

Novel approach to characterize developmental changes in pharmacokinetics across the human lifespan: application to the prediction of clearance in children Wang, C.

Citation

Wang, C. (2013, November 7). *Novel approach to characterize developmental changes in pharmacokinetics across the human lifespan: application to the prediction of clearance in children*. Retrieved from https://hdl.handle.net/1887/22108

Version: Corrected Publisher's Version

License: License agreement concerning inclusion of doctoral thesis in the

Institutional Repository of the University of Leiden

Downloaded from: https://hdl.handle.net/1887/22108

Note: To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden

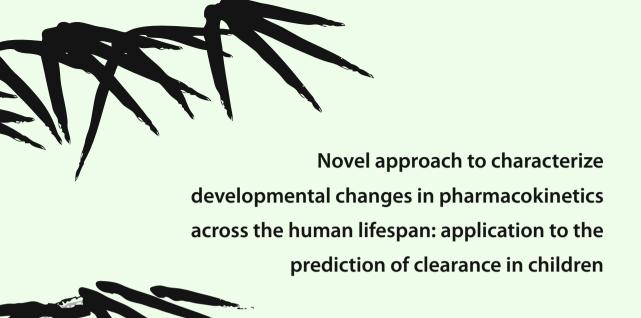


The handle http://hdl.handle.net/1887/22108 holds various files of this Leiden University dissertation.

Author: Wang, Chenguang

Title: Novel approach to characterize developmental changes in pharmacokinetics across the human lifespan: application to the prediction of clearance in children

Issue Date: 2013-11-05



NOVEL APPROACH TO CHARACTERIZE DEVELOPMENTAL CHANGES IN PHARMACOKINETICS ACROSS THE HUMAN LIFESPAN: APPLICATION TO THE PREDICTION OF CLEARANCE IN CHILDREN

Chenguang Wang

The research presented in this thesis was performed within the framework of project D2-104 of the Dutch Top Institute Pharma at the Division of Pharmacology of the Leiden Academic Center for Drug Research (LACDR), Leiden, The Netherlands

Thesis, Leiden University, the Netherlands

ISBN/EAN: 978-90-6464-712-3

 $Layout\ Cover\ and\ Thesis: Ferdinand\ van\ Nispen,\ Citroenvlinder-dtp.nl,$

Bilthoven, The Netherlands

Printed by: GVO | Ponsen & Looijen, Ede, The Netherlands

© Chenguang Wang, 2013, The Netherlands

All rights reserved. No part of this theis may be reproduced, distributed, stored in a retrieval system, or transmitted in any form or by any means, without the written permission of the author and the publisher holding the copyright of the published articles.

NOVEL APPROACH TO CHARACTERIZE DEVELOPMENTAL CHANGES IN PHARMACOKINETICS ACROSS THE HUMAN LIFESPAN: APPLICATION TO THE PREDICTION OF CLEARANCE IN CHILDREN

Proefschrift

ter verkrijging van

de graad van Doctor aan de Universiteit Leiden,

op gezag van Rector Magnificus Prof. Mr. C.J.J.M. Stolker,

volgens besluit van het College voor Promoties

te verdedigen op dinsdag 5 november 2013

klokke 11:15 uur

door

Chenguang Wang

geboren te Beijing, China in 1980

Promotiecommissie:

Promotoren: Prof. dr. C.A.J. Knibbe

Prof. dr. M. Danhof Prof. dr. D. Tibboel

Overige Leden: Prof. dr. P.H. van der Graaf

Prof. dr. J. Burggraaf Prof. dr. H.J. Guchelaar

Prof. dr. R.A.A. Mathôt (Universiteit van Amsterdam)

Contents

Chapter 1	General introduction to a novel approach to characterize developmental changes in pharmacokinetics across the human lifespan: application to the prediction of clearance in children	9
Chapter 2	Scope and intent of the investigations	29
Chapter 3	The allometric exponent for scaling clearance varies with age: a study on seven propofol datasets ranging from preterm neonates to adults	35
Chapter 4	A bodyweight dependent allometric exponent for scaling clearance across the human life-span	61
Chapter 5	Developmental changes in morphine clearance across the entire paediatric age range are best described by a bodyweight-dependent exponent model	93
Chapter 6	Population pharmacokinetics of paracetamol across the human age-range from (pre)term neonates, infants, children to adults	123
Chapter 7	Scaling of clearance across the human life span from neonates to adults: conclusions and perspectives	153
Chapter 8	Schaling van de klaring van geneesmiddelen over de levensduur van een mens van pasgeborenen tot volwassenen: conclusies en perspectieven	171
Appendix I	Body weight-dependent pharmacokinetics of busulfan in pediatric hematopoietic stem cell transplantation patients: towards individualized dosing	181
Appendix II	A novel maturation function for clearance of the CYP3A substrate midazolam from preterm neonates to adults	209

