

# Future Internet Public Private Partnership

## *Position Paper*



**NATIONAL TECHNICAL UNIVERSITY OF ATHENS**

**Department of Electrical and Computer Engineering**

**DISTRIBUTED KNOWLEDGE AND MEDIA SYSTEMS GROUP**

**Contact persons:**

Professor Theodora Varvarigou

Email: [dora@telecom.ntua.gr](mailto:dora@telecom.ntua.gr)

Dr Vassiliki Andronikou

Email: [vandro@mail.ntua.gr](mailto:vandro@mail.ntua.gr)

## Large-scale Collaborative Clinical Trial Design and Execution

### Introduction

*Large-scale collaborative clinical trial design and implementation* comprise an interesting and important application area with great potential of benefit from the Future Internet Platform. Given the great wealth of clinical and non-clinical research information distributed across the Internet in various forms as well as the established medical knowledge, investigators face a great challenge of reaching proper decisions and exploring a wide range of alternatives when designing and executing clinical trials. In the meanwhile, the temporal and budget-related requirements of clinical testing in the pharmaceutical industry lead to capital and valuable human resources being locked up in pre-clinical and clinical phases. With the average cost of clinical trials reaching € 800 million per drug candidate, the new drug development timeline being on average 11.3 years and the world economy shrinking, the pharmaceutical industry faces reduction in the allocation of funds for new research followed by declining innovation and reducing productivity; a phenomenon that has direct impact on scientific research as well as the world population. Within this context, *drug repositioning* comprises a current trend that pharmaceutical companies tend to follow to gain more profits from drugs that either are about to go off patent or are already off patent. In the meanwhile, clinical trials quite often fail to demonstrate any beneficial effect and sometimes underestimate risks and overestimate treatment efficacy with their results having *low external validity*.

### Bridging the gap between clinical research and clinical care

Clinical and non-clinical research results are published worldwide on a wide range of areas that are not necessarily unlinked; a clinical trial may be investigating an irrelevant test of hypothesis – treatment X for disorder Y – but it may encapsulate indirect, hidden knowledge valuable to other investigators' clinical trials in other fields. Moreover, Electronic Health Records are gradually being adopted forming a potential significant pool of information on patients who could be eligible for participating in clinical trials.

The Future Internet platform can significantly boost, advance, improve and speed up the clinical trial design and implementation processes by proving the infrastructure for more efficient management and semantic linking of currently available dispersed information, as well as allowing for the effective management of the constantly evolving knowledge in the medical domain. Hence, by effectively combining dispersed medical research knowledge across the Internet, investigators will be able to explore a variety of semantically linked and analysed clinical and non-clinical findings in order to form their test of hypothesis ("identify" novel treatments for disorders). Moreover, they will be able to perform "intelligent queries" that will be further elegantly analysed into a variety of "sub-queries" by taking advantage of underlying medical ontologies that will feed advanced data mining mechanisms for extracting knowledge from published findings. Thus, they will efficiently *design* their *clinical trial protocol* and *set the clinical study parameters* (sample size population, subject number, study duration, dosage scheduling, inclusion and exclusion criteria, statistical methods, etc) by exploiting and evaluating a great number of alternatives within a reasonable amount of time and thus getting higher chances of reaching a more "effective" choice. The term "effective" refers to choices which are well-documented,

are aligned with their research agenda and will allow for faster go/no-go decisions in the clinical research efforts.

Moving a step forward and by taking advantage of the gradual adoption of Electronic Health Records (EHRs) in clinical care and their potential of acting as an electronic umbrella over persons' health information, hospitals, clinics and research centres which will be collaborating with the system will form *a pool of potential subjects for participating in the clinical trial*. Thus, automatic patient selection from the available patient records will take place and the investigators will be presented with the list of patients who are eligible to participate in their clinical study.

Moreover, investigators will be able to take advantage of *adaptive clinical trial design*, during which they will take decisions based on the intermediate results of their clinical trials and decide upon early termination for safety/efficacy reasons or for more rapid entrance to the market as well as re-adjustment of study protocol parameters. The constant knowledge evolution of the system through regular feeds of information from published clinical and non-clinical findings will allow the researchers to enrich their study protocol with new or adjusted parameters. And what is more, intermediate patient results themselves will be used for adjustment of the future patients' assignment, by placing the latter to the best treatment identified.

Such a use case can be reversed at the scenario-level while maintaining the same underlying technologies; patients themselves could use such a platform to benefit from rapid and intelligent decision support when searching for clinical trials with expected or open recruitment that they could participate in. Hence, the system could analyse their Electronic Health Record and perform intelligent correlations with the available clinical study protocols in order to propose to them clinical trials for participation with the main criteria being driven by potential clinical efficacy and mitigation of patient risks.

Enabling the informational flow between these two highly related although currently unlinked domains, clinical research and clinical care, will also boost *outcomes research*, a research effort which focuses on examining the outcome of health care practices by linking health care outcomes, such as quality of life, with other factors, such as lifestyle or location.

### Future Internet Platform as an enabler of this use case

The suggested use case requires a wide range of technologies to be implemented. Medical ontologies allow for determining a common vocabulary when forming the clinical problem and setting the clinical study parameters. They, in fact, form the basis for semantically extending the medical searches across the Internet. Interoperability issues of these ontologies need to be effectively dealt with; ontology mapping will lead to the development of a *network of ontologies* able to describe the broader medical field. As such an approach aims at taking advantage of a great number of dispersed, heterogeneous data sources, advanced real time processing capabilities handling huge volumes of data are required. Moreover, given that numerous different workflows are built depending on the step in the clinical trial design and implementation phase as well as the decision that needs to be made, *advanced, dynamic service composition and mash-up* comprises a driving factor.

In order to achieve flexible interoperability among these systems which are disparate in technology, location, performance, and availability, the presented use case also requires:

- advanced orchestrators for integration of heterogeneous sources,

- approaches for temporal optimisation, which appears to be critical for expediting the clinical study process as a whole,
- synchronous and asynchronous invocation and execution of services
- advanced security and privacy preservation mechanisms including data confidentiality, rapid and reliable data pseudonymisation mechanisms, elegant access control, highly effective encryption techniques, given the sensitivity of the data involved (especially in Electronic Health Records)
- novel data models allowing for its efficient retrieval, indexing and management are required
- frameworks and functional systems for transfer, storage and access,
- dynamic, self-adjusting resources, including knowledge bases
- secure composability of real and virtualised resources, including computational resources, knowledge bases, data sources, networks, servers
- advanced trust establishment management for enabling the collaboration between the clinical research centers, the pharmaceutical companies and the clinical care providers (hospitals, clinical, private practitioners)

The broad large-scale testing of this platform will include multiple users as well as a variety of clinical research institutions and clinical care providers. Given the constantly evolving volume and variety of medical knowledge produced and published worldwide, high computational capacity for the processing, storing and management of the knowledge bases is required. Moreover, compliance to privacy and security policies posed by the legal framework whereas allowing for the interconnection of different administrative domains and technical interoperability especially at database level comprise two important requirements.

### Organisation role

The Institute of Communication and Computer Systems (ICCS) comprises a research organisation with great expertise in a wide variety of fields including Grid and Cloud technologies, Service Oriented Infrastructures, distributed systems, trust management, Quality of Service provision, semantic data representation as well as e-health, assisted living and decision support mechanisms. Having cooperated with a great number of European research organisations, academic institutions, large organisations as well as SMEs in a variety of application areas from Manufacturing, Filming and Logistics to Electronic Health and Knowledge Management, ICCS has the potential – as far as Usage areas are concerned - to propose truly innovative applications which should be expecting great benefits from the Future Internet Platform. Our research in these areas has allowed us to identify and analyse numerous infrastructural and application-level requirements in the aforementioned context in the presented use case that the Future Internet Platform shows the potential of covering efficiently and effectively and towards which our current research efforts are taking place.