

University of Groningen

Dry powder inhalation of biopharmaceuticals

Zijlstra, Gerrit

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2009

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Zijlstra, G. (2009). *Dry powder inhalation of biopharmaceuticals: from formulation to proof-of-concept*. s.n.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

**Dry powder inhalation of biopharmaceuticals:
from formulation to proof-of-concept**

Zijlstra, Gerrit Sietse

Dry powder inhalation of biopharmaceuticals: from formulation to proof-of-concept

Dissertation University of Groningen - with summary in Dutch

ISBN (printed version): 978-90-367-4074-6

ISBN (electronic version): 978-90-367-4073-9

Paranimfen

M.W. Stenekes

J.R. Toornvliet

Colofon

The research presented in this thesis was performed within the framework of the Groningen University Institute of Drug Exploration (GUIDE) and generously financially supported by the Dutch Cystic Fibrosis Foundation (NCFS), for the work on cyclosporine A.

Financial support for printing of this thesis was kindly provided by:

University of Groningen

Faculty of mathematics and natural

sciences of the University of

Groningen

Graduate school Groningen University

Institute for Drug Exploration (GUIDE)

Boehringer Ingelheim BV

Chiesi Pharmaceuticals BV

Grünenthal BV

Astellas Pharma BV

Novartis Pharma BV

Astra Zeneca

Schering-Plough

© Copyright 2009, G.S. Zijlstra

All rights are reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, mechanically, by photocopying, recording or otherwise, without the written permission of the author.

Cover & layout design: BiFab

Cover figure: scanning electron micrograph of a spray freeze dried inulin particle

Printed by: Gildeprint Drukkerijen - Enschede

RIJKSUNIVERSITEIT GRONINGEN

**Dry powder inhalation of biopharmaceuticals
from formulation to proof-of-concept**

Proefschrift

ter verkrijging van het doctoraat in de
Wiskunde en Natuurwetenschappen
aan de Rijksuniversiteit Groningen
op gezag van de
Rector Magnificus, dr. F. Zwarts,
in het openbaar te verdedigen op
vrijdag 11 december 2009
om 13.15 uur

door

Gerrit Sietse Zijlstra
geboren op 19 mei 1974
te Bolsward

Promotor:

Prof. dr. H.W. Frijlink

Copromotores:

Dr. A.H. de Boer

Dr. W.L.J. Hinrichs

Beoordelingscommissie:

Prof. dr. W. Jiskoot

Prof. dr. H.A.M. Kerstjens

Prof. dr. C. Vervaet

'Nature has its own religion'
Pearl Jam

Aan Pauline, Roderick en Lennart

CONTENTS

Chapter		Page
1	General Introduction	1
2	The role of particle engineering in relation to formulation and de-agglomeration principle in the development of a dry powder formulation for inhalation of cetrotorelix <i>Eur J Pharm Sci. 2004 Oct;23(2):139-49</i>	49
3	Characterization of a Cyclosporine Solid Dispersion For Inhalation <i>AAPS J. 2007 Jun 15;9(2):E190-9</i>	73
4A	Efficacy of a New Pulmonary Cyclosporine A Powder Formulation for Prevention of Transplant Rejection in Rats <i>J Heart Lung Transplant. 2009 May;28(5):486-92</i>	101
4B	Cyclosporine A Solid Dispersion for Inhalation: Effect of Dose on Pulmonary Reaction in Rats <i>Not published</i>	119
5	Formulation and process development of (recombinant human) deoxyribonuclease I as a powder for inhalation <i>Pharm Dev Technol. 2009 Mar 12; 14(4): 358-68</i>	131
6	Pharmacoeconomic review of recombinant human DNase in the management of cystic fibrosis <i>Expert Rev. Pharmacoeconomics Outcomes Res. 4(1), (2004)</i>	161
7	Dry powder inhalation of hemin to induce heme oxygenase expression in the lung <i>Eur J Pharm Biopharm. 2007 Nov;67(3):667-75</i>	189
8	Concluding remarks and future perspectives	213
9	Summary	221
Appendices		
	CsA klinisch studie protocol	229
	Samenvatting	269
	List of publications	279
	Dankwoord	283
	Curriculum Vitae	289

