

DRUG RESEARCH AND DEVELOPMENT
– CASE SCENARIOS, DEVELOPMENT PROCESS, RISKS AND BENEFITS

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The thesis is based upon the following papers:

I. Paciorek PM, Burden DT, Burke YM, Cowlrick IS, Perkins RS, Taylor JC, Waterfall JF. Preclinical pharmacology of Ro 31-6930, a new potassium channel opener. *Journal of Cardiovascular Pharmacology* 1990;15:188-197.

II. Paciorek PM, Cowlrick IS, Perkins RS, Taylor JC, Wilkinson GF, Waterfall JF. Evaluation of the bronchodilator properties of Ro 31-6930, a novel potassium channel opener, in the guinea-pig. *British Journal of Pharmacology* 1990;100:289-294.

III. Kainz A, Harabacz I, Cowlrick IS, Gadgil SD, Hagiwara D. Review of the course and outcome of 100 pregnancies in 84 women treated with tacrolimus. *Transplantation* 2000;70:1718-1721.

IV. Cowlrick I, Delventhal H, Kaipainen K, Krcmar C, Petan J, Schleibner S. Three-year follow-up of malignancies in tacrolimus-treated renal recipients - an analysis of European multicentre studies. *Clinical Transplantation* 2008;22:372-377.

V. Hedner T, Cowlrick I, Wolf R, Olausson M, Klofsten M. The changing structure of the pharmaceutical industry – perceptions on entrepreneurship and openness. In “Entrepreneurship and Technological Change”, Eds. Cassia L, Paleari S, Minola T. Edward-Elgar Publishing, in press 2011.

VI. Cowlrick I, Hedner T, Wolf R, Olausson M, Klofsten M. Decision making in the pharmaceutical industry: Analysis of entrepreneurial risk and attitude using uncertain information, accepted for publication 2011.

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ABSTRACT

BACKGROUND AND AIMS. Drug development has been classically associated with large pharmaceutical companies developing ‘blockbuster’ drugs aimed at large patient populations through high market penetration and multiple indication life cycle management. Higher costs and lower output have rendered this model inefficient and unsustainable. The aims of this thesis were to assess: suitability of test procedures, benefit to risk profile during development, importance of stages of discovery and development for benefit/risk and entrepreneurship, expert judgement in making ‘go/no-go’ decisions, and implications for innovation.

METHODS. Literature review was used to identify why drugs fail and characterise drug regulation history. Examples of drugs in different development stages were critically reviewed for choice of test procedure and assessment of benefit/risk in context with knowledge and scientific expertise today. An 18-step model of drug discovery and development was defined. Using web-based questionnaires, health experts were asked the importance of each step for assessing benefit/risk, and entrepreneurial input. Individual judgement using real drug case scenarios was studied by scoring ‘go/no-go’ decisions on a Likert scale. Relative importance of assessment of risk versus entrepreneurial need was compared on the model. Influence of entrepreneurial characteristics on the expert assessments and on decision making was explored.

RESULTS. Drugs failed development for inefficacy and toxicity. Choice of test procedure confirmed anti-hypertensive and anti-asthmatic efficacy of K⁺ channel openers in the laboratory, but these models were poor predictors of clinical potential. Alternative indications and potential routes of administration were left unexplored. Advances in molecular biology and screening have still failed to yield a product with full clinical potential. Retrospective case studies and prospective multicentre studies for an approved immunosuppressant proved valuable approaches for assessing risk of malignancy and risk during pregnancy. Identifying risk factors helps patients and carers in counselling to reach better outcomes. Health experts perceived toxicology, clinical trials, and pharmacovigilance most important for benefit/risk assessment. In contrast, drug discovery and later phases of development were of entrepreneurial importance. Results modelling revealed in-house entrepreneurial ‘core’ and external outsourcing opportunity. Experts showed marked variability in individual judgment for making ‘go/no-go’ decisions despite having the same information. Expert risk perception and decision making were not consistently influenced by entrepreneurial character. Optimised decision making was identified to be critical for effective drug development.

CONCLUSIONS. These findings reinforce the opinion that restructuring and opening up drug discovery and development to more external input is likely to increase the innovative capacity and efficiency of the whole drug discovery and development process.

KEY WORDS: drug discovery and development, benefit and risk, decision making, entrepreneurship, open innovation

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