




Österreichische Agentur für Gesundheit
und Ernährungssicherheit GmbH


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**Anpassung der Fach- und Gebrauchsinformation von
Kinderarzneimitteln als Ergebnis des „Paediatric
Worksharing Projects“**

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EU-Regulation (EC) No 1901/2006

- *Kinder sind keine Mini-Erwachsenen – eine Dosisreduzierung ist nicht gleichbedeutend mit der proportionalen Reduzierung der Wirkung und Nebenwirkung. Ca. 50% der zur Behandlung von Kindern eingesetzten Arzneimittel sind weder an Kindern geprüft noch für Kinder zugelassen.*
- Ziel: Entwicklung von Arzneimittel für Kinder und Jugendliche im Rahmen einer qualitativ hochwertigen, kontrollierten Forschung
- Optimierung der medizinischen Versorgung der Kinder und Jugendlichen
- Transparenz der Information zu und aus klinischen Prüfungen an Kindern – PIP. Zulassungsstudien für pädiatrische Indikationen, insbesondere der Sicherheitsaspekte und Notwendigkeit der Studien.

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Conditions and challenges



- Worksharing is only possible when submitted data are identical in all MSS; starting position and dossiers can be very different
- No formal procedures in place- decision is national
- No legal framework available – Update of the Var.Reg.
- For communication mailboxes and network needed;
- Coordination of procedures at EU level is needed
- Who has the mandate to discuss any scientific question?

EU Worksharing procedure on paediatric data



Heads of Medicines Agencies (HMA) agreed on a procedure to assess existing paediatric data in a coordinated way by using assessment reports prepared by Rapp and CoRapp.

Aim

- Making information available for Health professionals by publication of PARs and inclusion of information in the SPC
- Harmonised information in EU on use of medicines in children
- No duplication of national assessments, Worksharing

Timing Worksharing



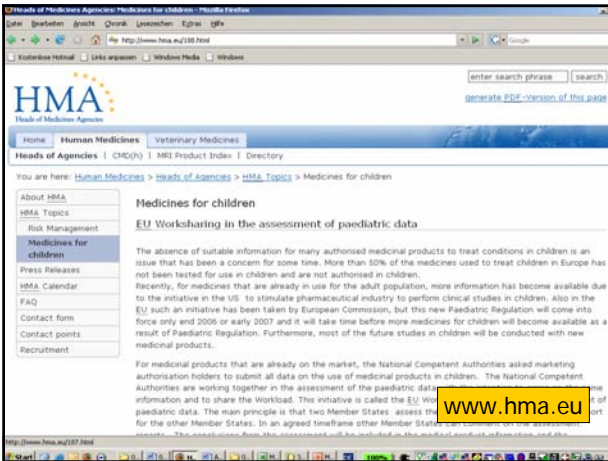
Why starting EU worksharing?

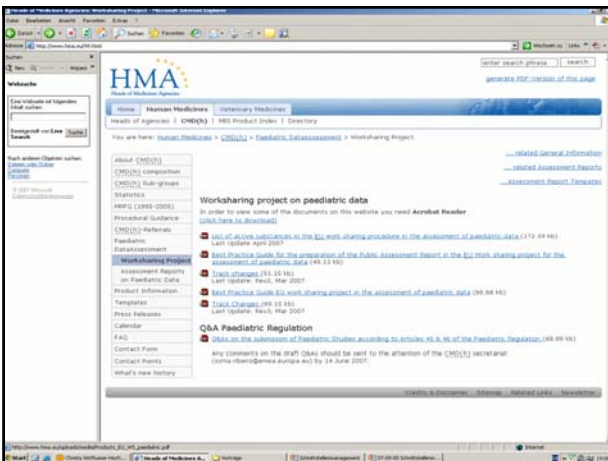
- New Paediatric Regulation focus mainly on new products
- Many medicinal products already on the market are used in children 'off label'
- FDA started Paediatric initiative- many studies in children were not submitted in EU
- Parallel national assessments of these data is duplication of work for agencies and industry and risk of non-harmonised outcomes

Timetable



- Proposal for Worksharing agreed in HMA-hum meeting Iceland 24 February 2005
- Letters to request paediatric data sent out April 2005
- Assessment of first wave started around September 2005
- Lists of products (MRP and nationally approved) selected
 - 1st wave finalised, variations awaited
 - 2nd wave ongoing
- Assessment of the studies submitted by MAH according Art. 45





Rapporteur:	Netherlands
Co-Rapporteur:	Sweden
Paediatric assessment Procedure start date:	21 September 2005
Deadline for (Co)-Rapporteurs's preliminary report (Day 70)	7 December 2005
Clockstop	6 January 2006
Deadline for Rapporteur's final report (Day 90)	7 July 2006
Deadline for member states final comments (Day 115)	10 August 2006
End of procedure (Day 120)	15 August 2006
Date of this Report	10 October 2006

IV. PROPOSED CHANGES IN THE SPC

Paediatric data of Pharmacokinetics Study CA124001 of AUC of carboplatin as measured platinum in plasma ultra filtrate are considered of no clinical value, as inadequate sample processing at the clinical sites may have taken place.

An integrated overview of published reports of paediatric trials where carboplatin was used has been given by the MAH. It shows that carboplatin is used in a range of children malignancies including both CNS and non-CNS solid tumours, but it could not provide an acceptable dosing recommendation for children for carboplatin. The literature shows that there is a large between patient variability in carboplatin AUC.

Rapporteurs consider the Applicant's acknowledgment of lack of data to give a dosing recommendation for children acceptable. The MAH does not seek an indication for the paediatric population.

The Applicant acknowledges the differences in the information included in current SPC regarding paediatric wording across Europe, and would suggest, as already included in the majority of the local SPCs, to include the following information:

4.2. Posology
 Paediatric patients: there is insufficient information to support a dosage recommendation in the paediatric population.

5.1. Pharmacokinetics/Pharmacodynamics
 Paediatric patients: safety and efficacy in children have not been established.

The Rapporteurs endorse the Applicant's recommendation that this wording be implemented across Europe.

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Rapporteurs agree with the MAH that, today, there is no conclusive information on paediatric use of carboplatin and any of these data in the SPC would thus be of limited use to prescribing oncologists. The SPC can only state the insufficiency and limitations of the data. Nevertheless, the variability of carboplatin pharmacokinetics could be mentioned in the SPC section 5.2.

The following text is proposed:

"Carboplatin clearance has been reported to vary by 3- to 4- fold in paediatric patients. As for adult patients, literature data suggest that renal function may contribute to the variation in carboplatin clearance."

Experiences Paediatrics (1)



Positive

- Assessors worked together in procedure, good interaction, only in a few cases no agreement
- Many MSs involved in procedures
- Industry first hesitating, now requests to submit data in context of Worksharing
- Data on paediatric use has become available to authorities and health professionals

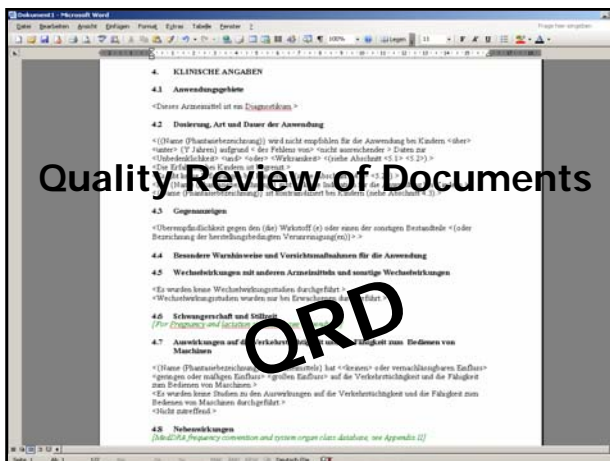
Experiences Paediatrics (2)



Difficulties – room for improvement

- Procedures difficult to follow; long clockstops
- For some nationally approved products difficult to find consensus (major differences in indications)
- End of procedure difficult to monitor (type II variations submitted?)
- Is industry committed to update SPC?
- Not discussed how to update SPC of generic products
- Workload for (co)- rapporteurs, however it is Worksharing
- HMA agreed with proposal, no clear mandate for CMD to coordinate

⇒ Now we have the Paed. Regulation



Quality Review of Documents



Thank you!



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