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ORBIS (Open Research Biopharmaceutical Internships Support) – building bridges between academia and pharmaceutical industry to improve drug development

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Open Research Biopharmaceutical Internships Support (ORBIS) is an international, Horizon 2020 project funded by Maria Skłodowska-Curie Actions, Research and Innovation Staff Exchange (RISE) programme. Six academic institutions and four pharmaceutical companies from seven countries cooperate with the aim to improve the preclinical pathway of medicine development through increased Research and Development (R&D) productivity, especially focusing on processes and technologies which address the challenge of poor drug bioavailability. The RISE scheme supports secondments, meaning that early stage and experienced researchers are sent to consortium partner institutions to advance studies on pharmaceutical preformulation, dosage forms and drug delivery systems and methods of biopharmaceutical evaluation. The ORBIS project enables secondees to gain news skills and develop their competences in an international and intersectoral environment, strengthening the human capital and knowledge synergy in the European pharmaceutical R&D sector.

Introduction

ORBIS (**O**pen **R**esearch **B**iopharmaceutical **I**nternships **S**upport, grant agreement no. 778051) is an international and intersectoral project awarded €2,268,000 by the European Commission under the

Research and Innovation Staff Exchange (RISE) call of Marie Skłodowska-Curie Actions (MSCA), Horizon 2020 programme (H2020-MSCA-RISE-2017). This four-year project was launched on 1st March 2018.

ORBIS (Figure 1) is one of the largest projects and consortia of the RISE programme, comprising 10 beneficiaries and partners; these include six academic institutions and four pharmaceutical companies located in seven countries (Figure 2). This project will enable over 200 researchers to advance their research and other skills through secondment placements. Poznan University of Medical Sciences (PUMS, Poland) is the project coordinator and the grant is managed by the project chair, Professor Janina Lulek, Head of the Chair and Department of Pharmaceutical Technology at PUMS.

Figure 1. *ORBIS official logo*

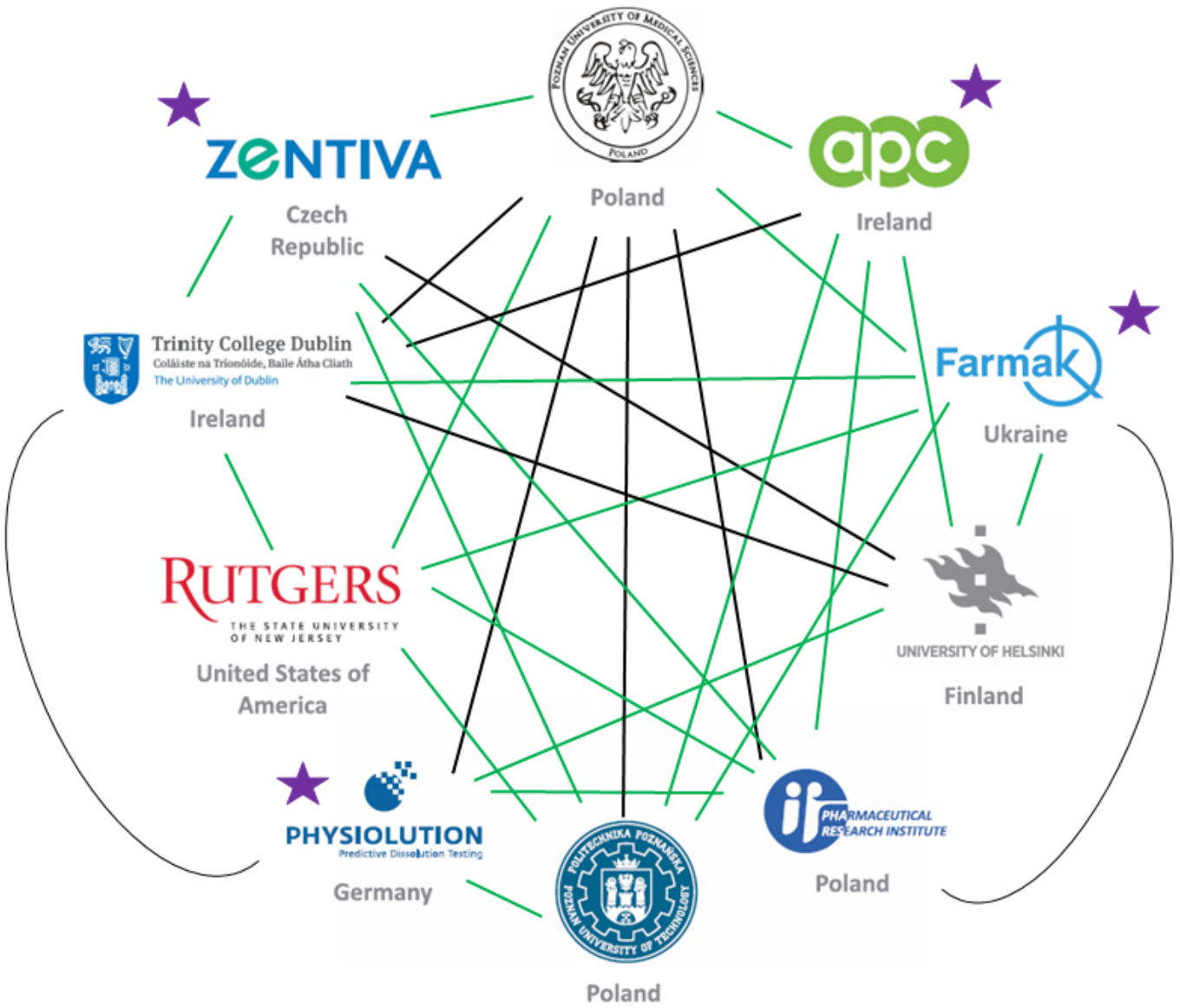

Figure 2. *ORBIS network. Pre-ORBIS collaboration (black lines) and new ORBIS collaboration (green lines). Industry partners are marked with a star*

Research Project Objectives

The current process of drug development is lengthy and inefficient. When developing a new chemical entity only one out of approximately 10,000 molecules enters the market as a drug. The situation is no better for generic or value-added medicinal products, where the active pharmaceutical ingredient (API) is already well-known: commencing from the first laboratory trials, it takes a minimum of four years of intensive activities for the simplest generic drug product to reach the market. The societal demand for more effective medicines has created a challenge of supply within the pharmaceutical industry. To address this gap, ORBIS proposes that the time for the medicinal product to reach the patients might be reduced by improving early stage R&D productivity. The overarching objective of ORBIS is to form an international and intersectoral academic and industrial network to address this challenge (Table 1). This consortium was built on pre-existing collaboration that has expanded into the current ORBIS group (Figure 2). The project aims to improve the preclinical pathway of medicine development, concentrating on processes and technologies to address poor drug bioavailability.

Institution name and acronym	Location	Project role / short description
Poznan University of Medical Sciences (PUMS)	Poznan, Poland	Project beneficiary and coordinator. Apart from the project management and organization, several departments of Faculty of Pharmacy are engaged in sending and hosting secondees. PUMS expertise includes: pharmaceutical preformulation, drug design and delivery, physical chemistry, pharmaceutical and biopharmaceutical analysis, pharmacokinetics.
APC Ltd. (APC)	Dublin, Ireland	Project beneficiary. APC specializes in integrating innovative process performance across a medicine's life cycle, from early Phase development to manufacturing support. APC's research platforms and associated information deliverables help the global bio/pharma sector accelerate the development and launch of their medicines.
JSC Farmak (FMK)	Kyiv, Ukraine	Project beneficiary. FMK is the leading Ukrainian developer of generic and innovative dosage forms. Small, pilot and large-scale manufacturing facilities.
Łukasiewicz Research Network - Pharmaceutical Research Institute (PRI)	Warsaw, Poland	Project beneficiary. PRI develops API manufacturing technologies, translating academic research into practical solutions for industry. Expertise covers laboratory scale synthesis and scale-up, development of formulations, analytics and pharmacokinetic studies. API manufacturing facilities .
Physiolution GmbH (PHY)	Greifswald, Germany	Project beneficiary. PHY develops biorelevant test methods for assessing in vitro biopharmaceutical properties of the drug substances and drug products.
Poznan University of Technology (PUT)	Poznan, Poland	Project beneficiary. Researchers of the Institute of Chemical Technology and Engineering, Faculty of Chemical Technology, provide knowledge in areas of inorganic and organic chemical technology, chemical engineering, polymer technology, chemical analysis and biotechnology.
University of Helsinki (UH)	Helsinki, Finland	Project beneficiary. The Formulation and Industrial Pharmacy unit of the Division of Pharmaceutical Chemistry and Technology focuses on the translation of a drug molecule into a medicine. Expertise is offered in novel spectroscopic techniques and manufacturing technologies of oral solid dosage forms.
Trinity College Dublin (TCD)	Dublin, Ireland	Project beneficiary. Trinity Pharmacy & Pharmacology is joint 45 in the world by subject (Pharmacy and Pharmacology) and the School of Pharmacy and Pharmaceutical Sciences is the leading Pharmacy educator in Ireland. The expertise includes pharmaceutical preformulation, engineering of solid-state materials and advanced oral and pulmonary formulations.
Zentiva (ZNT)	Prague, Czech Republic	Project beneficiary. ZNT is an international pharmaceutical company that develops, manufactures and

		distributes generic and value-added medicinal drug products for oral and parenteral drug delivery.
Rutgers, the State University of New Jersey (RUTG)	New Jersey, USA	Project partner. RUTG is a member of the “Big 10” top universities in the U.S. with 70,000 undergraduates & graduates &over $750.8 million in research monies. The School of Pharmacy is in the top ten pharmacy schools in the US. Center for Dermal Research founded in 2011 is the only academic Center in NJ dedicated to pharmaceutical skin research.

Table 1. *Institutions participating in ORBIS project*

The close research cooperation between the project partners, as well as knowledge synergy and transfer between the academic and industrial sectors, has created a stimulating environment for employees and PhD students to advance their individual career and transferrable skills during research visits (ORBIS secondments) and those interactions are the core enablers of the consortium objectives (Table 2).

To improve the process development of drug substances by innovating synthesis and evaluation of active materials and their physical forms.	To enable hands-on and relevant industrial training of early stage researchers including a range of “soft skills”.
To advance pharmaceutical preformulation studies by developing new industry-relevant methods of evaluation of drug substances physical forms in the biopharmaceutical context.	To foster “communal” academia-industry open collaboration.
To formulate advanced drug delivery systems and optimize manufacturing of oral dosage forms.	To support industry-academia research leading to joint publications, presentations and enabling staff transfer between these two sectors.
To better understand drug transport across the skin and develop topical and transdermal delivery systems.	
To innovate the biopharmaceutical evaluation of dosage forms and drug delivery systems by improving the testing approaches and methods of bioanalysis.	

Table 2. *ORBIS project objectives*

Research Plan and Basic Concept

The core and vehicle for accomplishing the ORBIS project objectives are secondments, i.e. 1- to 12-month long research and training visits of early stage and experienced researchers at partner institutions. PhD students and employees from the European universities can travel abroad to pharmaceutical companies and Rutgers University, while staff from the industrial members visit foreign academic partners, meaning that all secondments must be international and mostly intersectoral.

ORBIS activities are organized in 7 Work Packages (WP), each addressing a specific project objective to streamline the scientific progress, knowledge transfer or dissemination.

The aim of **WP1: Drug substances and pharmaceutical preformulation** is to translate the discovery synthesis of a drug substance (API) into technology development and investigate the solid-state physicochemical characteristics of APIs. The overarching goal is to improve unfavourable biopharmaceutical characteristics of APIs, i.e. poor solubility and/or dissolution. To accelerate small molecule process design, several technological platforms are explored to deliver an improved product better suited for further formulation development. Research employs advanced analytical equipment to investigate the intrinsic, solid state and derived properties of the APIs and their

forms.

The purpose of **WP2: Dosage forms and drug delivery systems** is to design, develop and test new drug carriers and dosage forms for oral and topical delivery of drugs. Examples of oral formulations are novel liposomes, polymeric nano- and microparticles, minitablets, self-microemulsifying systems or mesoporous materials, while topical pharmaceutical dosage forms include liquid (ionic liquids, microemulsions), semi-solid (hydrogels, organogels, creams) and adhesive (patches). This work package employs a variety of advanced methods to analyse the developed formulations, including novel imaging and structure analysis techniques and *in vitro* skin permeation tests.

WP3: Biopharmaceutical evaluation of dosage forms and drug delivery systems focuses on the development of biorelevant methods for *in vitro* dissolution and release testing, simulating conditions that act on dosage forms during their gastro-intestinal passage. An additional aim is to advance bioanalytical methods, including biological sample preparation techniques, reducing HPLC analysis time and assessing validation parameters according to the European Medicines Agency guidelines [1].

In addition to the scientific WPs, ORBIS is supported by four other WPs. **WP4: Training** especially concerns early stage researchers. Secondments are an opportunity to become familiar with new research topics and intersectoral environments, learn new methodologies and techniques as well as develop transferrable scientific and “soft” skills, further increasing employability of the young researchers. **WP5: Management** deals with the strategic management and organization of this large consortium, while **WP6: Communication and dissemination** increases the project impact, visibility and dissemination of results. **WP7: Ethics** monitors the handling of ethical issues related to the project and it is supported by the Honorary Ethical Advisory Board, an independent body of external experts.

Research Methodology

Methods include API synthesis, preformulation studies, manufacturing, analytics (including bioanalytics), continuous processing, quality by design and new testing methodology design. Also, a blend of experimental and computational techniques is used to accomplish the research goals. Experts in the various research areas from the consortium are involved in the design of the methods and approaches, amalgamating the expertise in the multidisciplinary, international and intersectoral consortium. The partners are integrating their common research protocols and filling gaps in individual infrastructures.

Measurable effects and expected results

Several deliverables and milestones are aligned with the objectives of the ORBIS project. The WP1 team will demonstrate a continuous operation of synthesis/crystallisation processes for APIs relevant to ORBIS and develop a strategy to improve the solubility/permeability of BCS class II and IV APIs. A public report on perspectives of API manufacturing and advances in preformulation studies will be jointly prepared.

The WP2 milestones comprise the demonstration of oral formulation advancements accomplished as a part of ORBIS (e.g. minitablets, novel drug carriers) and improvements in formulation of transdermal dosage forms. A WP2 deliverable will be a public report on new insights into oral dosage forms and delivery systems as well as novel approaches in topical and transdermal drug delivery.

The main impact of WP3 will be the successful evaluation of bioanalytical methods for selected APIs. The WP3 team will prepare a report on pharmacokinetics driven development of dosage form

specifications and estimation of pharmacokinetics based on *in vitro* data.

To date, after 24 months of project activity, 221 months of secondments have been completed and have started to deliver tangible research outputs, such as new research collaborations and publications [2-6].

Apart from the scientific deliverables and milestones, the progress of the ORBIS project is measured by completing activities related to training, management and dissemination. Four summer schools and workshops for ORBIS participants are the outcomes of WP4 (Table 3). These events involve lectures delivered by world-class researchers, hands-on workshops and demonstrations of relevant techniques, as well as are an opportunity to showcase the organizing partners' capabilities and the results of secondments. The summer schools and workshops are also excellent networking events for strengthening the relationships and formulating new ideas for cooperation between the ORBIS partners and reaching beyond the timeframe of this project.

Event name	Organizing institutions	Place and date
1st School on pharmaceutical preformulation testing of APIs and dosage forms.	TCD & APC	Dublin, 12-14th June 2019
Open Workshop on process development of drug substances.	FMK	
2nd ORBIS Summer School on Oral Dosage Forms: Fundamentals, Challenges and Future Opportunities	UH & ZNT	Helsinki, 18-20th September 2019
ORBIS Workshop on Dosage Forms and Drug Delivery Systems	UH	
3rd School on topical and transdermal drug delivery systems	PUMS & RUTG	Poznan, 29th September- 1st October 2020
4th School on biopharmaceutical evaluation of dosage forms and drug delivery.	ZNT & PRI	Prague, September 2021
Open Workshop on biopharmaceutical evaluation of dosage forms and drug delivery systems.	PHY	

Table 3. *Overview of ORBIS summer schools and workshops*

To date, the project has also successfully achieved its managerial deliverables – including two out of the three major consortium meetings (kick-off, mid-term and planned final conference) and one out of the two progress reports. Project activities and outputs can be followed on the ORBIS website and social media channels established as dissemination deliverables [7].

A goal of ORBIS is to have 504 months of secondments achieved by February 2022. This will lead to over two hundred researchers from European academia and pharmaceutical companies gaining new skills and experience in an international and interprofessional environment. A key impact of the ORBIS project will be increased competence and employability of researchers in the European pharmaceutical sector. Through new personal ties, academic and industrial institutions will form close cooperation and partnerships beyond the scope and duration of ORBIS. The project will enhance the transfer of knowledge in the pharmaceutical sector, ultimately strengthening human capital in research and innovation under the MSCA-RISE action.

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