



Universiteit
Leiden
The Netherlands

Development and use of biomarkers in clinical development of new therapies for chronic airway disease

Zuiker, Robertus Gerardus Johannes Antonius

Citation

Zuiker, R. G. J. A. (2016, April 6). *Development and use of biomarkers in clinical development of new therapies for chronic airway disease*. Retrieved from <https://hdl.handle.net/1887/38706>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/38706>

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

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/38706> holds various files of this Leiden University dissertation

Author: Zuiker, Rob

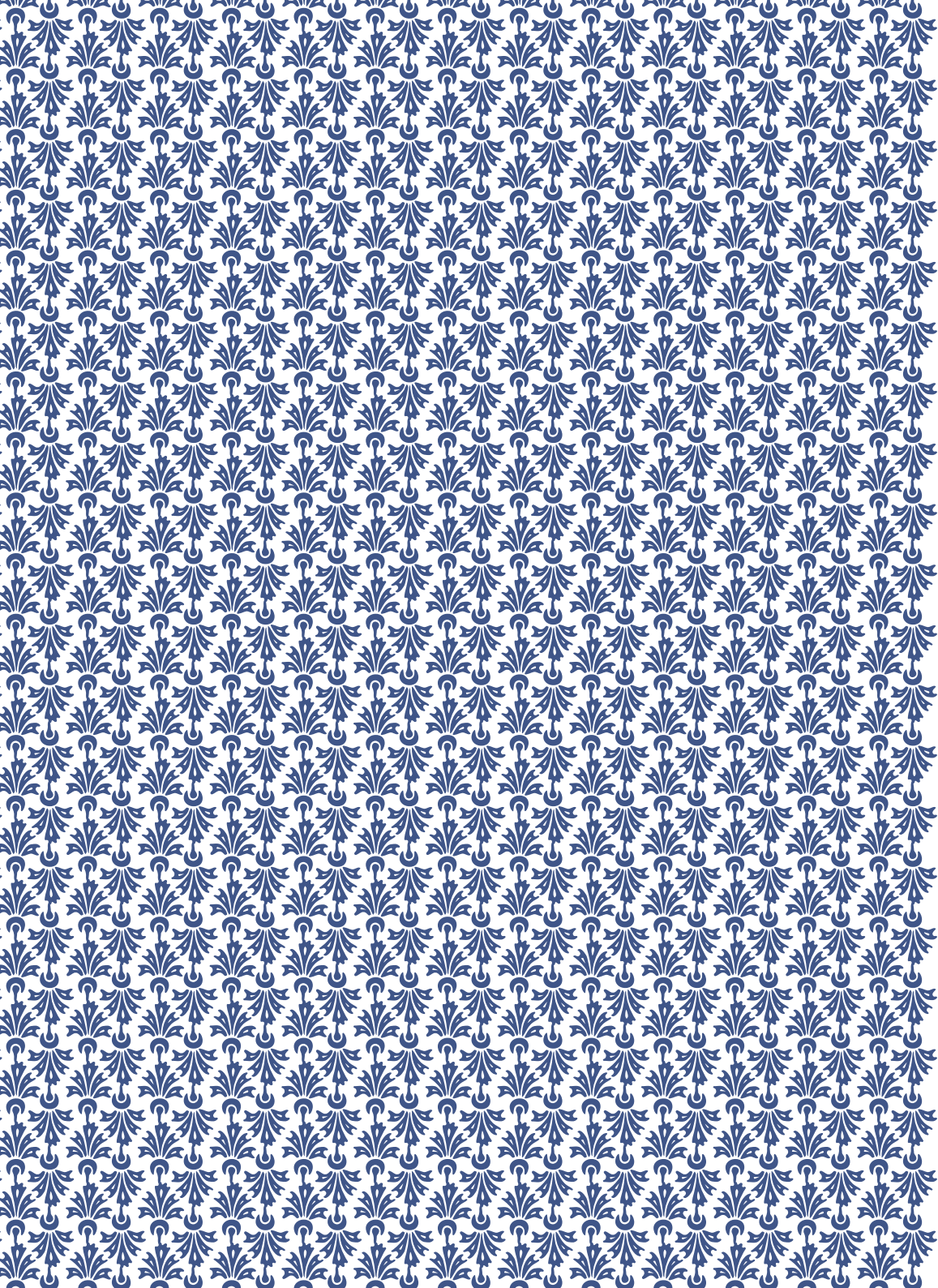
Title: Development and use of biomarkers in clinical development of new therapies for chronic airway disease

Issue Date: 2016-04-06



DEVELOPMENT
AND USE OF
BIOMARKERS
IN CLINICAL
DEVELOPMENT OF
NEW THERAPIES
FOR CHRONIC
AIRWAY DISEASE

ROB ZUIKER



PROMOTORES

Prof. dr. J. Burggraaf
Prof. dr. A.F. Cohen

LEDEN PROMOTIECOMMISSIE

Prof. dr. P.S. Hiemstra
Prof. dr. P.J. Sterk (Universiteit van Amsterdam)
Prof. dr. C. Taube

**DEVELOPMENT AND
USE OF BIOMARKERS IN
CLINICAL DEVELOPMENT
OF NEW THERAPIES FOR
CHRONIC AIRWAY
DISEASE**

DESIGN

Caroline de Lint, Voorburg (caro@delint.nl)

ACKNOWLEDGEMENTS

The publication of this thesis was financially supported by the foundation
Centre for Human Drug Research (CHDR), Leiden, the Netherlands

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 woensdag 6 april 2016 klokke 15.00 uur
door Robertus Gerardus Johannes Antonius Zuiker geboren te Wognum in 1968

	CHAPTER 1
8	Introduction

SECTION I BIOMARKER DEVELOPMENT AND EVALUATION

	CHAPTER 2
26	Kinetics of TH2 biomarkers in sputum of asthmatics following inhaled allergen

	CHAPTER 3
46	Sputum RNA signature in allergic asthmatics

	CHAPTER 4
68	Sputum induction with hypertonic saline reduces fractional exhaled nitric oxide in chronic smokers and non-smokers

	CHAPTER 5
76	Reproducibility of biomarkers in induced sputum and serum from chronic smokers

SECTION II CLINICAL STUDIES WITH A NEW ANTI-ASTHMATIC DRUG

	CHAPTER 6
92	Utilizing an adaptive trial design to assess the effects of the combined phosphodiesterase 3/4 inhibitor RPL554

	CHAPTER 7
112	Repeated dosing of RPL554, a novel inhaled phosphodiesterase 3/4 inhibitor, elicits sustained bronchodilator effects in allergic asthmatics

	CHAPTER 8
126	Discussion, Summary and cv