FACULTY OF HEALTH AND MEDICAL SCIENCES
UNIVERSITY OF COPENHAGEN

Copenhagen Centre for Regulatory Science

Progress Report
2015-2017

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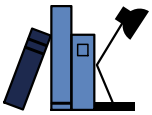

Reflections on 2016-2017

Letter from the Director of the Copenhagen Center for Regulatory Science (CORS)

I would like to start my letter by expressing appreciation to our partners, Steering Committee and Scientific Advisory Board. All of them played an important role in the establishment of the CORS, contributing to the strategic, financial, educational and administrative development of the center.

This report aims to capture the dynamics of the center and provide a clear picture of the CORS' work. CORS is built on full transparency and cooperation with the industry, academia, regulators, and patients. Thus, we would like to provide you with a detailed account of our activities and projects.

These years brought new opportunities regarding research and collaboration and helped us move forward towards our aim of becoming an international leader for research and education in Regulatory Science. It was a great honor for me to be inaugurated as a Professor in Regulatory Science at the University of Copenhagen. Moreover, it was a pleasure to welcome the last two years more than 80 participants to our annual CORS conferences, which featured speakers from relevant stakeholder groups, e.g., regulators, industry, academia, and patients. It is of great importance for CORS to advance the regulatory research and facilitate the dialogue around regulatory decision-making with all the involved stakeholders.

Hence, I would like to reiterate CORS' commitment to organizing new conferences and events in future, where professionals with diverse backgrounds can share their insights regarding regulatory science and its main challenges.

Finally, I would also like to emphasize my gratitude to CORS staff members. They worked with diligence throughout the year and helped fortify the center right from its start.

CORS is open for new cooperation and inputs from the outside world. I am pleased to inform you that CORS is involved at the moment in a couple of international research projects, and you can read more about it in our Research output section. I would like to encourage our readers to look into our materials on the website and follow the latest updates regarding our research and upcoming events.

Sincerely yours,
Marie Louise (Marieke) De Bruin

CORS Profiles

Marieke De Bruin
CORS Director, Professor in Regulatory Science

Marie Louise (Marieke) De Bruin was trained as a pharmacist and epidemiologist and has combined academic research with working for the regulatory authorities. She is an affiliate at the Utrecht University, WHO collaborating centre for pharmaceutical policy and regulation in the Netherlands. Furthermore, she was appointed by the European Commission as an independent scientific expert of the Pharmacovigilance Risk Assessment Committee (PRAC 2012-2018), that meets monthly at the European Medicines Agency in London; she is on the steering group of the European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCePP 2017-2019); and she is associate editor of the journal 'Pharmacoepidemiology & Drug Safety'. Her research focusses on developing new tools, standards and approaches to evaluate the efficacy, safety, quality and performance of medical products in order to assess benefit-risk and facilitate a sound and transparent regulatory decision making.

Christine E. Hallgreen
Assistant Professor

Christine Eriksrup Hallgreen has a background in Engineering Physics, with a PhD in non-linear dynamics of biological systems, from the Technical University of Denmark. During the past 5 years, Christine's research has focused on methodologies to support medical benefit-risk decision making. This includes development and assessment of formal qualitative and quantitative methods to assess benefit-risk of pharmaceutical products, probabilistic methods to assess the effect of uncertainty in outcome data and preference values, and methods to collect preference values to support benefit-risk assessment.

Louise C. Druedahl
PhD Fellow

Louise C. Druedahl (MSc Pharm) focuses on the regulatory landscape of biosimilars in her PhD project. She looks into how different stakeholders interpret biosimilarity and how this further impacts the approval, development, and use of biosimilars. Previous research areas include ADHD medication from young adults' perspectives and the future of the pharmacy profession.

Mathias Møllebæk
PhD fellow

Mathias Møllebæk holds an MA in Rhetoric from the University of Copenhagen and has previously worked as a communication consultant in the health sector. His research focus includes regulatory drug risk communication, public participation in regulatory decision-making and interdisciplinarity of health and social sciences.

Asbjørn Nohr-Nielsen
PhD fellow

Asbjørn Nøhr-Nielsen is a PhD candidate at CORS and the Department of Drug Design and Pharmacology, University of Copenhagen. In his PhD project, he focuses on the conditions for development of fixed-dose combination (FDC) drugs. This includes an assessment of the body of evidence submitted with a Marketing Authorization Applications (MAAs) to obtain approval for authorization of FDCs in the EU, with a specific focus on the number and size of clinical trials, characteristics of FDC, dose selection process including dose ratio, in order to propose strategies to improve the development process of FDC products.

Mikkel Lindskov Sachs
PhD Fellow

Mikkel Lindskov Sachs hold an MA in experimental immunology specialized in T-cell communication. He held temporary and permanent positions at the Danish Medicines Agency from 2010 to 2014 where he, after leading the introduction of computationally driven signal detection to the Agency, assessed and approved clinical trials. In his PhD project, he works with Patient involvement in regulatory decisions with the assessment of rare serious adverse events as a primary focus.

Per Sindahl
Guest researcher

Per Sindahl is a trained pharmacist and hold a BA in Philosophy from the University of Copenhagen. He has a broad and extensive experience within pharmacovigilance including 7 years at the Danish Medicines Agency as a senior assessor. His research focus on evaluation of post-authorisation drug regulation and patient safety.

Natalia Ghincul
Project Coordinator

Natalia Ghincul holds an MA in Journalism, Media, and Globalization from Aarhus University and the University of Amsterdam. She has previously worked in journalism and communication within education and research. At CORS, she provides project support to CORS and its director, also focusing on communication tasks.

Center Activities

2015

May 12
Establishment of CORS

May 6
Workshop: patient involvement in Medicines Development and Approval

November 23
Conference: Mapping the Scientific resources within CORS

2016

November 23
CORS research seminar

November 24
CORS Conference: The Present and Future of Regulatory Science

April 21
Workshop on the future directions in regulatory science

November 23
Inauguration of Marieke De Bruin

2017

April 20
CORS joins Pharmacoepidemiology Research Collaboration (PRC)

March 27
Symposium: Research and education in Regulatory Science

October 2
CORS Conference: Transparency in drug regulatory decision making

CORS Conferences. Numbers.

73 participants	October 2, 2017
89 participants	November 24, 2016
55 participants	November 23, 2015

Research Projects

PhD Projects

- Factors ensuring effective Direct to Healthcare Professional Communication of Risk Mininization

This project aims to identify and understand the factors that determine the effectiveness of drug safety communication such as Direct to Healthcare Professional Communication and educational materials and sets out to present suggestions on how to improve the existing communication process.

Collaboration between the University of Copenhagen departments of Pharmacy (Health and Medical Sciences), Media, Cognition and Communication (Humanities) and Ferring Pharmaceuticals. Funding CORS partner: Ferring Pharmaceuticals.

PhD candidate: Mathias Møllebæk.

- The development of fixed-dose combinations (FDCs) through improved methodology

This project will monitor and explore the conditions for the development of FDC's taking into account the differences in the available data for categories.

Collaboration between the University of Copenhagen departments of Pharmacy; Drug Design and Pharmacology; Public Health (Health and Medical Sciences), and Contera Pharma. Funding CORS partner: Novo Nordisk.

PhD candidate: Asbjørn Nøhr-Nielsen.

- Similar but not identical: the changing regulatory landscape of biosimilars from the regulator, industry, professional, and patient perspectives

The project aims to explore how different stakeholders interpret "similar," and how these views impact the approval, development, and use of biosimilars.

Collaboration between the University of Copenhagen department of Pharmacy (Health and Medical Sciences) and the Centre for Advanced studies in Bio-medical Innovation Law (Faculty of Law). Funding CORS partner: LEO Pharma.

PhD candidate: Louise C. Druedahl.

Collaborative projects

- How best to protect public health: a comparative analysis of regulatory safety warnings on medicines in Australia, Canada the European Union and the United States.

Mintzes B, Roughead E, Lexchin J, Bero L, Dormuth C, Kesselheim A, Lipworth W, De Bruin ML, Gnjidic D, Puil L; National Health and Medical Research Council (NHMRC)/Project Grants.

University of Copenhagen (Copenhagen Centre for Regulatory Science) (DK), University of Sydney, University of South Australia (Aus), University of British Colombia and York University, Toronto (Ca), Harvard School of Public Health (US), King's College London (UK) and Utrecht University (NL).

Coordinator of the project, Dr Barbara Mintzes, University of Sidney

- What works best to protect public health? An international comparison of post-market regulatory risk communication on prescription drugs.

Dormuth CR, Mintzes BJ, Sketris IS, Bero L, Davis C, De Bruin ML, Kesselheim A, Lexchin J, Mangin D, Moore TJ, Puli L, Roughead EE, Wiktorowicz ME; Canadian Institute of Health Research (CIHR). More details about the projet (link).

Coordinator of the project, Colin Dormuth, University of British Columbia

- Characterising the risk of major bleeding in patients with Non-Valvular Atrial Fibrillation: non-interventional study of patients taking Direct Oral Anticoagulants in the EU.

As a subcontractor to Utrecht University (NL), CORS participates through the Pharmacoepidemiology Research Collaboration Copenhagen (co-investigator prof Morten Andersen) in this EMA requested multi-country study (EUPAS 16014)
Other ENCePP centres participating in the project are University of Bordeaux (FR), Ludwig-Maximilians-Universitaet Muenchen (DE), Fundació Institut Català de Farmacologia (ES), Spanish Agency of medicines and medical devices (ES) and Aarhus University (DK).

- Dynamic relations between regulation and development of gene and cell based therapy products.

Coppens DGM, Hoekman J, De Bruin ML, Leufkens HGM; WHO Collaborating Centre for Pharmaceutical Policy and Regulation.
Prof De Bruin is one of the co-supervisors on this PhD project that aims to provide insight into the dynamic relations between regulation and the development of gene and cell based therapy products (GCTs).

- Pharmaceutical regulation in the EU: exploring (dis)connections between science, regulation and clinical practice.

Klein K, Stolk P, De Bruin ML, Leufkens HGM; WHO Collaborating Centre for Pharmaceutical Policy and Regulation

Prof De Bruin is one of the co-supervisors on this PhD project that aims to get a better understanding of the crossroads of science, regulation and clinical practice in innovative and developing pharmaceutical areas, by identifying key drivers for the designing of new regulations, evaluating the impact of regulations in the area of practice and assessing how we can learn from regulatory evaluations in order to improve current and future regulations.

Publications

Vestergaard S, Ravn P, Erikstrup Hallgreen C, Kaae S. Differences and similarities in medicine use, perceptions and sharing among adolescents in two different educational settings. Int J of Adoles Med Health. 2017 Nov 23.
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Rietbergen C, Stefansdottir G, Leufkens HG, Knol MJ, De Bruin ML, Klugkist I. Evidence synthesis in drug safety assessment: the example of rosiglitazone. Front Med. 2017 Nov 28.
doi: 10.3389/fmed.2017.00228 [Epub ahead of print]
Lindskov Sachs M, Kälvemark Sporrong S, Colding-Jørgensen M, Frokjaer S, Helboe P, Jelic K, Kaae S. Risk Perceptions in Diabetic Patients Who Have Experienced Adverse Events: Implications for Patient Involvement in Regulatory Decisions. Pharm Med. 2017 Aug;31(4):245-255.
doi: 10.1007/s40290-017-0200-z.

But A, De Bruin ML, Bazelier MT, Hjellvik V, Andersen M, Auvinen A, Starup-Linde J, Schmidt MK, Furu K, de Vries F, Øystein Karlstad Ø, Ekström N, Haukka J. Cancer risk among insulin users: comparing analogues with human insulin in the CARING five-country cohort study. Diabetologia. 2017 Sep;60(9):1691-1703.
doi:10.1007/s00125-017-4312-5.

Nyeland ME, Laursen MV, Callréus T. Evaluating the effectiveness of risk minimisation measures: the application of a conceptual framework to Danish real-world dabigatran data. Pharmacoepidemiol Drug Saf. 2017 Jun;26(6):607-614.
doi: 10.1002/pds.4203.

Bouvy JC, Blake K, Slattery J, De Bruin ML, Arlett P, Kurz X. Registries in European post-marketing surveillance: a retrospective analysis of centrally approved products, 2005-2013. Pharmacoepidemiol Drug Saf. 2017 Dec;26(12):1442-1450.
doi:10.1002/pds.4196.
Engel P, Almas MF, De Bruin ML, Starzyk K, Blackburn S, Dreyer NA. Lessons learned on the design and the conduct of Post-Authorization Safety Studies: review of 3 years of PRAC oversight. Br J Clin Pharmacol. 2017 Apr;83(4):884-893.
doi: 10.1111/bcp.13165.

Aagaard L, Hallgreen CE, Hansen EH. Serious adverse events reported for antiobesity medicines: postmarketing experiences from the EU adverse event reporting system EudraVigilance. Int J Obes (Lond). 2016 Nov;40(11):1742-1747.
doi: 10.1038/ijo.2016.135.

Borup G, Bach KF, Schmiegelow M, Wallach-Kildemoes H, Bjerrum OJ, Westergaard N. A Paradigm Shift Towards Patient Involvement in Medicines Development and Regulatory Science: Workshop Proceedings and Commentary. Ther Innov Regul Sci. 2016 May;50(3):304-311.
doi: 10.1177/2168479015622668.

Hughes D, Waddingham E, Mt-Isa S, Goginsky A, Chan E, Downey GF, Hallgreen CE, Hockley KS, Juhaeri J, Lieftucht A, Metcalf MA, Noel RA, Phillips LD, Ashby D, Micaleff A; PROTECT Benefit-Risk Group. Recommendations for benefit-risk assessment methodologies and visual representations. Pharmacoepidemiol Drug Saf. 2016 Mar;25(3):251-62.
doi: 10.1002/pds.3958.

Spindler P, Bach KF, Schmiegelow M, Bedlington N, Eichler HG. Innovation of Medical Products: The Evolution of Regulatory Science, Research, and Education. Ther Innov Regul Sci. 2016 Jan;50(1):44-48.
doi: 10.1177/2168479015599810.

Teaching activities

- Teaching courses at the School of Pharmaceutical Sciences
- Supervising MSc projects
- Hosting international master exchange students
- Supervising PhD projects
- Teaching Master of Medicines Regulatory Affairs (MRA)
- Giving lectures at our partner centres and universities

CORS is actively involved in training the next generation of regulatory scientists and specialists. Centre's staff members are teaching courses at the School of Pharmaceutical Sciences and a supervising MSc projects. Since we have strong ties with other regulatory science research groups in Europe, we are also hosting international master students and supervise their master projects. CORS senior researchers are also supervising PhD projects, and the research outlines were mentioned in the Research Project section of our Progress Report.

Through our international collaborative projects, we are often invited to give lectures at our partner's universities. The recent example is that Marieke De Bruin gave the key-note lecture at the inaugural conference of the Regulatory Affairs MSc education at the University of Lisbon.

We are doing our best to create a unique atmosphere at CORS, where both emerging and senior researchers are learning from each other in an intercultural and interdisciplinary environment.

Master of Medicines Regulatory Affairs (MRA)

Additionally, CORS is also involved in the teaching of the courses for the Master of Medicines Regulatory Affairs (MRA). Students at MRA program have an international profile and a diverse background related to regulatory affairs.

MRA course lecturer and coordinator: Christine E. Hallgreen

'Drug Regulatory Science' course presents current perspectives on and innovations in drug regulation in clinical development with focus on four selected topics. It enables students to critically reflect and discuss guidelines, regulations and legislation within clinical development of medicine. Hereby giving the students tools to nuance their current knowledge on guidelines and regulations and work strategically with the regulatory processes.

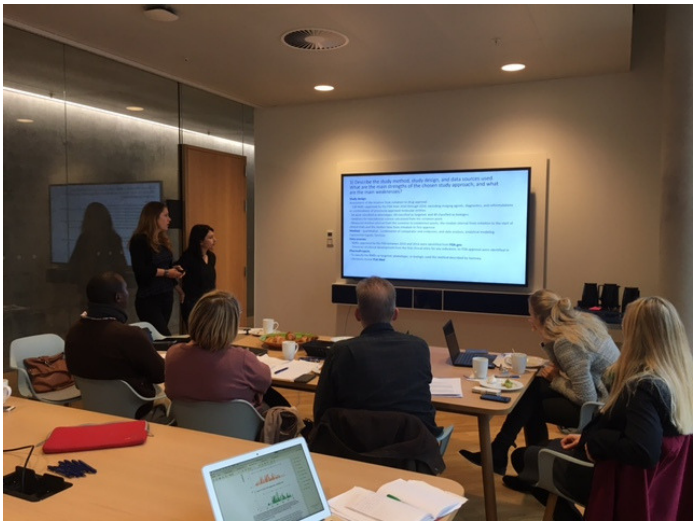
Feedback on MRA course from the students in 2017:

"The course helped us better understand how regulatory science can impact regulatory processes. We were not aware of some of the publications, which were quite relevant to us. It helped us rethink the evaluation of regulatory tools and better understand the gaps of these tools".

Araksya Topchyan (MRA student)

"I am looking forward to using the information I got during the course for my dissertation. It was a good balance of academic perspectives and industrial case studies".

Moses Kasigazi (MRA student)



MRA students during the group presentations

Assistant attorney-at-law Lise Aagaard (Phd Cand.jur, Bech-Bruun) teaching at the course

Assistant Professor Jarno Hoekman (Innovation Studies Copernicus Institute of Sustainable Development, University of Utrecht) teaching at the course