isoforms. Relationship of expression with age was studied with the Kruskal-Wallis test for age groups (fetal, 0–1.5 year, 1.5–6 year, 6–12 year and 12–18 year) and with Spearman correlation tests for age on continuous scale.

Results In 97 hepatic post-mortem tissues (gestational age median 16.4 [range 14.7–41.3] weeks, postnatal age 0.36 [0-17] years) 27 novel mRNA transcripts were detected. Of these, 13 were relevant: 2 isoforms are predicted to translate into amino acid sequences similar to the annotated isoform for OATP1B1, 9 isoforms may translate into truncated versions, and the expression of 8 isoforms was associated with age. None of the isoforms had an ORF that covered the SLC01B7 region.

Conclusion We showed that novel SLC01B1 mRNA isoforms potentially translate into OATP1B1 protein with unknown function, and that alternative splicing may well be a regulatory mechanism for SLC01B1 expression during development. This data provides a better understanding of age-related changes in the expression of OATP1B1, and, with that, potentially improves prediction of disposition of endogenous and exogenous substrates.

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