Executive Summary

EU-OPENSCREEN was included in the 2008 ESFRI roadmap and its preparatory phase project (11/2010-04/2015) was funded by the EC with 3.7 Mio. €. Currently, 13 governmental partners and one International Organisation either signed or intend to sign the Memorandum of Understanding and participate in the Transition Committee (TC): Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Netherlands, Norway, Poland, Romania, Spain, Sweden and EMBL. The Transition Committee already agreed on the overall budget for the research infrastructure, the prospective legal entity as a European Research Infrastructure Consortium (ERIC) and a roadmap with the aim to obtain the ERIC status at the latest at the end of 2016. The governance structure, the funding models and the draft statutes for the ERIC are currently being negotiated among the TC members. Germany has applied as the future host country of the ERIC and negotiations to obtain the required VAT exemptions are ongoing with the German Finance Ministry.

The primary objective of EU-OPENSCREEN is to offer access to a distributed research infrastructure which meets the needs of its users – scientists seeking a better understanding on how fundamental molecular processes act to govern biological function at the organismal, tissue, cellular and pathway levels. Using a well-founded collaborative working model, infrastructure users and EU-OPENSCREEN teams will identify and develop novel small chemical compounds which elicit specific biological responses on organisms, cells or cellular components. These bioactive compounds are identified by means of screening large collections of >100,000 molecules, in an automated process, using robotics-based high-throughput screening platforms. The majority of scientists in Europe, however, do not have access to suitable technology platforms and compound collections, which are generally expensive to purchase, operate and maintain. As a distributed large-scale research infrastructure with an 'open' pre-competitive character, EU-OPENSCREEN will cost-effectively overcome this limitation by involving and providing access to Europe's leading screening platforms and chemistry groups, constructing a jointly used compound collection, and operating an open-access bioactivity database which will be accessible on a global basis.
EU-OPENSCREEN will further our understanding of physiological and pathological processes as the basis for knowledge-based innovations. By doing so, EU-OPENSCREEN will advance the development of solutions for grand societal challenges such a "healthily ageing, growing population" and guarantee European competitiveness. EU-OPENSCREEN will extend the application of Chemical Biology and will develop novel research 'tools' for all fields of the Life Sciences, incl. molecular, cell, plant, structural and micro-biology; synthetic and medicinal chemistry; pharmacology and early drug discovery.
An objective of EU-OPENSCREEN is to drive quality and consistency in the generation and analysis of biological data. This will enormously benefit the search for new medicines by driving consistency in the process of target validation through the application of agreed experimental and data analysis standards. The framing of this objective is a response to recent reports indicating that over 50% of published pre-clinical data may not be reproducible when academic findings are transferred to an industrial setting.

The mission statement of EU-OPENSCREEN is: *"Progress the discovery of biologically active substances in all areas of the Life Sciences by providing transnational open access to the most advanced technologies, chemical and biological resources, and expertise and harnessing the rich chemistry knowledge of Europe in a common compound collection to advance the elucidation of the molecular mechanisms of complex biological phenomena."*

Summary description of project context and objectives

Chemical Biology is a fast-growing interdisciplinary research field that provides fascinating new opportunities to study biological processes in the post-genomic era. Chemical substances are developed and applied as tools for the directed manipulation of the function of biological target molecules (i.e. proteins) instead of conventional mutagenesis of these targets. A major approach for discovering such chemicals is by screening large compound collections for anticipated biological activities in appropriate assays. This approach, well-known from the pharmaceutical industry, is increasingly applied in academia. It is, however, demanding with respect to the logistics of handling several hundred thousand chemical samples, instrumentation for high-throughput screening (HTS), and robotics with sophisticated assay read-out technologies. All of this demands experienced personnel and up-to-date facilities.

EU-OPENSCREEN will provide access to such resources for researchers in academia and industry. It aims to satisfy the needs for new bioactive compounds in many fields of the Life Sciences and health research (e.g. human/veterinary medicine, systems biology, biotechnology, agriculture, nutrition).

EU-OPENSCREEN will comprise HTS centres at different sites in Europe with their special HTS and bio-assay expertise, chemical resources for optimisation of first hit compounds, bio- and chem-informatics capacities, and a publicly-accessible database combining screening results, assay protocols, and chemical information. A large collection of diverse compounds, representing the chemical knowledge in Europe, will be made available from a central storage facility.

The key objectives of the Preparatory Phase (PP) project are the development of a detailed business plan for construction and operation of the research infrastructure and to secure (financial) commitments from several countries. This involves

Legal, Governance and Logistical work: Selection of a future legal structure that is suited to a distributed, pan-European research infrastructure with partner facilities from different countries is required, which obtains support from all organisations involved, i.e. ministries, funding bodies and scientific institutions. Collaborations between institutions and users for an effective service will need a clear operational plan based on high quality standards, a legal framework of contracts and a governance structure to support efficient decision-making for day-to-day management. EU-OPENSCREEN's involvement with potential drug and target candidates requires careful consideration of intellectual property rights; suitable regulations will be established.

Strategic work: Involvement of all stakeholders is crucial for a refined user concept and coherent alignment with EU and member states. Especially a close interaction with ministries and funding agencies is important to ensure a high level of commitment for setting-up and operation of the research infrastructure. Activities in the various EU member states (not supported by this grant) will initiate further national consortia. Training programs for staff are required, to ensure high quality standards for all services offered.

Financial work: Implementation of EU-OPENSCREEN will primarily exploit existing centres that will upgrade their facilities and offer transnational services. A financial concept and management plan will be established that includes controlling mechanisms as well as a finance plan for a sustained operation of EU-OPENSCREEN, and will examine incentive investment models and funding options (i.e. structural funds, RSFF, sponsors, charities, public research funding).

Technical work: An optimized technical layout of the infrastructure facilities will match the EU-OPENSCREEN user concept. Common standards for exchange and deposition of data will be established and the created database will be linked to other European and global databases for the mutually beneficial sharing of knowledge.

Description of main S & T results/foregrounds

During the 4,5-year Preparatory Phase project all foreseen tasks were accomplished and all deliverables have been prepared. Thus all essential elements necessary for the foundation, construction and operation of the future research infrastructure have been elaborated and collated in EU-OPENSCREEN's business plan. The main achievements and the agreements that have been reached are summarised below.

Aim: EU-OPENSCREEN will develop novel research 'tools' for all fields of the Life Sciences. These chemical tools complement other genetic and molecular-biology methods and enable researchers to investigate the molecular mechanisms of physiological and pathological processes.

Layout: EU-OPENSCREEN will involve Europe's leading compound screening sites and chemistry groups, which provide access to cutting-edge technologies, services and resources required for the discovery and characterisation of biologically active substances. It brings together a multitude of academic groups, thereby integrating the individual biological, chemical and technological expertise only available in these local research groups. EU-OPENSCREEN will construct a jointly used, unique European compound collection and operate an openly accessible database to support maximal availability of generated research data. An open-access policy has been adopted to support maximal data dissemination and publication, where the same rules will apply to users from academia and industry. As legal structure a European Research Infrastructure Consortium (ERIC) is foreseen.

Services: EU-OPENSCREEN will support all stages of a tool development project. The core support is for the screening of the joint compound collection with the biological assays derived from the user's projects, while the final outcomes of the projects are the tool compounds. The submission of project proposals will be possible via a dedicated online portal. The proposals will include information on the aim of the project, scientific relevance, impact, exploitation plan, detailed description of the biological assay, screening protocol, etc. The assignment of the project proposals to one EU-OPENSCREEN service site will be based on technical, geographical and capacity considerations. Project moderators at the central office will assist the users throughout the project life cycle.

Training: A prerequisite for the successful construction and operation of a research infrastructure are well-trained staff including scientists, engineers and technicians. Therefore a dynamic package of theoretical and practical courses will be provided by the infrastructure and continuously optimized to ensure that EU-OPENSCREEN is at the forefront of screening and Chemical Biology. EU-OPENSCREEN will also take responsibility for contributing to the training of second (master) and third (PhD) cycle students as well as postdoctoral scientists and principal investigators in Chemical Biology by providing special introductory courses in high throughput screening and assay development. Such courses will help to foster the next generation of European researchers and ensure optimal use of the EU-OPENSCREEN infrastructure. Another important element is the synergy that can be achieved by interaction with the other ESFRI BMS RIs and with the European Medicines Research Training Network (EMTRAIN). Several pilot courses have already been organised by EU-OPENSCREEN.

Involved countries: During the third reporting period new partners from Hungary and Greece entered the consortium, thus increasing the number of involved countries to 16. At the level of the respective ministries/funding agencies, currently 12 countries (Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Netherlands, Norway, Sweden, Poland, Romania and Spain) and 1 International Organisation (EMBL) negotiate the setting-up of the EU-OPENSCREEN-ERIC.

Potential impact and main dissemination activities and exploitation results

The Preparatory Phase project ensures that EU-OPENSCREEN reaches the necessary level of technical, legal and financial maturity required to enable its successful foundation, construction and implementation. To this end a business plan was developed, which forms the basis for the negotiations between the countries interested to become involved in the future pan-European research infrastructure. The business plan comprises several elements, such as the overall concept, a description of the stakeholder community, the user service portfolio, the overall business description, the specific expertise and the contributions of the individual partner platforms, the legal structure of the infrastructure, the governance structure and the management plan, the IPR strategy, the construction plan, the operation plan, the financial plan for construction and operation, a risk assessment and details on quality and impact monitoring, a contingency plan, the development plan (inclusion of new partners, new operation sites and new services), the PR, exploitation and dissemination plan and the affirmative action plan.

EU-OPENSCREEN will integrate local expertise and resources in the field of Chemical Biology in a distributed network to provide open access to external researchers and thus contribute to the attractiveness of the European Research Area. Its successful implementation will have wide-ranging socio-economic impacts.
Understanding how chemicals, both natural and artificial substances, influence our lives and environment is of fundamental importance for the development of new and safer products – be they drugs to treat diseases, herbicides to protect crops, food additives for livestock, and many more. Any chemical released into the biosphere will in some way interact with living species, affecting them in ways both beneficial and potentially adverse, and so a detailed knowledge about these chemicals is vital. EU-OPENSCREEN will increase this knowledge by offering access to researchers from academia or industry aiming to identify compounds with specific biological activities, e.g. tumour growth inhibition, antibiotic, antiviral or herbicidal activity. These compounds will be used by biologists as tools for studying biological phenomena (signal transduction or metabolic pathways) that will lead to new insights into how these substances affect biological processes. These insights will then inspire the design of new drugs and many other marketable products. By testing systematically and repeatedly such a vast number of chemicals, the screening process generates enormous amounts of information about their biological activities and thereby steadily enriches our understanding.

The EU-OPENSCREEN infrastructure will be critical for satisfying the increasing need for bioactive compounds, and will meet these challenges by:
- broadening the basis for the scientific use of bioactive compounds;
- accelerating the discovery of biologically active substances in all areas of Life Sciences;
- harnessing the rich chemistry knowledge of Europe in a common compound collection;
- focusing on non-validated targets and identifying entirely new target classes;
- elucidating the underlying mechanisms of complex biological pathways;
- enabling wide, cross-experimental/disciplinary activity pattern and fingerprint analyses for the discovery of new Structure-Activity Relationships (SAR) from its database;
- creating a multitude of opportunities for new research collaborations;
- bridging the gap between academic research projects and the commercial development of bioactive compounds;
- securing IP from academic projects for commercialisation;
- providing efficient bio-profiling of novel synthetic compounds vs. a broad variety of protein targets;
- promoting the availability of safe and efficacious chemical products for so-far-unmet needs in medicine, nutrition and agriculture; and

- contributing to the training of a new generation of chemical biologists.

Public website address: www.eu-openscreen.eu