C O N F I D E N T I A L

Remote Decentralized **Clin**ical **T**rials **O**perating **S**ystem For Trials@Home (**CLINTOS**)

Acronym: CLINTOS
Call ID & Topic: ID: ECSEL-2020-3-IMI-ECSEL IMI-ECSEL Joint Activity Trials@Home

CLINTOS
The Operating System For Trials@Home

No	Participant organization name		Country
1	UTB: Universitatea Transilvania Din Brasov	University	Romania
2	BC5: Blockchain 5.0 OÜ	SME	Estonia
3	EMA: European Medical Association	Non-profit	Belgium
4	AFL: Autonio Foundation Ltd	Non-profit	UK
5	OT: Ozanteks Tekstil	Large Enterp	Turkey
6	SST: Stelar Security Technology Law Research GmbH	Research Org	Germany
7	ISS: Innovation Sprint SPRL	SME	Belgium
8	ABI: Abich SRL	SME	Italy
9	MIA: MIA Teknoloji	SME	Turkey
10	SBA: SBA Research Gemeinnutzige GmbH	Research Org	Austria
11	HBI: HeartBalance Innovations GmbH	SME	Austria

Special Trials@Home Advisory Board*

No	Advisory Organization name		Country
1	**CERTH: Ethniko Kentro Erevena Kai Technologikis Anapty***	Research Org	Greece
2	**MLC: Stichting MLC Foundation (MLCF)***	Research Org	Netherlands
3	**FHJ: FH: JOANNEUM Gesellschaft mbH***	University	Austria

***These third party contributors to the CLINTOS consortium are members of the **Trials@Home center of excellence** funded under IMI Joint Undertaking (JU), and were original partners in the CLINTOS consortium but were not able to join the consortium as regular part due to funding limitations imposed by their countries' funding agreement with ECSEL. Their engagement with CLINTOS as advisory board will ensure that this project will be "timed and tuned to facilitate a close complementary activity between Trials@Home.[1]

Our Vision:
To build a versatile, future-ready, user-centric, cloud based universally compliant Operating System for Trials@Home.

Our Mission:
To exploit ICT & wearable technologies for enabling a decentralized, universally compliant, user-centric ecosystem for conducting RDCTs (Remote Decentralized Clinical Trials).

Our Goals:
To build, test, validate CLINTOS (**Clin**ical Trial **OS**) as RDCT-as-a-Service platform, disseminate & exploit the cloud business model.

[1] ECSEL Joint Undertaking, Work Plan 2020, Version 16, page 16

Abstract

Clinical trials (CTs) are means of validating & receiving regulatory approvals for marketing new medical products for prevention, treatment & diagnosis of diseases. The average cost of bringing a new drug to market is estimated at $2.6 billion, with 2/3 of the cost going to CTs, about 90% of which fail. Moving CTs from the traditional clinic setting to the participant's immediate surroundings not only affords cost savings, but also makes it easier for larger, more diverse & remote populations to participate in CTs, enabling participants to visit a CT center less frequently, or not at all.

Remote Decentralized Clinical Trial (RDCT) is a promising new way to conduct CTs that also maximizes stakeholder engagement as investors, physicians, state, patient advocacy groups, and even the patients themselves can play a role in study design, implementation, analysis & optimization of the remote monitoring approach.

Despite many benefits, RDCTs pose a number of operational & regulatory challenges including privacy, security & interoperability (PSI). Most CT systems lack capabilities in securing, anonymizing & making acquired patient data interoperable. Almost all health data still exists in silos at the risk of privacy/security breaches. The RDCT-as-a-Service presented in this proposal builds upon a pending PSIaaS (PSI-as-a-Service) & 2 granted H2020 (XENO & COVID) projects, using wearable sensors that broadcast vital signs in real time. This decentralized patient-centered approach integrates PSI by design into any existing CT system, wherein patients remain in full control of their personal online data (POD), authorizing, access to HMS, CDMS of EHR, via APIs when required. Thus, this novel Trials@Home framework functions as a universally compliant CT Operating System (CLINTOS) of future RDCTs, seamlessly connecting with the entire care continuum as plug-n-play federated cloud ecosystem generating new financial opportunities for partner SMEs in the multi-billion CT industry.

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2 ECSEL JU Work Plan for ECSEL US Calls of 2020. Version 15. https://www.ecsel.eu/calls-2020-wp2020

[3] Privacy, security & Interoperability-as-a-Service: https://liquidus.info/consortium/

1. Excellence

Background

For the health and pharmaceutical industry, clinical trials are the means of validating new medical products for prevention, treatment and diagnosis of diseases. It is not only a mandated path to regulatory approvals of medicinal products, but also an opportunity to observe their real-world effects on patients before being marketed on a wider scale. Considering that the average cost of developing and bringing a novel pharmaceutical agent to market comes to around $2.6 billion, pharmaceutical companies are increasingly looking for ways to lower costs and maximize return on their investment. This scenario is also valid for the cosmetic industry. Despite being characterized by easier clinical trials, the impressive number of new cosmetics and personal care products launched every year (around 40.000) create the need for the optimization of tests on volunteers. Moreover, in the past decade end users become more and more skeptical about the real efficacy of commercialized beauty products, forcing most of the produced to adopt scientifically validated protocols. In particular, when it comes to skincare and makeup products various aspects can be revealed through different kinds of clinical trials. With this type of testing, the general credibility of a brand or product can be increased through claim substantiation, efficacy testing, dermal safety studies, and more. With their own eyes, potential customers will be able to view real life results through the information provided to them as a result of clinical trials. And to help buyers understand the true benefits of a product.

Remote Decentralized Clinical Trial (RDCT) is the way. Moving clinical trials from the traditional clinic setting to the participant's immediate surroundings makes it easier for larger, more diverse and remote populations to participate in clinical trials, enabling participants to visit a clinical trial center less frequently, or not at all. The remote monitoring approach to virtual clinical trials is also ideal for maximizing stakeholder engagement. All groups who have a vested interest in the success of a trial – including investors, physicians, government agencies, patient advocacy groups and even the patients themselves – can play a role in study design, implementation, analysis and optimization of the remote monitoring approach as a whole.

The first attempt to pioneer virtual clinical trial concept was made by Pfizer with their Research On Electronic Monitoring of Overactive Bladder Treatment Experience (REMOTE) trial conducted in 2011. Although Pfizer's REMOTE trial failed to reach its goals (basically because of severity the disease chosen and older population who have little or no online presence), the learning has helped in some initial successes as in Sanofi's VERKKO trial, Novartis' NASH trial & a few other RDCTs.

Despite many benefits, RDCTs pose a number of unique operational challenges including privacy, security and interoperability (PSI) of the sensitive data over the Internet. Currently, most pharma companies & contract research organizations (CROs) lack the systems needed to efficiently deal with the large amounts of data collected in securing, anonymizing and making them interoperable. Almost all health data still exists in centralized silos at the risk of privacy and security breaches.

The Trials@Home project is establishing a set of best practices and a selection of tools for all stages of RDCTs from trial design, to recruitment approval, management, analysis and outcomes.

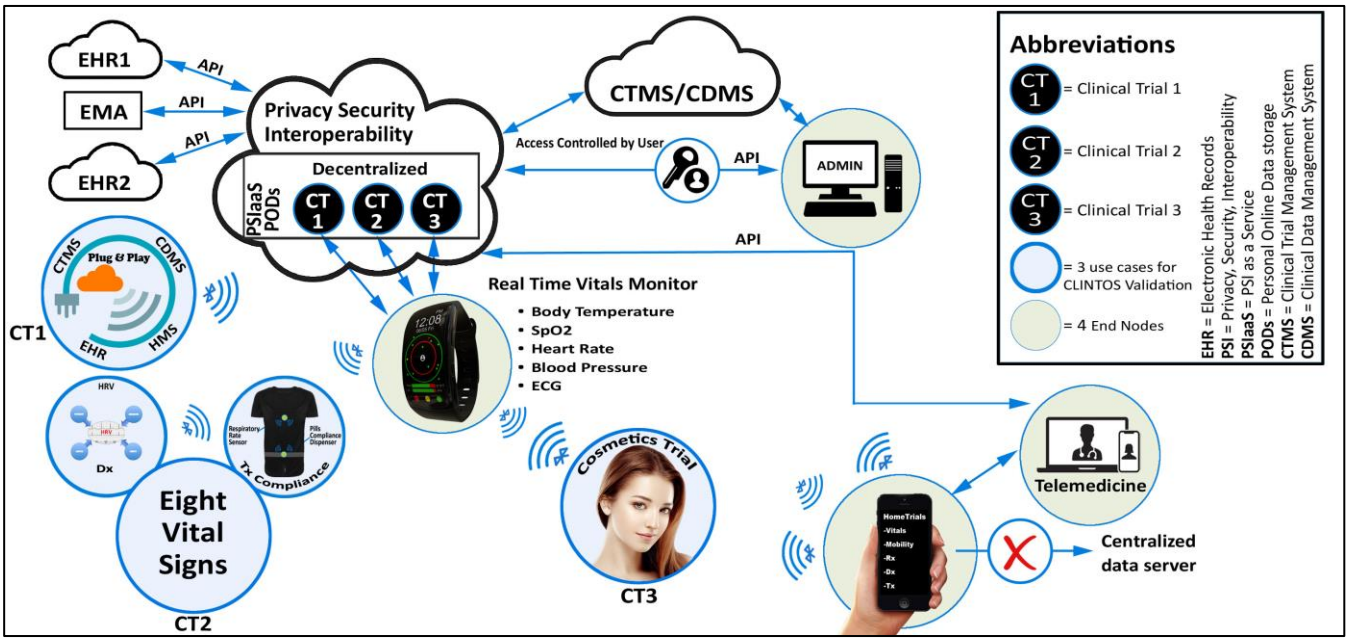
Today, when cloud computing has entered an era of 'Everything as a Service' (XaaS), we recently invented **PSIaaS** cloud infrastructure for embedding PSI as a plug-n-play service into any cloud application. The RDCT-as-a-Service presented in this proposal builds upon the **PSIaaS** project in addition to two other ongoing H2020 grants (**XENO** & **COVID**). It uses a wearable device with sensors that operates as the SmartHub of the this novel RDCT cloud infrastructure, and seamlessly broadcasts in real time, 7 vital parameters, without burdening the patient or the trial monitor. This decentralized patient-centered approach integrates PSI by design into any existing clinical trial software wherein the patients at all times remain in full control and ownership of their decentralized data as PODs (personal online data stores), authorizing, whenever necessary, access to hospitals, CROs or EHRs, via APIs. Thus this novel Trials@Home framework functions as the **Cli**nical **T**rials **O**perating **S**ystem **(CLINTOS)** of the future RDCTs.

In our ultimate vision the wearable device that monitors user's real time vital signs 24/7 and serves as the SmartHub of the **CLINTOS** ecosystem will eventually become a new norm that every citizen will have to wear to ensure safer and healthier communities in the changing post-COVID-19 world. It is also being pursued as a SmartHub of a first responder technology - MOONSHOT (**M**ishaps & **O**minous **O**rdeals **N**eutralizing **S**ystem of **H**igh **O**perational **T**oughness) by yet another H2020 consortium.

For validation and first market replication of CLINTOS, the proposal also presents at least 3 use cases spread across a diverse clinical trial scenarios. RDCTs will be a major asset and a significant game changer for the

Pharma industry. They are already very much here, and with **CLINTOS** they present a perfect opportunity to leapfrog into a new world of Trials@Home.

CLINTOS will align with and extend the Trials@Home practices by leveraging best practices and lessons learned by its rigorous literature and pharmaceutical practice review (T@H WP1 – BEST) as well as handpicking the best tools, practices and services from its technological platform (T@H WP2 – TECH) throughout its process. To ensure this, a Trials@Home advisory board with 3 members of Trials@Home center of excellence. These members are active in T@H BEST and TECH and all its streams: Technology Scanning, Platform Assembly and Quality Assurance; and its Building Blocks: Patient Engagement, Data Acquisition and Processing etc.



Bird's Eye View of CLINTOS Ecosystem & 3 Clinical Trials To Validate Its First Market Replication

1.1. Objectives

1.1a) Introduction - Context:

The evaluation of quality, safety and efficacy of medicinal products by regulatory agencies is a necessary step for obtaining marketing authorization in the European Union (EU). The cost of conducting multi-site clinical trials has significantly increased over time, with site monitoring, data management, and amendments being key drivers. Due to high cost of drug development estimated at around $2.6 billion, pharmaceutical companies are increasingly looking for ways to lower costs and maximize return on their investment. Clinical trial data management approaches typically rely on a central database, and require manual efforts to encode and maintain data capture and reporting requirements. To reduce the administrative burden, time, and effort of ensuring data integrity and privacy in multi-site trials, a European private public partnership (PPP) sponsored by IMI-ECSEL joint activity & EU, funded €40 million to launch an ambitious Trials@Home project[4] to explore the opportunities of moving clinical trials from the traditional clinic setting to the participant's immediate surroundings. Coordinated by University Medical Center Utrecht and Sanofi, the Trials@Home research to be conducted includes an inventory and evaluation of existing and new techniques for use in such *"remote decentralized clinical trials"* (RDCTs) as well as a pan-European pilot trial with an objective to develop and test remote decentralized methods to streamline data collection, participant recruitment and retention. At the same time, it will ensure the participation of a greater number of volunteers that are more representative of the population at large. By augmenting face-to-face interaction with remote procedures, larger geographic regions will be accessible to foster the participation of unrepresented relevant populations.

These RDCTs make use of new – digital – innovations and enable participants to visit a clinical trial center less frequently, if at all. This makes it easier for larger, more diverse and remote populations to participate in clinical trials. These trials are expected to be conducted faster, more efficiently, and provide results that are more representative, because the data is collected in the daily context of the participant (Real World Evidence).
We propose a novel cloud-computing infrastructure that provides a comprehensive ecosystem for conducting RDCTs by deploying a novel network of sensors, devices, algorithms and processes, and yet retaining the usage

[4] https://cordis.europa.eu/project/id/831458

of most of the existing clinical trial management systems (CTMS) and clinical data management systems (CDMS) as plug-n-play peripherals of the platform. Implemented in as-a-Service (-aaS) business model, our CLINTOS platform enables privacy, security and interoperability by default keeping the operation smooth, seamless and easy to use.

1.1b) RDCT vs VCT: What's in a name?

RDCT is a new terminology. A *"Remote Decentralized Clinical Trial"* search query in Google Scholar brings up only one peer-reviewed article,[5] which is authored by the participants of the Trials@Home consortium. However, "*Virtual Clinical Trials"* (VCT) is another term in use since National Academies of Sciences, Engineering and Medicine (NASEM) held a multi-stakeholder workshop in 2018, referring to such clinical trials as VCTs.[6] Although, both terms imply the same, the latter term was actually included in the NASEM workshop title. Even within the workshop, different terms were used by workshop participants to refer to clinical trials in which all or part of the study incorporates digital health technologies and enable remote participation outside of the traditional brick-and-mortar clinical trial site. The workshop terms such as *"decentralized," "remote,"* or *"site agnostic"* or *"direct-to-participant™", "location variable"* and *"mobile clinical trials"* that participants used, describe some types of trials that incorporate digital health technologies, but many study activities they discussed required a centralized location. Each of these terms highlights different aspects of how digital health technologies that may be incorporated into study design.

Nomenclature was a topic of discussion during the final session of the NASEM workshop, noting that an adequate umbrella term for the variety of clinical trials out there is not easy to define. Before embarking on our journey to solve the RDCT riddle, we took up the challenge. Even otherwise, we believe, it is important to clearly define the concept that you want to invent. So we looked for a clear and precise definition of RDCT, and found on the Trials@Home website, the closest that can be called a definition:

> *"The RDCT approach is an operational strategy for technology-enhanced clinical trials, that are more accessible to patients by moving clinical trial activities to more local settings. RDCTs can be applied in all stages of the drug development process, to generate evidence on safety, efficacy (as traditionally obtained from controlled phase I to IV clinical trials) or effectiveness (as obtained from more pragmatic studies aimed at guiding prescribing in routine clinical practice)."*

A technical definition is a definition in technical communication describing or explaining technical terminology. Technical definitions are used to introduce the vocabulary, which makes communication in a particular field succinct and unambiguous. For a highly regulated, fragmented and siloed specialty[7] such as clinical trials, technical definition of the same term may vary according to the regulatory regime. For example, European Medicine Agency (EMA) elaborates clinical trials in Annex 1 of Directive 2001/83/EC and defines[8] it as:

> *"A study performed to investigate the safety or efficacy of a medicine. For human medicines, these studies are carried out in human volunteers."*

NIH definition of a Clinical Trial[9] is a bit more elaborate:

> *"A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes."*

WHO definition[10] elaborates it further:

> *"Clinical trials are a type of research that studies new tests and treatments and evaluates their effects on human health outcomes. People volunteer to take part in clinical trials to test medical interventions including drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioral treatments and preventive care.*

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[5]Bolislis, Winona Rei; Corriol-Rohou, Solange; Hill-Venning, Claire; Hoogland, Hans; Joos, Angelika; King, David; Kitcatt, Victoria; Le Visage, Genevieve; Kühler, Thomas C. Orphan Medicines for Pediatric Use: A Focus on the European Union. Clinical Therapeutics, ISSN: 0149-2918, Vol: 41, Issue: 12 (Dec 2019), Page: 2630-2642

[6] National Academies of Sciences, Engineering, and Medicine. 2019. Virtual Clinical Trials: Challenges and Opportunities: Proceedings of a Workshop. Washington, DC: The National Academies Press. https://doi.org/10.17226/25502

[7]https://www.biospace.com/article/releases/new-survey-finds-fragmented-processes-and-system-silos-slowing-clinical-trials/

[8] https://www.ema.europa.eu/en/glossary/clinical-trial

[9] https://grants.nih.gov/policy/clinical-trials/definition.htm

[10] https://www.who.int/health-topics/clinical-trials

Our first order of business is to define RDCT as an umbrella term for the variety of clinical trials that it encompasses. We believe, without the complete understanding of what RDCT should ideally entail, one cannot scope the four corners of an ideal RDCT infrastructure. So for us the key question in defining RDCT is whether decentralization should only be in terms of the study subjects and trial sites, or also include decentralization of the data that originates from the decentralized subject population. In designing our solution our preference is for the latter as the decentralization of data by default automatically solves many of the privacy, security and interoperability issues that mar the legacy systems. Patient health records today face the biggest problem of data being locked up in data silos owned by service providers, and remains without any interoperability for privacy and security reasons. Hence, we believe decentralizing the subject data by design and placing the data ownership and control in study subject's hands, automatically addresses privacy, security and interoperability issues. So here's how our first cut on this new turf looks like:

> *RDCT is a clinical trial conducted without an elaborate clinical trial site, by remotely recruiting study subjects who mostly stay home during the course of such trial, to evaluate the efficacy of a clinical intervention, whether diagnostic, preventive, therapeutic or palliative, and who consent to real time electronic remote monitoring of the impact of the clinical intervention, on their vital signs and other pre-selected physiological parameters, and who personally own and control the flow of such data from a secure distributed storage to the study sponsor, to hospitals or to EHR for further processing that data for the specific purpose the study subjects specifically consented to.*

That's a generic definition of RDCT we arrive at integrating all the key elements of what RDCTs entail. However, for the purpose of designing our solution, we go a step further and define how the private, secure and interoperable decentralized data storage should be actually handled to further improve the two other major considerations of health data management - **latency** and **economy**. Hence, the RDCT definition that we give ourselves for building our solution reads:

> "*RDCT is a clinical trial conducted without an elaborate clinical trial site, by remotely recruiting study subjects who mostly stay home during the course of the trial. RDCT aims to evaluate the efficacy of a clinical intervention, whether diagnostic, preventive, therapeutic or palliative. Study subjects consent to real time electronic remote monitoring of the impact of the clinical intervention, on their vital signs and other pre-selected physiological parameters. Accordingly, study subjects own such data stored in secure decentralized PODs (Personal Online Data stores) and control its flow to the study sponsor, to hospitals or to EHR via APIs. This is needed for further processing those data for the purpose the study subjects specifically consented to."*

Therefore, our definition of RDCT has the following 9 elements:

1. Conducted without an elaborate clinical trial site;
2. Remote recruitment of study subjects;
3. Study subject mostly stay home during the course of the trial;
4. Evaluation of the efficacy of a clinical intervention;
5. Whether diagnostic, preventive, therapeutic or palliative;
6. Study subjects consent to real time remote monitoring of their vital signs and other pre-selected physiological parameters;
7. Study subjects own and control the sharing of their personal data;
8. Personal data of study subjects stored in secure decentralized PODs (Personal Online Data stores); and,
9. Study subjects share specific data via APIs with the study sponsor, hospitals, EDC, CTMS, eTMF, EHR or PODs for further processing that data for the purpose the study subjects specifically consented to.

Armed with those 9 crystal clear elements of what our Trials@Home solution for RDCTs should comprise of, we commenced our journey to invent the inventible.

Today, when cloud computing has entered an era of *"Everything as a Service"* (**XaaS**), we recently invented "*Privacy, Security & Interoperability as a Service"* (**PSIaaS**).[11] Deploying PSIaaS to embed *"Privacy, Security & Interoperability"* into our RDCT solution, we build it as a service on the cloud to serve as a backbone ecosystem for all types and variants of RDCTs. We call our RDCTaaS solution ***"Clinical Trials Operating System"*** (**CLINTOS**), as it is designed to interoperate with all the diverse range of stakeholder solutions, thus virtually serving as an OS for Trials@Home RDCTs.

[11] Privacy, security & Interoperability-as-a-Service: https://liquidus.info/consortium/

Thus, CLINTOS, while providing a universal framework to enable all types of RDCTs in general, allows other existing cloud applications that service clinical trial industry, such as CTMS, CDMS, eTMF, etc. to be plugged-in and integrated with CLINTOS as a federated cloud ecosystem, or as an OS for the RDCTs as a whole. The following specific objectives will take the CLINTOS Trials@Home infrastructure development from our TRL-4 technology to TRL-7:

Ultimate Vision	To become a new privacy-preserving, secure and resilient backbone of any scalable and cross-sectorally expandable Trials@Home infrastructure, for enabling telepresence of clinical trial subjects for remote delivery of telemedicine for testing and validating diagnostics, therapeutic, preventive and palliative interventions in clinical trials which will be conducted remotely without the need that study subjects having to physically visit a trial site frequently.
Current Mission	To provide a versatile privacy-preserving AI-powered wearable devices with sensors that monitor vitals and mobility of clinical trial study subjects in real time for remotely recording the impact of one or more diagnostic, therapeutic, preventive or palliative interventions in compliance with relevant regulations.
Goals	1) To design RDCT protocols using CLINTOS platform for validating the efficacy of clinical interventions using the CLINTOS platform in compliance with all the applicable regulations. 2) To get IRB approvals for the field trials to validate the usability of CLINTOS infrastructure. To test & validate CLINTOS with the following field trials: i) CT-1: Plug-n-Play operability of 3rd party apps; ii) CT-2: Validation of 8 built-in vital signs (including HRV & therapy adherance) for RDCTs; and, iii) CT-3: Validation of RDCT as tool for dermal/cosmetic product CT.To analyze test results for recommending refinements, enhancements and dissemination / exploitation activities.

As reasons therefore following are the specific objectives and the deliverables of our proposal:

		Objectives	Deliverables	WP
Research & Innovation	1	To define and draft requirements, specifications, decentralized architecture of the CLINTOS cloud computing platform, its software, hardware and BLE5 mesh-network based on improvements on COVID-PASS device to produce AI-powered, privacy-preserving RDCT SmartHub device, including companion app (iOS & Android) with telepresence UI, decentralized database powered with PSIaaS Health PODs (personal online data stores) & DLT (digital ledger technology) for securing user ID & data sharing smart contracts.	- CLINTOS specs, - SmartHub device -Companion app (iOS & Android) - PSIaaS / DLT network architecture - PSIaaS Health PODs - Secure ID & smart contract	**WP2** M1-M3
	2	To build Proof-of-Concept (POC) of the complete CLINTOS infrastructure deploying sensors that monitor study subjects vital signs in real time supported by privacy-preserving decentralized network architecture for securing data privacy / anonymity. Create a testbed for testing & validating 3 use-cases.	- 50 SmartHub devices for CE Marking. - DLT Testnet - CLINTOS testbed	**WP3** M3-M12
	3	To implement and manufacture 200 units of RDCT SmartHub wearable devices (wrist device & Smart T-shirt) for testing of the product (companion app and always-on mesh-networking for CE marking). IPR review and filing of patents.	- 200 RDCT SmartHub - CE Mark SmartHub & Smart T-shirt devices for testing CLINTOS use case - 2 patents	**WP4** M12-M20
Test	4	To design clinical trial (CT) protocols for field trials, get IRB (Institutional Review Board) approvals and conduct CTs for the following use-cases: i) CT-1: Plug-n-Play operability of 3rd party CT apps; ii) CT-2: Validation of 8 built-in vital signs (including HRV & therapy adherance) for RDCTs; and, iii) CT-3: Validation of RDCT as tool for cosmetic product CT.	- IRB approved protocols for CT-1, CT-2 & CT-3 - CT-1 results - CT-2 results - CT-3 results - CLINTOS validation report	**WP5** M18-M32
PEDR	6	To plan for exploitation and dissemination of results (PEDR). Connect, interact & exchange CLINTOS data with European health services, CROs, pharma industry and EMA to establish alliances, collaborations, accreditations. Build a diverse transnational RDCT	- Project website - Business Plan - 4 social media channels - 4 workshops including 1	**WP6** M1-M36

		community by engaging with public, health and Trials@Home advocacy groups, NGOs and healthcare / stakeholders at all levels to achieve cooperation for collaborating and interacting with external entities to engage, educate and clarify technological nuances to potential beneficiaries, end-users, developers, policy-makers, healthcare, IoT & ICT industries, scientific community & potential investors. Build a long term Business Plan (BP) of CLINTOS ecosystem for Trials@Home.	for young women - 6 webinars - 3 conferences - 2 press releases - 2 TV/Web shows	

1.2. Relation to the ECSEL JU Annual Work Plan 2020 & ECSEL MASP 2020[12]

This proposal builds on two ongoing Horizon 2020 Fed4FIRE+ grants[13] and two pending H2020 proposals, PSIaaS[14] & ZEROV[15]. As much as CLINTOS draws from PSIaaS and COVID-PASS, these technologies enable *"closer interaction between users of technology and technology developers"* and *"ensure that technologies are developed in a more focused, accelerated, efficient manner, without reinventing the wheel i.e. attempting to develop technologies that already exist"*

Addressable Areas Within The Scope Of The Call
"to accelerate the medicines development process and to implement a suite of processes in drug development."
This project **firstly** draws up the elements that constitute an ideal definition of RDCT, **Secondly**, builds upon those elements to design and develop a proof-of-concept (POC) that enables seamless implementation of diverse types of RDCTs in a universal cloud computing framework that ensures privacy, security and interoperability of the ICT infrastructure in different clinical trial scenarios integrating existing CRO tools and applications, **Thirdly**, tests and validates the functionality of the components of the POC framework in the most popular "Everything as a Service" (XaaS) cloud computing service model, and, **Fourthly**, tests and validates CLINTOS as RDCTaaS business model as a comprehensive suite of processes involved in medicinal product development, with at least 3 real world use cases representing clinical trials for preventive, diagnostic and therapeutic products. Thus, for all the above reasons CLINTOS is versatile enough to provide a universal private, secure and interoperable RDCT infrastructure for plugging in any and all existing clinical research tools and applications for conducting Trials@Home to accelerate and economize development of medicinal products.
should address the issues and gaps to bring all the scattered activities, technologies, platforms to a higher TRL level by addressing the technical, regulatory, compatibility and acceptability issues that at the moment block endorsement by pharma and hospitals: ▪ Lack of accuracy (compared to clinical instruments) ▪ Data integration (into the workflow of hospitals and pharma) ▪ User friendliness (should be straightforward for non-technical staff and elderly) ▪ Data security and Privacy (most hospitals don't want to have data outside the hospital) ▪ Patch to patch communication (how to prevent latency)
The first attempt to pioneer remote or virtual clinical trial concept was made by Pfizer with their Research On Electronic Monitoring of Overactive Bladder Treatment Experience (REMOTE) trial in 2011. Since then several successful attempts have been mad by Sanofi's (VERKKO trial), Novartis' (NASH trial) & others. These attempts do establish that RDCTs are the future of drug development process, and early adaptors are indeed optimistic about the future. However, these scattered activities did bring forth several technical, regulatory, compatibility, privacy, security, interoperability and of course general acceptability issues, which defy their mainstream adaption by hospitals, CROs and pharmaceutical companies. CLINTOS addresses all of those issues and resolves most of them by developing a low-latency cloud computing ecosystem that's designed to ensure privacy, security and interoperability of the platform, while being easy to use for non-technical staff as well as technically naïve study subjects, and seamlessly integrates and interoperates via APIs with

[12] ECSEL JU Work Plan for ECSEL US Calls of 2020. Version 15. https://www.ecsel.eu/calls-2020-wp2020

[13] Fed4FIRE+ project has received funding under grant agreement No 732638 from the Horizon 2020 Research and Innovation Programme, which is co-funded by the European Commission and the Swiss State Secretariat for Education, Research and Innovation. See https://myxeno.org and https://www.bc5.eu/moonshot/covid.html

[14] Privacy, security & Interoperability-as-a-Service: https://liquidus.info/consortium/

[15] **ZEROV** (**Zero V**ulnerability Computing Devices) **https://www.bc5.eu/ZEROV-Consortium/**

applications that manage the workflow of hospitals, CROs, pharma and EHRs.

Additionally, to improve latency and connectivity issues the CLINTOS framework deploys a novel 4-layered cloud computing continuum we recently disclosed in another project (PSIaaS),[16] and also BLE5 mesh networking protocol, which is currently under testing in an ongoing H2020 (Fed4Fire+) grant.[17]

The proposal should start for the running IMI JU project (Trails@Home) and complement to and extent on the technology scan activity of the project which will identify barriers, enablers and data management for the Remote Decentralised Clinical Trials. In an end-to-end journey, aspects as quality and data integrity, security, connectivity, communication interface, stakeholders' feedbacks such as patients, principal investigators, regulators, sponsors will be assessed over an broad technology range (available or with a validated proof-of-concept) in order to enable a seamless communication, data monitoring and collection from distant location for these RDCT.

CLINTOS is basically an enabling technology platform that can be deployed for remotization of any type of clinical trial, with capabilities of integrating the diverse range of available clinical research tools for implementing procedures that are key to regulatory approval of a medicinal product. CLINTOS consortium already has 3 partners who are also the participants in IMI JU's flagship project- **Trials@Home**, which is driving the RDCT development in EU to the next generation. CLINTOS consortium is also in direct communication with the Trials@Home coordinator and has also won their support (We can provide a support letter from our client(s)). As such, the CLINTOS consortium is in perfect sync with and complements the Trials@Home mission and objectives. CLINTOS components, modules and architecture are designed ground up in alignment with the Trials@Home principles. The joint concept is developed under the scrutiny of Trials@Home partners themselves for quality, data integrity, security, connectivity, communication interfaces that enable a robust seamless communication, data monitoring and collection from distant locations of the study subjects by means of network of sensors, devices, nodes, servers, algorithms and processes.

Thus, enabling all processes, tools, diverse functions and algorithms to run clutter-free and seamlessly, CLINTOS virtually functions as an operating system (OS) for future Trials@Home, making sure all the benefits of RDCT are available to CLINTOS OS users.

1.3 Concept and Methodology

a) The CLINTOS Concept: State-of-the-art and Beyond

Since the first RDCT attempt by Pfizer in 2011 with the REMOTE trial, several attempts have been made to conduct and improve remote trials. Although Pfizer's pioneering attempt failed, it carved the road to the future of clinical trial industry. The failure of Pfizer's remote clinical trial was basically because of the selection of a disease indication that was predominantly in an older age group that was most unlikely to be active on the Internet or social media. While Pfizer's trial had recruitment issues using social media strategies, Sanofi's trial has been successful in recruiting participants using the same strategy. As previously mentioned, a great advantage of the RDCT model is the ability to conduct the trial from a single study site, thereby minimizing infrastructure and overhead costs. Hence, pharmaceutical companies and contract research organizations (CROs) are increasingly looking for ways to lower costs and maximize return on their investment. But, currently, they lack the systems needed to efficiently deal with the large amounts of data collected, and, to do it in a way that is in compliance with GDPR and other regulatory agencies. Nevertheless, inspired by early efforts by Pfizer, Sanofi and others there has been a score of initiatives to build solutions that support aspects of remote trials. The ongoing Covid-19 pandemic has further expedited these fragmented and piecemeal activities.

While there are many innovations that may serve as components of the Trials@Home vision, there's none that provides a complete ICT fabric for any and all kinds of RDCTs, whether validating a therapeutic, preventive intervention or diagnostic accuracy of a diagnostic procedure. Moreover, privacy, security and interoperability (PSI) is the most important attribute of any cloud computing solution, more so when the cloud ecosystem supports any clinical trial setting. Our CLINTOS framework embeds PSI into any CTMS application by default.

Remarque Systems, dedicated to effective trial continuity even during Covid-19, helping trials stay on track and adapt to the existing circumstances. Promeditec offers a Virtual On Site Monitoring (VOS) package that enables you to carry out remote monitoring of your clinical trial, leading to significant reduction in time and cost by

[16] Privacy, security & Interoperability-as-a-Service: https://liquidus.info/consortium/

[17] Fed4FIRE+ project has received funding under grant agreement No 732638 from the Horizon 2020 Research and Innovation Programme, which is co-funded by the European Commission and the Swiss State Secretariat for Education, Research and Innovation. See https://myxeno.org and https://www.bc5.eu/moonshot/covid.html

eliminating the need for monitor relocation. Biosphere claims delivering intelligent clinical trial monitoring services that are in alignment with international compliance standards. Florence claims to go beyond remote monitoring and offer Risk Based, Remote, and Centralized Monitoring in Clinical Trials to advance clinical research through software for managing document and data flow between research sites and sponsors. While Veeva simplifies operations and reduces the administrative burden as much as possible with their Veeva SiteVault for remote monitoring, RealTime CTMS offers remote clinical trial solutions to help your trial stay on track through the pandemic.

Although, these scattered activities do establish that remote monitoring is indeed the future of drug development, the fabric that weaves these piecemeal digital health technologies together seems to be missing. CLINTOS provides that fabric.

1.3a)1. CLINTOS: The Missing Fabric For Integrating RDCT Components:

Once we formulated a comprehensive definition of RDCT and ripped it off to its elements, it became clear how we could use our ICT expertise and prior experience in building our solution for the Trials@Home challenge, particularly our innovations that build: i) decentralized network that ensured privacy, security and interoperability by design, ii) body wearable sensors that securely and anonymously monitored user vitals and mobility parameters, iii) the APIs that allow integration with other third party applications, iv) the end node client interfaces that make the interactions with the ecosystem smooth and seamless. Our CLINTOS concept will be a lot clearer if we first detail the two major subsystems of our solution, which make up the backend and frontend respectively of the CLINTOS framework. But before that it is pertinent to answer the question:

Why "RDCT-as-a-Service" business model for the next generation clinical trials?

1.3.(a)1.1 Benefits of "-as-a-S" Cloud Computing Model

From Amazon's EC2 data storage services to almost everything on the cloud X-as-a-Service (XaaS), the cloud computing market has expanded at a rapid pace. The exponential growth is obviously due to a range of advantages cloud computing provides both for organizations and end-users. Some of those benefits are:

- **Scalability** (outsourcing provides access to unlimited computing capacities, storage space, RAM, etc.): A company essentially can quickly and seamlessly scale its processes up and down depending on requirements without worrying about additional deployments or downtimes)
- **Cost- and time-effectiveness** (no capital expense or delays in setting software infrastructure): Companies don't have to purchase and deploy personal equipment, saving much time and money. A pay-as-you-go model is quite beneficial. Thus "**as-a-service**" model cuts costs and simplifies IT deployments.
- **Flexibility:** Cloud computing helps in distributing workloads across the company and can be remotely accessed by end-users, irrespective of their location. Companies could even hire a global and, perhaps, cheaper workforce when they use cloud computing.
- **Elasticity**: In cloud computing, elasticity is defined as "the degree to which a system is able to adapt to workload changes by provisioning and de-provisioning resources in an autonomic manner, such that at each point in time the available resources match the current demand as closely as possible"
- **Feeds And Facilitates Innovation:** Cloud computing has given businesses an edge that drives innovative solutions that can be implemented speedily and step up motivation within the company.
- **Focus on core competencies** (no need to set up apps and programs or conduct training for employees): Companies can concentrate on their direct duties and achieve better performance.
- **The high quality of services** (professional support and maintenance of IT infrastructure and systems): Cloud computing vendors provide the latest updates, guaranteeing the quality of services.
- **Provides Great Efficiency at a Lower Price:** Cloud computing is very cost-effective as companies need not invest in expensive, heavy infrastructure, making it inexpensive and faster.
- **Minimizes Maintenance Hassles:** Shifting to cloud computing takes away the huge cost associated with the maintenance and upgrade of software, renewal of licenses, maintenance of infrastructure as well as the employment of technically skilled staff for software upkeep. Cloud computing is based on a 'pay-as-you-go' expense model.
- **Increased Resource Sharing:** The resource acquisition and release can be dynamically and cleverly managed.

- **Better Collaboration:** Employees can share files and documents on the cloud. This increases collaboration and reduces unnecessary duplications or generation of multiple versions of documents.
- **Enables Better Backup:** Recovery from disasters such as hardware failures are much faster and have the least impact on the business, due to cloud-based solutions.
- **Better customer experience:** The above-mentioned pros lead to customer satisfaction and increase customer loyalty.

Besides the aforementioned advantages cloud computing facilitates business agility, smoothens business transformations, and can be environmentally sustainable. SMEs tend to benefit the most from cloud computing.

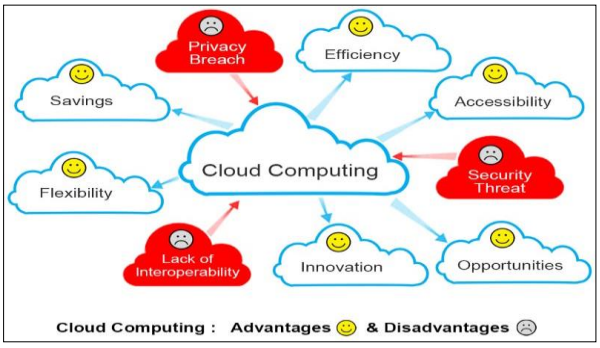
1.3(a)2. PSIaaS (Privacy, Security & Interoperability as a Service): A Radical Thinking:[18]

This project deploys LIQUIDUS[19]**(Linkable Quarantined Internet Data of Unique Subjects)**, a novel network decentralizing technology that solves the hitherto unsolvable cloud conundrum by creating personal online data stores (PODs) that secure user data away from centralized hack-prone legacy servers, and delivers a

comprehensive "Compliance by Design" solution in an easy to deploy ***"-as-a-Service"*** cloud computing model (PSIaaS).

PSIaaS is a novel Web 3.0 cloud-computing ecosystem that disrupts the current status quo in the multibillion Euros cloud computing industry, which remains vulnerable to the triple whammy of privacy, security & interoperability, costing trillions in annual global losses.

Despite its serious shortcomings cloud computing is the preferred business model for most businesses for it many advantages. In 2019, 90% of companies[20] used one or the other cloud computing service. Data centers will handle 94% of the global workload in 2021. Cloud Computing's "**-as-a-Service**" model is projected to hit $623 Billion by 2023. It is such a hot tech category that Forbes runs a special Cloud 100[21] series on top 100 cloud computing companies since 2016. NIST defines Cloud Computing[22] as:



"a model for enabling ubiquitous, convenient, on-demand network access to a shared pool of configurable computing resources (e.g., networks, servers, storage, applications, and services) that can be rapidly provisioned and released with minimal management effort or service provider interaction."

Trends indicate that usage of cloud computing among businesses is fast approaching 100%, and not sparing the health industry – ***"the cloud is igniting the clinical trial revolution."***[23]

The PSIaaS project expands the current cloud continuum horizontally & vertically from current 3-layered continuum to a more secure 4-layered continuum based on a "Compliance by Design" architecture that adds

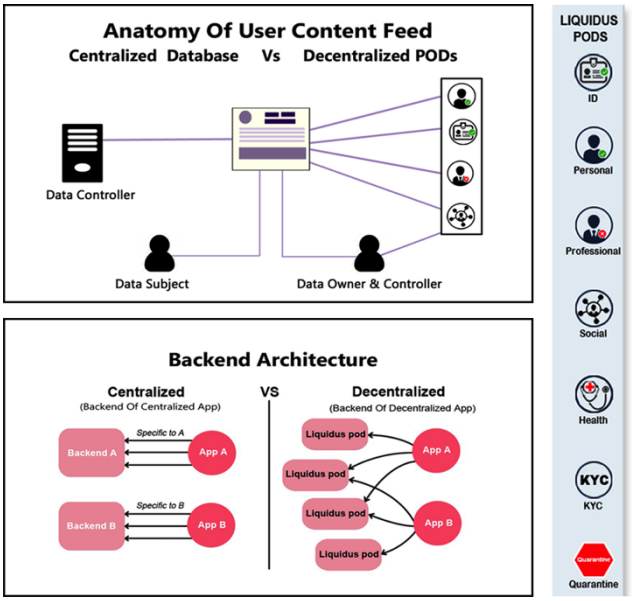
[18] Privacy, security & Interoperability-as-a-Service: https://liquidus.info/consortium/
[19] LIQUIDUS is based on SOLID (Social Linked Data), an open source project conceptualized by Tim Berners Lee, the inventor of Web: https://www.csail.mit.edu/research/solid-social-linked-data
[20] https://hostingtribunal.com/blog/cloud-computing-statistics/#_blank
[21] https://www.forbes.com/cloud100/#_blank
[22] https://csrc.nist.gov/publications/detail/sp/800-145/final#_blank
[23] https://www.cleardata.com/news/cloud-clinical-trial-revolution/

privacy, security & interoperability (PSI) to any legacy cloud service in a PSI-as-a-S model to federate a multi-cloud ecosystem. PSIaaS achieves this by deploying **LIQUIDUS** technology that creates user-friendly decentralized **p**ersonal **o**nline **d**ata **s**tores (**PODs**) for users & makes such personal data available to any app that needs it via an API at the user's behest, enabling PSI by default in the world's first commercially viable PSI-as-a-S business model. The LIQUIDUS innovation is user friendly providing seamless service environments for end-users, who need no extra training or extra steps than they are conventionally used to in classical IT systems. In delivering PSIaaS, LIQUIDUS creates new opportunities for developers by providing them APIs to integrate PSI into new cloud apps they develop or upgrade any existing service for GDPR compliance. However, the biggest beneficiaries are companies that use cloud computing to service their customers, and spend large amounts in retaining full-time compliance teams vis-à-vis PSIaaS. Almost all companies providing clinical trial services are cloud-based. Therefore, with GDPR in force the timing for PSIaaS cloud infrastructure adaptation is opportune across all sectors, particularly when we are developing the next generation infrastructure for future clinical trials.

In current state-of-the-art, storing, processing, sharing freely without the need of a centralized data controller is inconceivable in any cloud-computing ecosystem. Currently all data storage, processing, sharing is centralized with little or no user control. Like all other privacy laws, EU's recent GDPR assumes that personal data[24] of a "data subject" will always be controlled by a "data controller" & processed by a "data processor". Nevertheless, the GDPR mandate puts data subjects in control of their personal data with more stress on the sensitive personal data[25]. All references to personal data limits to its GDPR / EC definition, and explicitly excludes gigabytes of data that users accumulate or save during their online activities.

1.3(a)2.i Anatomy Of The Decentralized Private, Secure and Interoperable (PSI) PODs

There is a prominent difference between the architecture of conventional databases and Liquidus powered PSIaaS framework. While in traditional centralized databases all content of users is stored in a single centralized server, PSIaaS platform creates separate personal online data storage (PODs) for each unique user. Such PODs can be stored either locally at an End Node (client node) or at any remote location of user's choice. The PODs can be linked to any application via APIs in such a way that the corresponding application interface does not exhibit any difference between the data retrieved from that application's own centralized server and the data served from a remote POD location. User data populates the application only if the user authorizes the access via API, and only to the extent and time period the user authorizes the data access.



The advantage of keeping the PODs at the client computer or End Node is that the data becomes available without latency only when the user is online. But the disadvantage is the inaccessibility of the linked data 24/7. The disadvantage may also be the permanent loss of data on account of any adverse event at the End Node. In a practical PSIaaS implementation this is remediated by provisioning backup PODs in the cloud within the PSIaaS remote server.

LIQUIDUS not only puts users in full control of their personal data, but also transforms a "**data subject**" to "**data owner**." Liquidus' "**Compliance By Design**" architecture is GDPR compliant, freeing companies, CROs, clinical trial sponsors, hospitals and other cloud service providers from liability, as they don't control the user

[24]**GDPR's Art 4(1) defines** '**personal data**' means any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person.

[25]**European Commission** considers the following personal data as 'sensitive' and is subject to specific processing conditions:

- personal data revealing racial or ethnic origin, political opinions, religious or philosophical beliefs;
- trade-union membership;
- genetic data, biometric data processed solely to identify a human being;
- health-related data;
- data concerning a person's sex life or sexual orientation.

data at all.

The following figures illustrate the frontend and backend architecture of the basic decentralized POD design. The users can create as many PODs as they desire depending on the type of personal data ranging from personal profile, self-sovereign identity, professional profile, social data, health data, etc. Such user-controlled segregation of personal data away from a service provider's central database, not only protects user's privacy, but also has beneficial impact on the security and interoperability of the data as discussed in subsequent paragraphs.

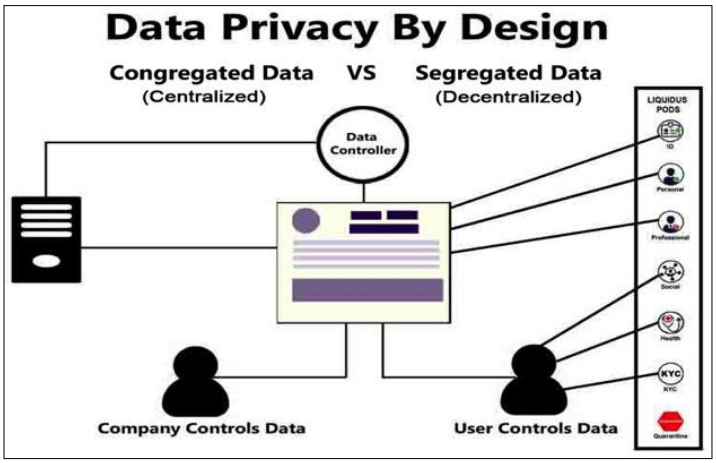
Taking cue from the legendary Sir Tim Berners-Lee's work on privacy via socially linked data (SOLID)[26] secured in personal online data stores (PODs), we extended the concept of decentralized segregation of user data, beyond privacy, and designed it as a cloud computing service to federate with any third party cloud solution to render it GDPR compliant. Collectively, these concepts create an ecosystem that is very extensive, encompassing pretty much every activity that is performed on the Web, basically qualifying PSIaaS as a key **Web 3.0** enabler. These breakthrough concepts are herein discussed in some detail.

Privacy By Design

Since 1995, "**Privacy By Design**,[27]" has been a very compelling concept for protecting user privacy on the Web. But, in well over two decades of its existence, no one ever succeeded in creating a commercially viable software that had privacy built in as default. It is only recent advances in decentralization that have made it possible to get rid of the root cause of privacy breaches – centralized databases.

While developing the Liquidus concept, we aimed to accommodate all the 7 principles of "**Privacy By Design**" originally conceived and developed by Ann Cavoukian[28] and formalized in a joint report on privacy-enhancing technologies[29] by a joint team of the Information and Privacy Commissioner of Ontario[30] (Canada), the Dutch Data Protection Authority[31] and the Netherlands Organization for Applied Scientific Research[32] in 1995. Here are those principles:

1. Proactive not Reactive, Preventative not Remedial
2. Privacy as the Default
3. Privacy Embedded into Design
4. Win-Win For All, No trade-offs
5. End-to-End Security
6. Visibility and Transparency
7. Respect User Privacy



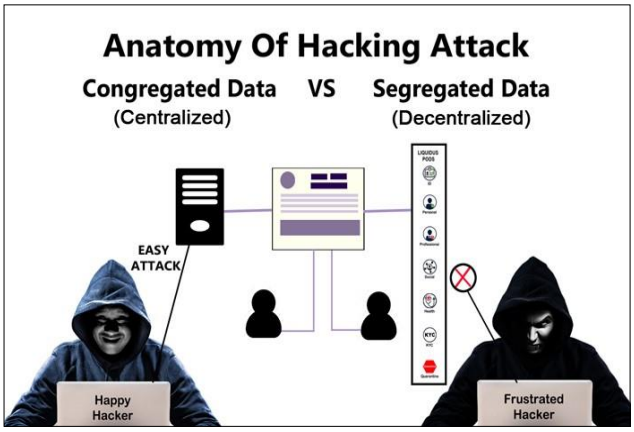
Liquidus creates decentralized personal online data (POD) storage for user, and makes such personal data available to any app that needs it via APIs at user's behest, enabling data privacy, security & interoperability by design. Liquidus PODs can be hosted wherever the user desires, and any app can be authorized to request the data. The user retains complete ownership and control of data in the PODs: what data each pod contains, where each pod is stored, which data is quarantined, and which apps have permission to use the data. This does not mean that the users are burdened with any extra complexities of managing their personal data. The ecosystem operates autonomously once users authorize data access. It's no more hassle than users are currently used to.

Security By Design

Security by design means that the software has been designed from the foundation to be secure, wherein security is built in the system from the ground up and starts with a robust architecture design. In the conventional approach design decisions are often based on well-known security tactics, and patterns defined as reusable

[26] https://solidproject.org/
[27] https://iapp.org/media/pdf/resource_center/Privacy%20by%20Design%20-%207%20Foundational%20Principles.pdf
[28] https://en.wikipedia.org/wiki/Ann_Cavoukian
[29] https://en.wikipedia.org/wiki/Privacy-enhancing_technologies
[30] https://en.wikipedia.org/wiki/Information_and_Privacy_Commissioner_of_Ontario
[31] https://en.wikipedia.org/wiki/Dutch_Data_Protection_Authority
[32] https://en.wikipedia.org/wiki/Netherlands_Organisation_for_Applied_Scientific_Research

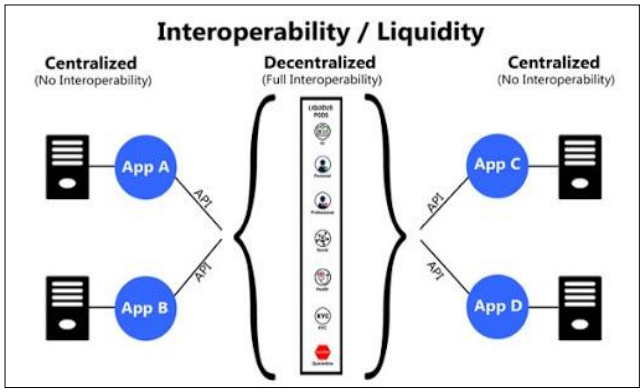
techniques for achieving specific quality concerns. However, this approach assumes that the user data, as a rule, will always be collected, congregated and centralized at a single server location controlled by data controller.



However, our approach in building the concept took a complete 360 degrees departure from the universal assumption that **all user data will always be residing in centralized data servers**. If we dispose of that notion and rethink the user-data-company relationship all over from the ground up, then all the known security tactics become irrelevant. And, our concept design for a robust decentralized cybersecurity solution that disincentivizes a data hacker by disenfranchising the conventional data servers from holding any of the user data becomes straightforward.

Interoperability / Liquidity By Design

Data liquidity is a new concept signifying seamless flow of consumer data **'to where it is needed and when it is needed'** throughout a given ecosystem, as a function of data portability. Data on the Internet mostly exists in silos with very limited ability to move. Interoperability of data, particular in healthcare industry is crucial in saving hundreds of billions in added costs. Besides breaking the data silos, introducing semanticity into the interoperable data is an important function of interoperability.



As much as service providers / vendors harbor an epic misunderstanding[33] on ownership rights of consumer data, it is the consumer who owns it. Data portability / interoperability / liquidity in our current centralized systems, particularly in **EHR** (electronic health records), is prone to compromising privacy / confidentiality during data exchange between third parties. Liquidus breaks the silos and makes the personal data easily accessible to diverse databases in a structured logical.

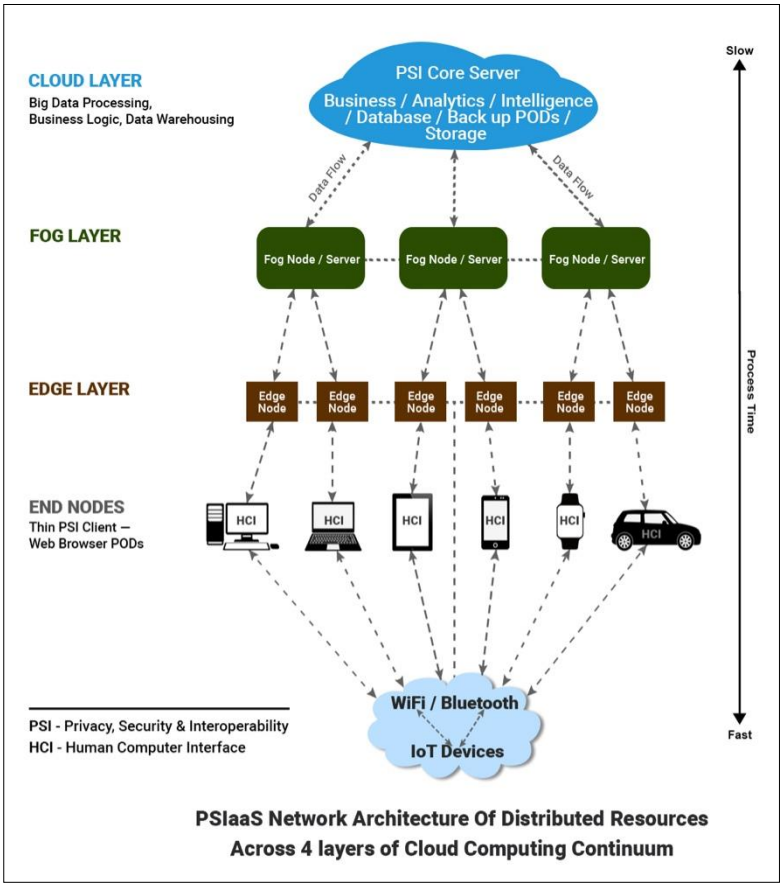
1.3(a)2.ii. Four-Layered PSIaaS Network Architecture

As part of cloud computing continuum, both fog and edge computing systems shift the processing of data closer to the source of data generation. The main focus of doing so is to reduce the amount of data sent to the cloud. Therefore Fog & Edge[34] computing brings processing close to the data source improving the speed and performance of data transport. This helps in decreasing latency and thereby improving system response time.

Traditionally, client computers (End Nodes) in general and web browsers in particular haven't had much role in sharing computing responsibilities within a cloud continuum other than just as user interfaces. As much as the industry talks about the core, the fog, the edge and even the last mile of the cloud-computing continuum, it mostly ignores resources at the End Node or web browser at the client computer that can be exploited to privacy, security and the interoperability of cloud computing. In the conventional cloud continuum, it is considered no more than a user interface that comes with plenty of *End Node Problems*[35], actually warranting its exclusion from the continuum. On the contrary, we demonstrate that End Node resources can be beneficially exploited to ensure user privacy, security and interoperability. In the PSIaaS network design of the cloud-computing continuum; it is no less important than the servers that have always been the principle focus of the core, the fog or the edge of the cloud computing architecture.

[33] https://www.cio.com/article/3346022/the-great-conundrum-of-data-liquidity-in-healthcare.html
[34] https://www.cisco.com/c/en/us/solutions/enterprise-networks/edge-computing.html#_blank
[35] https://edgeinducedcohesion.blog/2015/04/24/the-end-node-problem/

To maximally leverage a cloud-computing continuum, integration of resources at the core, at the edge, at the End Node and along the data path is imperative to support dynamic and data-driven application workflows. However, the cloud-computing continuum of prior art ignores the EN client, although client interface could be an important computing resource besides the cloud, fog or edge servers themselves.



The End Node or the HCI, or the client, or the web browser isn't just an epicentre of Web 3.0, but as equal a component of the cloud-computing continuum, as the data servers in the cloud, fog or edge are. The problem is, cloud companies do not see EN / HCI/ client web browser as another home for implementing and anchoring cloud computing resources that can empower the user and actually secure the client end of the continuum. One possible reason, as indicated by the cloud innovation trends, is that cloud computing innovations are mostly hardware driven, engineered by hardware companies that market servers, routers and switches. Their motivation to innovate is to sell hardware such as routers and switches, rather than deal with the End Node software, which in any case is considered as a problem and risk to the security of the cloud network. Companies often prohibit their employees accessing their corporate portal using any computer other than authorized by the company because of the ***End Node Problems***. No wonder, the fog & edge computing terms were coined by Cisco[36], the networking hardware major. Contrary to the convention, we believe whether it is enabling the Web 3.0, or resolving the PSI Triple Whammy, the solution mostly lies in including End Node or the client end of the last mile within the cloud continuum. Not just the edge, but at the termination of the edge—the End Node (client device). It not only extends the continuum beyond the edge nodes but also resolves the End Node Problem, by securing the client computer.

The extended four-layer Cloud-Fog-Edge-EndNode infrastructure of the PSIaaS ecosystem serves as a foundation for a complete computing continuum that's capable of federating infrastructures, programming applications and services, and composing dynamic workflows. Because of its network architecture that redistributes resources across four layers, the PSIaaS ecosystem is *resilient, energy-efficient and* capable of efficiently reacting in real-time to unpredictable data sizes, availability, locations, and data transmission rates. This will provide **application developers** with greater control over network, computing and data infrastructures and services, and the **end-user will benefit from seamless access to continuous service environments**.

PSIaaS' four-layered architecture and its Compliance by Design ecosystem thus not only optimizes performance on all fronts but responds to the future digitization needs of industry and the public sector, and significantly contributes to the technological ambitions of the Next Generation Internet (NGI).

1.3(a)2.iii. Redefining Data Ownership: LIQUIDUS is a radical new way to reclaim the user's privacy and security that has been under siege from technology for eons. PSIaaS is based on the vision of Sir Tim Berners-Lee, the inventor of the World Wide Web. PSIaaS is advancing his original approach to ensuring privacy of personal data on the Web, to data protection against security breaches, and the much-ignored interoperability of the traditional silos of databases via a versatile PSIaaS cloud computing service.

Like all other privacy laws, EU's recent GDPR assumes that private data of a "**data subject**" will always be controlled by a "**data controller**" and processed by a "**data processor**." However, its mandate puts data subjects

[36] https://www.cisco.com/c/en/us/solutions/enterprise-networks/edge-computing.html#_blank

in control of their personal data.

We defined LIQUIDUS (**L**inkable **Q**uarantined **I**nternet **D**ata of **U**nique **S**ubjects) as:

> **Liquidus is a decentralized user-controlled linkable personal online data storage (PODs), the software architecture of which is designed to provide data privacy, security and liquidity by default.**

So basically, it's a personal data storage system that's decentralized and made linkable to any other piece of data, at the behest of the user who owns the data. Cloud computing has its origin in data storage services. Hence let's look at the four essential elements that define Liquidus in the context of cloud computing from historical perspective.

i) Personal Data Storage: If we look at the history[37], we find that CompuServe made the very first effort at cloud storage in 1983, offering its consumers a small amount of disk space to store any files they chose to upload. This was followed by PersonaLink Services, launched by AT&T in 1994. But, the real cloud storage was first introduced by Amazon in 2006 as Amazon Web Services, which gained widespread popularity eventually moving much of the Internet onto "cloud storage". Most of the apps we use on a daily basis have our data stored in server farms owned by Amazon, Google, or Microsoft. The cloud storage industry is now on track to reach $100 billion in next few years. Data storage can either be decentralized, semi-decentralized, or hybrid.

ii) Decentralized: The trend began with the release of blockchain software by Satoshi Nakamoto in 2009. Since then, developers have increasingly turned to decentralizing their apps including the cloud storage as a way to avoid censorship, server outages, and hacks. Decentralized storage is where data is stored on a decentralized network, across multiple locations by users who are incentivized to join, store, and keep data accessible. People, rather than a single company host the computers serving decentralized storage. Decentralized storage imposes no restrictions and data is stored on random nodes; semi-decentralized storage selects a subset of nodes responsible for storage and management of data of all the users of the system; the hybrid approach relies on third-party storage such as public cloud providers. Decentralized storage first caught global attention when Filecoin raised $257 million[38] in a record breaking ICO in 2017 for commercializing IPFS (Inter Planetary File System), the decentralized storage protocol first released in 2015. Some of the decentralized storage providers that followed are Sia, Storj, Swarm, etc.

In a 2017 paper, Pham et al suggest that a decentralized architecture[39] may be a promising solution for preserving privacy in social networks. However, most decentralization protocols still face major usability challenges, particularly those features that suite following scenarios in legacy systems:

- **Searchability**: Searching through all the users of the network may not be as seamless in decentralized networks as in the legacy systems, such as LinkedIn, Facebook, because availability of data may not be guaranteed in some decentralized networks.
- **Discoverability**: Recommendations or discovery of people with common interests is another area that relies on central indexing and aggregation but is not practical in decentralized networking scenarios.
- **Faking**: Fake profile/content detection becomes much more difficult in decentralized settings because data is distributed which makes detecting patterns and anomalies a lot complicated compared to centralized systems.
- **Differential Privacy**: Differential privacy (DP) is a strong, mathematical definition of privacy in the context of statistical and machine learning analysis. According to this mathematical definition, DP is a criterion of privacy protection, which makes it possible for tech companies to collect and share aggregate information about user habits, while maintaining the privacy of individual users. This is because whenever the data are aggregated for statistical or predictive purposes and becomes public, not only does the single piece of data remain private, but even a small perturbation on the public data cannot make a potential adversary infer too much about a single individual. But DP can also be breached as evidenced by the Netflix hack in 2006-7.[40] Such breaches can also happen in decentralized systems especially when the data are aggregated for statistical or predictive purposes.

[37] https://en.wikipedia.org/wiki/Cloud_storage
[38] https://www.coindesk.com/257-million-filecoin-breaks-time-record-ico-funding
[39] https://digital-library.theiet.org/content/journals/10.1049/iet-net.2017.0137
[40] https://www.diva-portal.org/smash/get/diva2:1113852/FULLTEXT01.pdf

LIQUIDUS, however overcomes those shortcomings of the current decentralized networks.

iii) Linkable: Almost a decade ago at MIT's Computer Science & Artificial Intelligence Lab (CSAIL), the inventor of World Wide Web, Sir Tim Berners-Lee conceived the idea of personal data storage space in the cloud that could be linked to any application. The academic idea took the shape of SOLID (socially linked data)[41], which was released in 2016 as an open source platform. It differed from other decentralized storage in that it could be linked to any application through API ensuring data subject's data ownership and privacy.

Linked Data is nothing but a set of best practices prescribed for how data is structured, published and linked to an application, and made discoverable. In any case, not all data is created at the same place, but Web standards can help build a Web of Data or the Semantic Web.

Presently, Linked Data is based on two central pieces: RDF and HTTP. RDF (Resource Description Framework), which is semantic extension of OWL (web ontology language), is a W3C Recommendation that allows expressing facts using triples. More on RDF, OWL and semantic web in Methodology section (Section 1.3. (b) 2.i Application Development)

iv) Who Owns The Data? One, who collects, stores and processes it, or own who is the subject of that data? The data controllers often think that they own the data. Even **GDPR** (General Data Protection Regulation) is ambiguous on the data ownership. But, what does follow from the GDPR however is that data subjects should be in control of their personal data. This project categorically places the ownership of personal data in the hands of the subject of the data.

Thus, integrating the PSIaaS backend architecture into the CLINTOS platform not only ensures compliance with privacy and security, but also provides a universally compatible fabric that enables all third party applications to be seamlessly plugged in and operated interactively with rest of the subsystems of the CLINTOS ecosystem for enhancing the RDCT experience.

1.3(a)2iv. Enabling PSI by Default Enables "Universal Compliance by Design (UCbD)"

Although "Compliance by Design" has been a concept in the minds of cloud developers for quite some time, it remains a theoretical compliance continuum of six compliance positions[42] that range from *Avoidance, Ignorance, Knowledgeable Non-Compliance, Approaching Compliance, and Establishing Compliance.*

The concepts described in the previous sections, collectively, form the building blocks of an ecosystem that makes **Universal Compliance by Design (UCbD)** possible. Patient / CT participant can create as many PODs as required to comply with the HL7 / EEHRxF standards, or as required by GDPR/CTR or other local regulations. Such patient-controlled segregation of personal CT data away from the CT sponsor or CRO's central database, not only protects user's privacy, but also has beneficial impact on the security and interoperability of the data, which are the building blocks of any regulatory requirement as discussed herein.

Clinical trials are highly regulated by international (GDPR & CTR) as well as diverse national regulations. Therefore, implementing regulatory compliance is a highly heterogeneous concept, varying widely with jurisdictions and regulatory regimes. Within the constrains of the centralized legacy systems, homogenizing and universalizing compliance is inconceivable. However, in the context of patient data logistics, regulations of different states predominantly rely on patient data integrity, protection, ethics and the state interest. Universal compliance can be potentially built around the decentralized PSI framework deployed in the CLINTOS ecosystem. That's what this project seeks to build. In doing so, it redesigns the legacy cloud continuum, and transcends the state-of-the-art in many respects. While a true technological 'universal compliance by design' solution is completely missing in the prior art, there are quite a few EU-funded (Horizon 2020) projects that focus on catering to the rapidly growing need to move data ownership and control to the patients.

Privacy is our fundamental right. It is explicitly stated under Article 12 of the 1948 Universal Declaration of Human Rights. It has been defined as[43]:

"The right to control access to one's personal information," or "the right to be in control of how the information flows"

[41] https://en.wikipedia.org/wiki/Solid_(web_decentralization_project)
[42] https://jhengstler.wordpress.com/2014/04/24/the-compliance-continuum-fippa-bc-public-educators/
[43] https://www.researchgate.net/publication/294836170_Social_Media_Privacy_A_Facebook_Case_Study

As most regulations are designed to protect the rights of patients, and balance it with public interests; privacy, security and interoperability (PSI) of the patient data becomes the mainstay of any regulatory policy that upholds data integrity / protection, and meets the rigors of ethics. If PSI is technologically dealt with, the other norms are automatically met within the architectural design of the conceptual framework of CLINTOS. Thus CLINTOS has the potential to automatically comply with the core requirements of any regulation irrespective of their jurisdiction. The capabilities of CLINTOS architecture to federate additional protocols / procedures as modules or standalone apps in a multi-cloud setting makes CLINTOS ecosystem 100% compliant across all jurisdictions.

1.3(a)2v. UCbD Vs Rule/Policy Based Compliance: As much as CLINTOS project deploys a radical data decentralization approach that makes patients, the ultimate owners and controllers of their personal data, it provides UCbD by default. In the centralized legacy systems what makes implementing PSI difficult, cumbersome and expensive is that it's rule / policy based approach that warrants 24/7 monitoring by a dedicated team. Integrating LIQUIDUS tech as cloud architecture into CLINTOS platform not only ensures PSI compliance, but also provides a universally compatible fabric that enables all third party applications to be seamlessly plugged in and operated interactively with rest of the subsystems of the CLINTOS ecosystem for empowering the clinical trial participants with full and complete control of their personal data.

Thus, our **"CLINTOS"** ecosystem not only makes RDCTs homogenously compliant across all jurisdictions, but embeds universal compliance in all third party applications that run within the CLINTOS ecosystem.

1.3(a)2vi. Does Study Subject's Total Control & Ownership Of Data Undermine Sponsor/State Interests?

A cursory read into the CLINTOS' network architecture and it's radical approach to make study subjects owners and controllers of their personal data, may give an impression that CLINTOS will strip the study sponsors / medicinal product developers or so called data controllers / owners of the legacy systems of their right to the clinical trial (CT) data. A detailed analysis of the new regulations pertaining to clinical trials in Europe will greatly help us in comprehending the intricacies in answering the question:

> *Whether decentralizing the clinical trials data, and making study subjects owners and controllers of their personal data will deprive the clinical trial sponsors and stakeholders of their right to the CT data?*

So, here's a brief overview of the applicable clinical trial (CT) regulations.

The new US/European policy[44] initiatives and new legislation, such as the European Medicine Agency (EMA)'s Policy 0070 and the European Union (EU)'s new clinical trial regulation (CTR) 536/2014,[45] have considerably increased public access to clinical trials data (CTD). The new disclosure rules[46] not only encompass the results of clinical studies, but also pertain to GDPR[47] mandated privacy and anonymized patient-level data and other detailed information from clinical trials' dossiers. In simple terms, CTD transparency implies that decisions and data from clinical studies are widely shared with other researchers, clinicians, and the public. These new initiatives are generally perceived as much welcomed developments for the enhancement of science, scientific collaboration, trust, and open innovation. While in line with the increased openness in the private and public sector, these developments also highlight concerns about how to balance the intrinsic tensions between closed and open innovations.

There's absolutely no doubt that study sponsors, who invest in the clinical trials, or states that uphold public interest, have legitimate interest in the research data that clinical trials generate. That's as fundamental as study subjects' rights to their own data under GDPR or CTR and would be a fairly valid concern that would never let any concept that's contrary to those interests takeoff. But, that's absolutely not the case. On the contrary CLINTOS' personal data handling not only empowers the study subjects, but also safeguards sponsor interest and public interest in the research results that clinical trials deliver. Just because study subjects become owners of

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[44] EMA (2014) *EMA policy on publication of clinical data for medicinal products for human use*, POLICY/0070, EMA/240910/2013, (London, UK; pubd online Oct 2014)

[45] Regulation (EU) 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (referred hereafter as 'Regulation (EU) 536/2014').

[46] Timo Minssen, Neethu Rajam, Marcel Bogers, Clinical trial data transparency and GDPR compliance: Implications for data sharing and open innovation, *Science and Public Policy*, scaa014, https://doi.org/10.1093/scipol/scaa014

[47] The EU's General Data Protection Regulation (GDPR) entered into force on 25 May 2018. It replaces the EU's previous legal framework that dates back to 1995; while retaining the overall regulatory approach of its predecessor, the GDPR also introduces a number of new compliance obligations, including higher sanctions than those available under the previous framework.

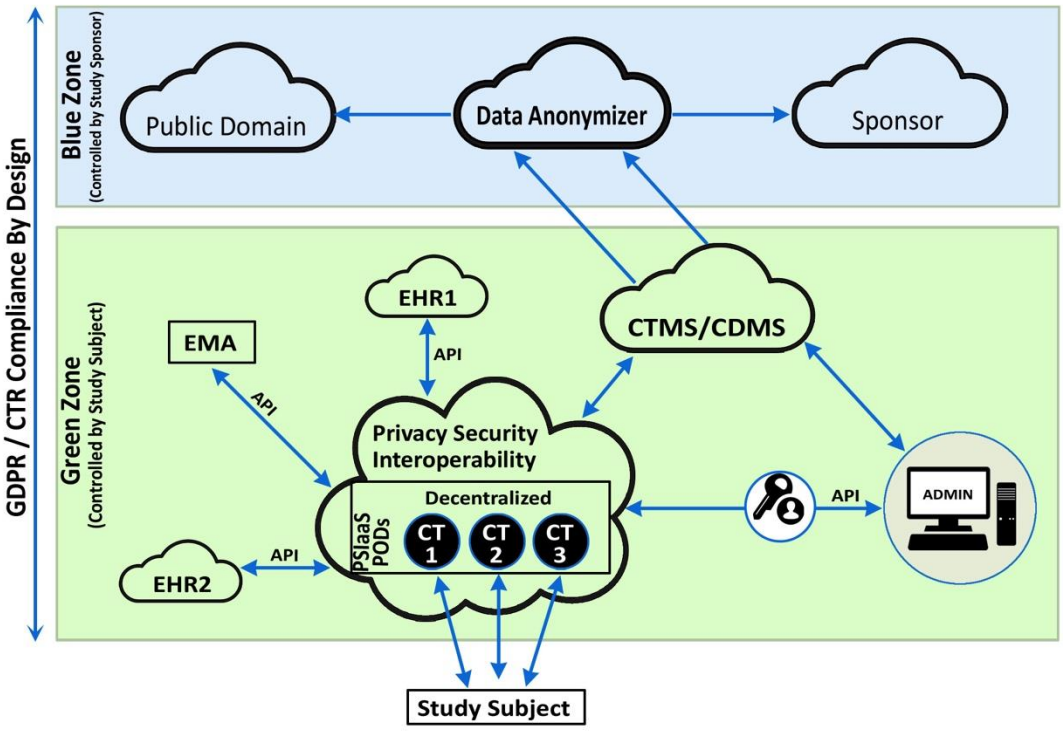
their personal data in CLINTOS ecosystem, does not mean that sponsors have to relinquish their rights to use the data for the product approval. So, how does CLINTOS balance study subjects' rights against sponsors / states' rights? It does, and does it better than any legal system.

The decentralized CLINTOS framework is designed for GDPR compliance by design. Any personal data that pertains to citizens has to be GDPR compliant. However, GDPR regulations were written assuming that data controllers will always process all data, and users will always be data subjects. This is because the state-of-the-art at the time did not put forth the possibility that data can be fully owned and controlled by users and there may not be any need for a data controller or data processor. So the GDPR mandate was to enforce citizen privacy via implementing privacy rules, policies and protocols rather than have it technologically built into the solution. For the same reason the CT's sponsors' handling of the CT data is tightly regulated, because the data is centralized under sponsors' control, and beyond the control of the study subjects. Conversely, such tight regulations will be redundant if a technology made users owners, controllers and decision makers of their personal data on one hand, and gave CT sponsors unflinching and unrescindable rights on the other. Access to data can be guaranteed with smart contracts that are not rescindable. This is explained in the following paragraphs.

Conducting clinical trials is a lengthy, risky, and expensive process involving huge investments with often fairly low success-rates. Any intervention that places that investment at risk will not fly. By decentralizing the data of the study subjects and bestowing them with full data ownership and control, CLINTOS is not depriving study sponsors, hospitals, CROs of the data they invested in or leaving them at the mercy of study subjects, but just opening up new possibilities that create Win-Win situation for all the stakeholders.

As far as informed consent is concerned, whether CTR or GDPR, study subjects can withdraw consent at any time, so there is nothing new here. In EU, if study subjects withdraw half way in the clinical trial, that data may be subjected to study subjects right to be forgotten (Article 17, GDPR), and may be a loss to the sponsor and to the state, unless of course they can establish "public interest" exception that Article 17 provides. However, the public interest exception is not a blanket right that universally applies to all CT scenarios. For example, it didn't apply in the recent Covid-19 contact tracing apps issue for containing the pandemic. In the context of Covid-19 pandemic, the Counsel of Europe still upheld citizens right to privacy over public interest tracing citizens infected with the pathogen, clearly stating that,

> *"Users of the digital tracing system must not be directly identified, and digital contact tracing systems should only use unique and pseudonymised identifiers, generated by and specific to the system. Those identifiers must be renewed regularly and must be cryptographically strong."*
> https://rm.coe.int/covid19-joint-statement-28-april/16809e3fd7 page 6.



If the data is anonymized, the privacy regulations are not applicable. Simply put, GDPR's Article 17 "public interest" exception may acknowledge sponsor's / state's right to the study data, but it does not prevent the study subjects from litigating their Article 17 right to be forgotten in a court of law. On the other hand, in CLINTOS' PODs system, if the study subjects refuse to authorize their personal data in the middle of a CT, all may not be lost or at least may not be a subject of debate or resource consuming litigation. This is because the CLINTOS ecosystem will segregate the personal data obtained from the study subject into two zones. When the data stays in Green Zone, it is fully controlled by the study subject, but once it flows into Blue Zone it is anonymized by the system, and by default relegates beyond the scope of GDPR, and study subjects cannot deprive CT sponsor / state claiming GDPR privileges. Whether, it is CT sponsor or state, their legitimate interest in study data is still met as GDPR does not apply to anonymized data, and unanonymized data of study subjects personal nature in any case does not serve any legitimate public interest purpose.

Hence, contrary to any spontaneous perception that disenfranchisement of the clinical trial sponsors and pharmaceutical companies from ownership of study subjects' personal data that CLINTOS ecosystem implements will harm their interests is misplaced. It will actually work to their advantage by eliminating any ambiguity that exists in legacy systems that place the erstwhile data controllers at risk of liability and protects their rights, securing them from any risk of legal contest by privacy advocates.

1.3(a)3. The CLINTOS SmartHub of 8 Vital Signs:

While PSIaaS builds the decentralized, secure, privacy-preserving and interoperable backend fabric of the RDCT that provides sort of an RDCT operating system for the diverse and scattered applications that services RDCTs, the second major subsystem that completes the CLINTOS ecosystem is a wearable SmartHub with sensors that securely and anonymously monitor user vitals, mobility parameters and treatment adherence / compliance, which are the key measurable variables in almost all clinical trials. It does it all in real time, a huge advantage over the legacy processes.

Traditionally **Vital signs** (also known as **vitals**) are a group of the four to six most important medical signs that indicate the status of the body's vital (life-sustaining) functions. These measurements are taken to help assess the general physical health of a person, give clues to possible diseases, and show progress toward recovery. More the number of vital signs recorded, the better. In the state-of-the-art this depends on the ease and ability to record those signs.

The Seventh Vital Sign: In a recent expert analysis report, Magid & Ho proposed a 7th vital sign[48] – Medical adherence. It is defined[49] as the "*active, voluntary, and collaborative engagement of the patient in a mutually acceptable course of behavior to produce a therapeutic result.*"[50] In simple terms it is patient's medication-taking behavior and the degree to which a patient follows the prescription regimen that was mutually established with his or her health care provider.[51] While medication adherence can vary from total noncompliance to perfect adherence, prior studies suggest that overall patient adherence to medications is about 50%.[52] As medication non-adherence is common in real life scenarios, it is also important in various clinical trial scenarios, and therefore an essential component of the CLINTOS infrastructure.

The Eighth Vital Sign: Heart rate variability (HRV) is fast emerging as a sensitive diagnostic / prognostic aid for several morbid conditions.[53] HRV is the beat-to-beat variation in either heart rate or the duration of the R-R interval. These temporal fluctuations in heart rate exhibit a marked synchrony with respiration (increasing during inspiration and decreasing during expiration—the so called respiratory sinus arrhythmia), and are widely believed to reflect changes in cardiac autonomic regulation (Billman, 2011). Accordingly it has become a popular clinical and investigational tool (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996; Billman, 2011). In 2016, the term "heart rate variability" yields nearly

[48] Delamater AM. Improving patient adherence. *Clin Diabetes* 2006;24:71-7.
[49] Meichenbaum D, Turk DC. *Facilitating Treatment Adherence: A Practitioner's Guidebook*. New York, NY: Plenum Press; 1987.
[50] Delamater AM. Improving patient adherence. *Clin Diabetes* 2006;24:71-7.
[51] Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med* 2005;353:487-97.
[52] Nieuwlaat R, Wilczynski N, Navarro T, et al. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2014;11:CD000011.
[53] Sammito, Stefan; Bockelmann, Irina. Factors influencing heart rate variability. International Cardiovascular Forum Journal, [S.l.], v. 6, may 2016. ISSN 24093424.

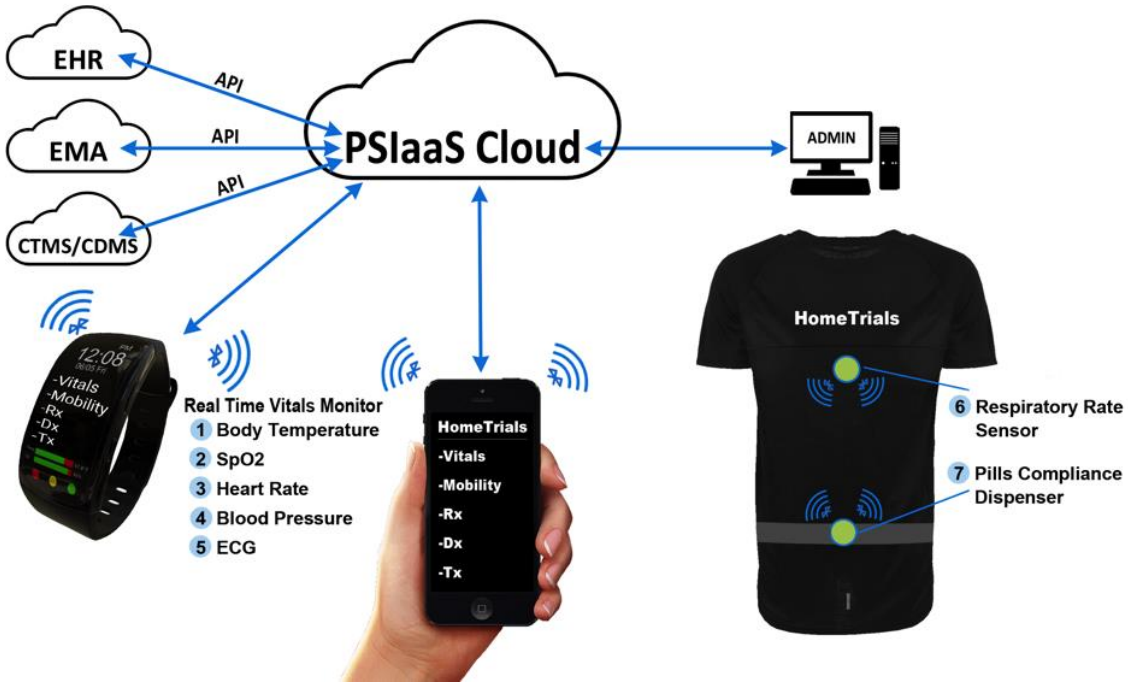
18,000 “hits” when placed in the pubmed search engine. Today it is 49,000. A search for “heart rate variability” on the clinicaltrials.gov site brings up 1901 registered trials as compared to other popular markers such as “pulse oxymetry” (1109), “SpO2” (1109), Xray chest (1634).

The role of HRV in clinical investigational evaluation of a new pharmaceutical agent is particularly important, as it is a very sensitive marker of cardiotoxic and neurotoxic effects of a new investigational drug. Providing HRV analysis in real time as a core feature of CLINTOS brings tremendous advantages to RDCTs conducted using the CLINTOS ecosystem.

The CLINTOS’ SmartHub subsystem goes beyond the state-of-the-art, and makes it possible to record all the vital signs including the new, so called, 7th and 8th vital signs, and that too remotely in real time in any RDCT setting. It constitutes of two IoT wearable modules:

i) the core SmartHub, which records 6 vital signs and operates as epicenter of the CLINTOS ecosystem, and,
ii) an auxiliary Smart T-Shirt, which assists in recording the remaining 2 vital signs.

These wearable modules and their networkability within CLINTOS infrastructure are illustrated in the following illustration:



The CLINTOS SmartHub’s Capability To Record Eight Vital Signs

1.3(a)3.i The Core SmartHub: Evolution and Technical Specifications

Our expertise in building privacy, security and anonymity into wearable IoT devices dates back to 2017, when XENO IoT entered and reached semi-finals of the global $1 million Xprize foundation global challenge for a Women’s Safety Device. Since then the original wearable device has evolved and its variants are currently under development in at least two ongoing H2020 funded projects (XENO & COVID). Another H2020 consortium is also deploying the features of the COVID wearable device to build a holistic solution for an H2020 call that addresses first responder needs: **MOONSHOT** (**M**ishaps & **O**minous **O**rdeals **N**eutralizing **S**ystem of **H**igh **O**perational **T**oughness).

Evolution of RDCT SmartHub Wearable Device

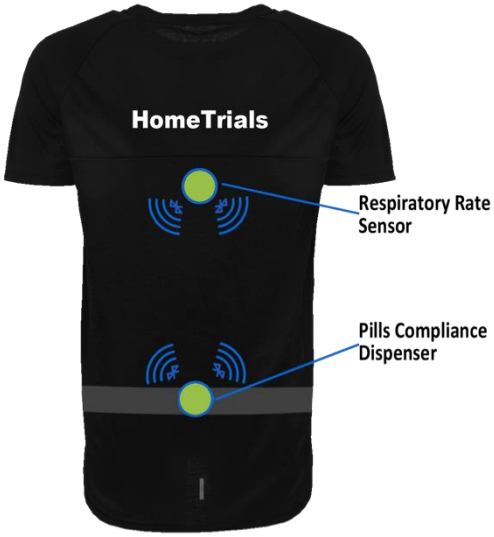
While the RDCT core SmartHub wearable device may be a revolutionary entry into the remote clinical trials arena as the frontend of the CLINTOS ecosystem, its evolutionary history makes a compelling case for our expertise in designing and building it to highest standards of quality, robustness and resilience to threats due to known, predictable, unknown, unpredictable, uncertain and unexpected adverse events or data breaches. In our vision its evolutionary future is a Health Passport for every citizen.

More details on the current technical specifications of the SmartHub wearable device are provided herein. However, these technical specifications will be revised in WP2 when the final requirements, technical specifications and architecture of the novel CLINTOS ecosystem is delivered for building the CLINTOS proof-of-concept and the SmartHub devices are manufactured for testing, validation and CE marking of the hardware.

RDCT SmartHub Lite Hardware Configuration		
MCU		Nordic52832
Storage	RAM	512 KB
	ROM	4MB
Display	Type	TFT Multi-touch
	Size	1.08 inch
	Resolution	128 * 220
Battery		104mAh Lithium Polymer 7-10 days standby time
Bluetooth		BLE 4.2
Sensors	SpO2	Maxim-MAX32664
	Temperature	T1-LMT70
	Heart Rate	Goodix-GH3011
	Accelerometer	BOSCH Sensortec BMA400
Charging		Standard USB charging
Language		Multi-Laungauge support
Certifications		CE, FCC, UN38.3 Safety

As the term indicates SmartHub functions as the Hub of the CLINTOS ecosystem, wherein its sensors monitor in real time vital signs like SpO2, body temperature, heart rate, Blood pressure, ECG in addition to study subject's mobility. It constitutes one of the four End Node interfaces of the CLINTOS ecosystem. The technical specifications presented herein are for the CE marked lite version that we inherited from the COVID project to build the basic framework of the CLINTOS platform. It will be upgraded to incorporate electrocardiogram and blood pressure. The remaining 2 vital signs will be integrated in a smart T-Shirt, which serves as the auxiliary node to the SmartHub node as described in the next paragraph.

1.3(a)3.ii Auxiliary SmartHub T-Shirt



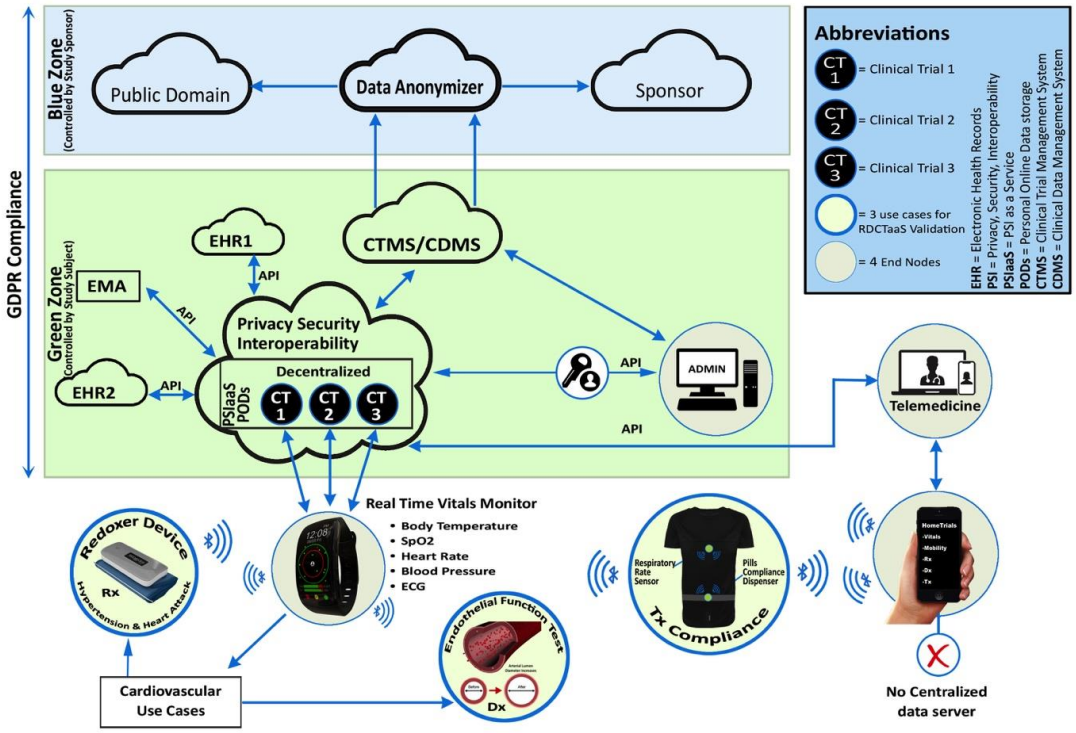
Wearable technology that measures body parameters has become increasingly popular in recent years. When wearable devices first emerged, they came in the form of smartwatches and fitness bands, helping people to increase their fitness level, monitor their mobility, and get better quality sleep. But new and emerging wearables can do a lot more than monitor your heart rate or count steps.

Since we decided to include treatment compliance as the 7th vital sign to monitor the RDCT study subjects, we designed a Smart T Shirt as an auxiliary to complement the SmartHub and integrate into the CLINTOS infrastructure. The design deploys flexible PCB technology to embed respiration sensor, piezoresistive pressure sensor and Bluetooth Low Energy (BLE) into the fabric of specially designed T-shirt. The respiratory rate data from the respiration sensor is transmitted to the SmartHub and saved to the study subject's POD to feed into the CDMS application of the RDCT or send instant alert in case any abnormality detected.

Our smart T-Shirt design integrates a soft pills dispenser pouch that houses sachets of medications, each sachet containing a single dose of single or combination medication. One or more sets of piezoresistive pressure sensors are embedded in a flexible PCB in the pills compliance dispenser pouch, which keeps track of the medication sachets removed from the dispenser pouch, assuring adherence to the treatment protocol by broadcasting compliance alerts across to the SmartHub and across the system via the BLE network.

1.3a)4. CLINTOS Architecture & GDPR/CTR Compliance:

The CLINTOS framework satisfies all the 9 elements of the RDCT definition that we formulated, and while ensuring privacy, security and interoperability makes it easy for third party applications to be plugged in to the ecosystem to enhance user experience and make the entire operation seamless.



The PSIaaS decentralized patient-centered approach (discussed in section **1.3a)1.i)**, that powers RDTaaS embeds Privacy, Security & Interoperability (PSI) by design not only in the CLINTOS framework, but also into any existing CTMS or CDMS system that plugs into the CLINTOS ecosystem. Once in the CLINTOS ecosystem, the study subjects / patients at all times remain in full control and ownership of their decentralized data as PODs (personal online data stores), authorizing, whenever necessary, access to hospitals, CROs, sponsors or EHRs, via APIs. Thus, not just the CLINTOS framework is GDPR compliant, but the novel architecture renders all other applications that enter into the CLINTOS ecosystem, GDPR compliant.

CLINTOS uses novel wearables with sensors that basically function as the epicenter of the CLINTOS ecosystem, seamlessly and autonomously broadcasting in real time, the study subject's vital data, without burdening the subject or the trial monitor. The PSIaaS decentralized patient-centered approach of CLINTOS is also capable of integrating 3rd party eClinical platforms that collect Real World Data about the patients as plug-and-play modules, like the Healthentia platform discussed in 1.3(b)2.vi. The CLINTOS framework also allows easy integration of existing clinical trial facilitating applications, such as CTMS (clinical trials management system), CDMS (clinical data management system), HMS (hospital management system), EHR (electronic health records), etc.

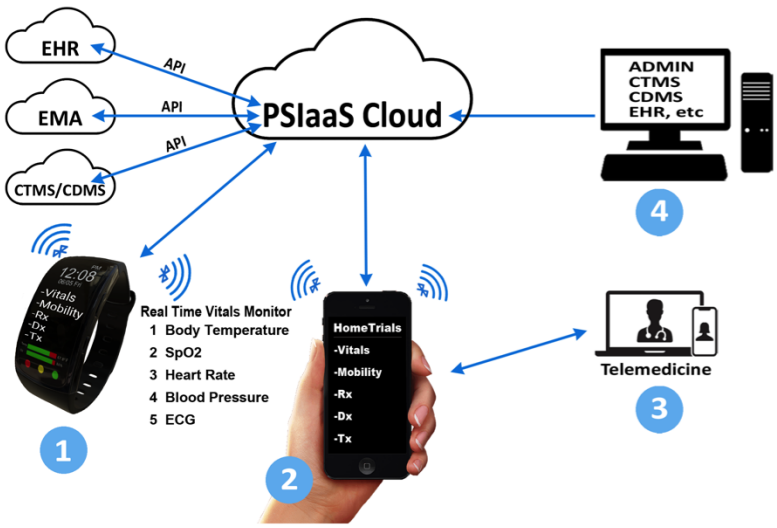
The CLINTOS architecture is designed to rid the legacy systems of their centralized data structures. Decentralization using PODs (personal online data stores) not only secures the data from hacking attacks, but makes the data private and interoperable. The security of PODs is further enhanced by deploying post quantum cryptography (PQC) techniques, and to a limited extent with blockchain / DLT (digital ledger technology), using DLT only for authoring data movement across service providers and not for the data storage. This is because storing data on blockchain recording every activity related to the data is a lot more expensive than the traditional data storage. Moreover, every bit of database activity need not be recorded on blockchain or executed in a smart contract. Only the data access / transfer that needs to be authorized to a third party warrants a DLT smart contract. All and sundry database activities / transactions neither need smart contracts, nor have to be recorded on the ledger. Hence, our approach is to use PSIaaS cloud architecture to decentralize the CLINTOS framework economically and efficiently, and use blockchain / DLT only to authenticate user ID and record any data transfer to any third party data transfer under smart contract recorded on the DLT ledger.

Data is the driver for clinical trials, and faster seamless access to data allows us to react to results faster. And, if a new digital innovation enables that delivers a more representative data in real time from participants without a visit to a clinical trial center, nothing like it. More details on the components, subsystems and modules of the CLINTOS architecture are presented in the Methodology section.

The Figure illustrates at least 4 types of End Node (Client Node) interfaces:

i) *The Wearable SmartHub*,
ii) *Study Subject's Mobile phone*,
iii) *The Study subject's personal computer* (either laptop or desktop), and,
iv) The *Web interface* for the system administrator, the study monitor, or any third party stakeholder.

The first three End Node Interfaces are installable native applications, while the fourth node is a general-purpose web interface for all stakeholders for accessing the CLINTOS ecosystem.



Four End Nodes of CLINTOS Framework

The CLINTOS architecture drawing also illustrates the relationship and interoperability of the CLINTOS framework with various clinical trial stakeholders who use a wide range of clinical trial facilitating applications. Even the regulatory authorities, such as EMA (European Medicines Agency) can receive direct feed from RDCT activities in real time, thereby streamlining the product review process and considerably reducing the regulatory approval time. All the components, modules and subsystems are discussed in detail in the Methodology section.
To illustrate the relevance of the CLINTOS ecosystem in implementation of real world use cases, Figure 1.3a)4

also depicts 3 use cases that will be tested in the proposal to validate the CLINTOS ecosystem. These use cases are spread across diverse clinical trial scenarios, viz.

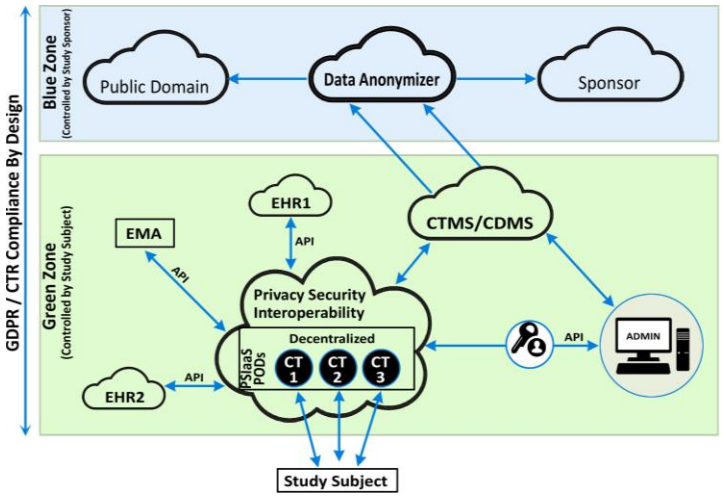
i) CT-1:Plug-n-Play operability of 3rd party apps;
ii) CT-2: Validation of 8 built-in vital signs (including HRV & therapy adherance) for RDCTs; and,
iii) CT-3: Validation of RDCT as tool for phase-IV dermal /cosmetic product trials.

Although, the Trials@Home does not mandate a full-fledged clinical trial for testing and validating the solution, but complete testing of the components and modules of CLINTOS will be best demonstrated only in a real clinical trial setting. Hence, we pick up the above use-cases which are neither as much resource consuming in terms of time and cost, as traditional clinical trials are, nor involve any significant risk to study subjects. The first two use cases serving as demonstrations of preventive and diagnostic interventions are actually interlinked and requires only analysis of data output from the devices that study subjects already use. Neither extra devices, nor new study subjects are required, nor it changes the timeline. The third use case is adherence to regimen of any prescribed oral medicine under trial. This use case is to establish that CLINTOS ecosystem can ensure and keep a record of compliance to the prescribed medication remotely. This use case also recruits the same study subjects as in the first and second trial, and deploys sham medications (Vitamins / placebo) to test the system. All three trials run concurrently and conclude within a period of 4-6 weeks (excluding recruitment time). More details on the use cases are presented in the Methodology section.

1.3a)5. Regulatory Compliance & Returning Clinical Trial Data To The Participants:

In recent years there is growing consensus that citizens' right to their personal data, transparency and clinical decision-making and public interest in general far outweigh the risks that status quo entails. There is an increasing awareness that greater transparency and engagement with study participants are needed in clinical research, and that the return of study participants' clinical trial data can address those needs. However, disrupting the status quo comes with its own challenges, such as:

- Privacy, security & interoperability of the personal clinical data
- Seamless integration of the clinical trial data within EHR
- Lack of common data format, processes or infrastructure;
- Compliance with ICH (International Council for Harmonization), GCP (Good Clinical Practice), CTR (EU Clinical Trial Regulation) and GDPR (General Data Protection Regulation) across EU Member States, for use and sharing of individual clinical trial data (personal data).



These challenges are further compounded by the fact that today's EHRs, CDMS, HMS, so on and so forth, silo patient data, and the efforts to breaking those silos haven't produced much success despite over a decade of intensive efforts worldwide. This is because there are over 1,100 EHR providers and many more CDMS, HMS providers and connecting them all will mandate either changing the structure of their centralized databases or deploying thousands of different APIs, either of which is an extremely difficult endeavor. Existing operational silos make returning clinical data to study participants meaningless if it moves from one silo to another. Moreover, returning clinical data back to the trial participants will carry little value unless there is an infrastructure to securely receive it in a privacy-preserving manner and render it portable enough to be easily shared for clinical decision-making in any scenario across the care continuum.

> *An important attribute of data should be that it flows to where it is needed and when it is needed without compromising privacy, security and confidentiality.*

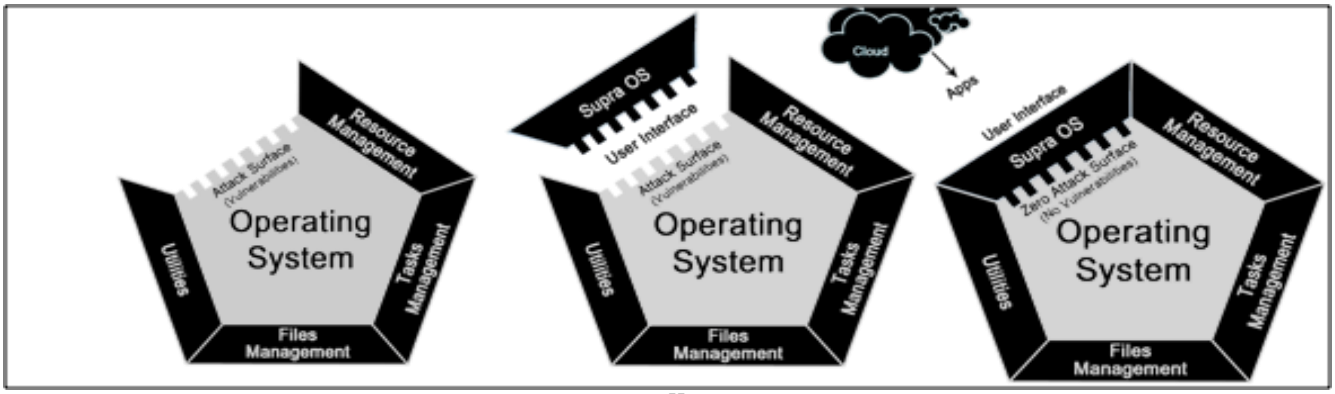
Inspired by that maxim, and drawing up on our previous work on embedding Privacy, Security & Interoperability (PSI) as a Service (**PSIaaS**) into any cloud computing application, and taking cues from **several *"previous or ongoing EU-level activities on citizen-centric access to health records"*** projects, particularly those that bestow ownership and control of personal data to patients via decentralization, such as MH-MD, CUREX, SERUMS,

FeatureCloud and PANACEA (each of those projects deploys blockchain for immutability of data), we are using a new user centric concept of decentralized universally compliant PODs (Personal Online Data) that meets the currently insatiable needs of patients' clinical trial data. PODs are user owned and controlled units of decentralized database that by default implement Universal Compliance by Design (UCbD) ensuring PSI of stored personal data making it available to any app that needs it via an API at the user's behest. This essentially means that PODs can exchange data with EHRs, CDMSs, HSMs and seamlessly connect using just a single API. Since almost all regulatory regimes focus on securing patient's interest in their personal data, once CLINTOS vests full ownership and control in patients, all national or international regulatory regimes such as GDPR/CTR/GCP/ICH so on and so forth, UCbD will be potentially achieved by default. Conversely, legacy systems' protocol / rule-based compliance is cumbersome and resource consuming, and most importantly will only offer a palliative solution, keeping the problem of returning clinical data perpetually alive forever.

1.3a)6. Rendering CLINTOS End Nodes Unhackable

ZEROV (Zero-Vulnerability) is a technology under development that builds a Supra OS (SOS) layer to obliterate attack surfaces that every computing device harbors. The four End Nodes CLINTOS that users use to interface with the system will implement ZEROV infrastructure.[54]

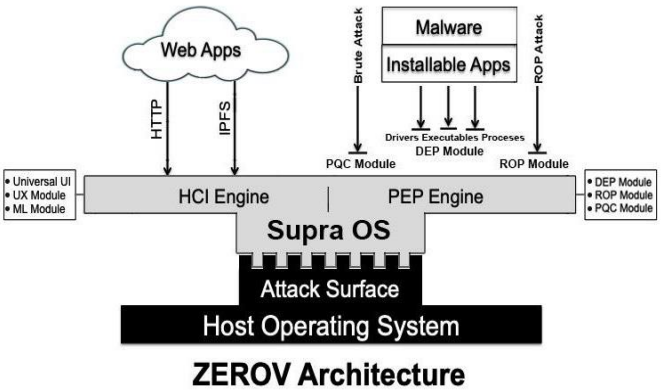
ZEROV: What is it?



i) a **Program Execution Prevention (PEP)** engine[55] that includes one or more anti-executable modules to disable drivers, processes, executable and thus prevent direct installation and execution of all third party end-user software applications, executable applets or scripts on the host OS, completely eliminating the potential attack surface of the host OS and,

ii) a **Human Computer Interface (HCI)** engine that includes a universal user interface (UUI), a user experience (UX) module and a machine learning (ML) module that runs and analyzes all the diverse third party end-user software applications delivered via network.

The delivered software may vary according to the scope of the computing device (e.g. productivity software, entertainment apps or web browsing software). Such a versatile user interface allowing all third party apps to run online on the SOS software program layer in online as well as offline mode with all of their native functions (**as progressive web apps**) without direct installation on the host OS. The PEP engine obliterates the attack surface of the host OS, preventing direct installation & execution of malicious software program, securing the computer from malicious attacks.

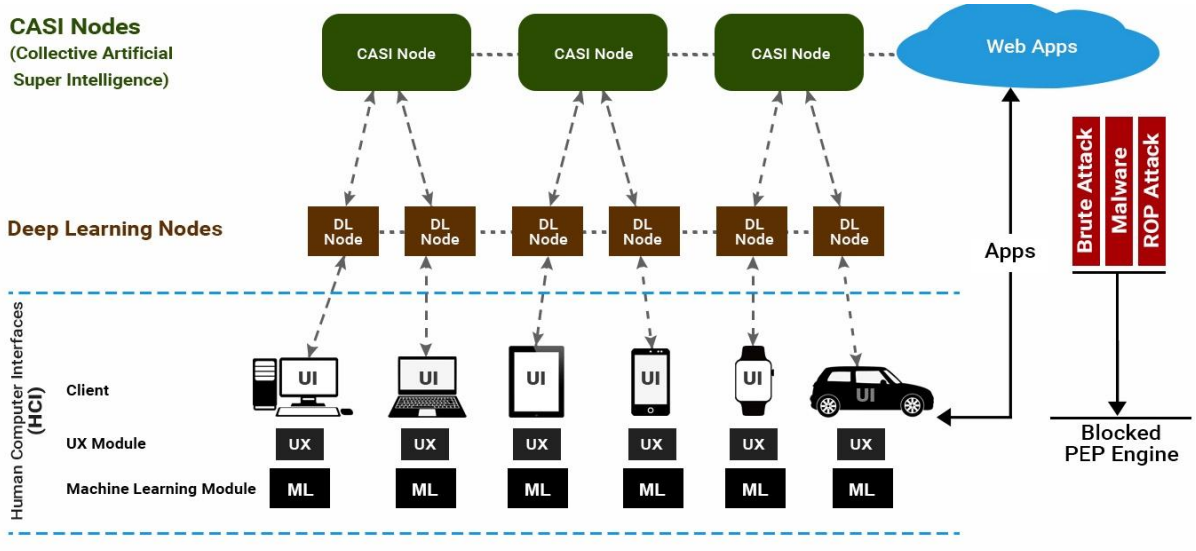


ZEROV Architecture

[54] https://www.bc5.eu/ZEROV-Consortium/
[55] Jackson, T., Salamat, B., Wagner, G., Wimmer, C., & Franz, M. (2010, September). On the effectiveness of multi-variant program execution for vulnerability detection and prevention. In Proceedings of the 6th International Workshop on Security Measurements and Metrics (pp. 1-8).

The network communication (remote application delivery) and the user authentication will be secured by applying PQC primitives for long-term security guarantees, such as FHE (Fully Homomorphic Encryption, VDF (Verifiable Delay Functions).

The ZEROV device's network architecture provides real time environment to run a desktop, laptop, tablet, handheld device, or an IoT device, all kinds of network-delivered third party decentralized as well as centralized applications with all of their native features and functions retained, eliminating the need for direct installation on the host OS thus rendering total freedom from app stores. The ZEROV can be compatible with any commercially available Operating Systems, such as Microsoft Windows, Apple macOS, Linux, Google Android, iOS, Chromium, OxygenOS, by developing the relevant SOS module. The SOS can also support offline apps. AI will



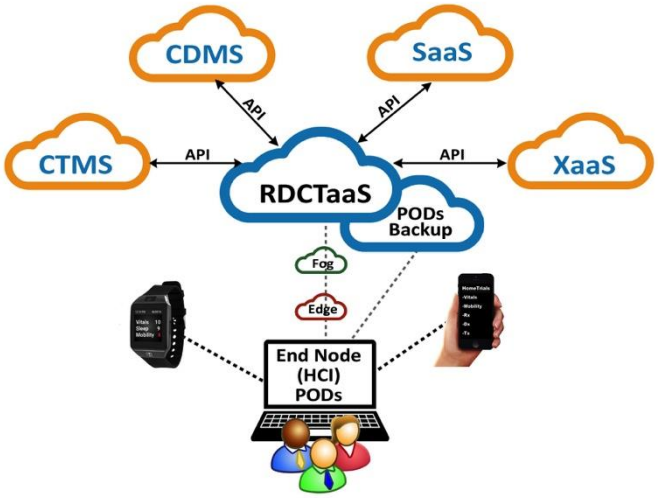
support user experience and interaction and therefore will enhance security from the user awareness perspective.[56]

Thus, in addition to the network security of the PSIaaS architecture, the four End Nodes of the CLINTOS can be further rendered unhackable by deploying the novel ZEROV / SOS middleware.

As CLINTOS provides a comprehensive ecosystem for all types of clinical trial tools for implementing RDCTs, it not only functions as backbone support to all of those CTMS tools and approaches out there, but also extends its security and unhackability attributes to those different applications, introducing some level of homogeneity in this otherwise heterogeneous field.

1.3a)7. CLINTOS: The Operating System (OS) Of The Future Clinical Trials

Novel CLINTOS architecture design creates an ecosystem that facilitates Plug-n-Play integration of the diverse clinical trial applications and tools available on the market. The third party app integration is developer-friendly via simple APIs. The developers can build various RDCT solutions to address clinical trial pain points, test it on CLINTOS testbed and deploy it as part of the CLINTOS ecosystem. They get the CLINTOS tools to combine various execution platforms safely and securely for ubiquitous and seamless execution of diverse computing environments in compliance with regulations. It is the easiest and fastest and developer friendly way to implement "**Compliance by Design**" without any significant changes to their current cloud solution. It is simply by adding



[56] Q Yang. The Role of Design in Creating Machine-Learning-Enhanced User Experience. 2017 AAAI Spring Symposium Series. 506-511

another -aaS offering to the current landscape of diverse range of XaaS offerings. The developers will be provided easy to implement CLINTOS APIs that they can use to plug-in their cloud solutions such as CTMS, eTMF, etc. to be integrated with CLINTOS as a federated cloud ecosystem. They can also use CLINTOS resources to upgrade their existing cloud applications to implement "**Compliance by Design**."

Thus, from technical perspective CLINTOS virtually functions as an operating system (OS) for future clinical trials or RDCTs. Any standard OS, be it Microsoft Windows, Apple Mac, or mobile systems like Android or iOS, also executes routines based on user commands issued through keyboard, mouse-clicks or screen-taps where all the tasks get completed locally on the End Node device. The same concept is extended to the use of CLINTOS as an OS for the network nodes executing processes to implement RDCT in a smooth and clutter-free manner. All the benefits of RDCT are available to CLINTOS OS users.

1.3a)8. Trans-Disciplinary Considerations & Stakeholder Knowledge & Engagement:

The CLINTOS Consortium is built to meet all the diverse trans-disciplinary considerations required to develop, test, implement, validate and exploit the CLINTOS infrastructure. The 12 consortium partners bring all relevant expertise ranging from ICT, IoT, privacy, security, social and ethical aspects of CLINTOS implementation, exploitation and dissemination, and of course, the clinical expertise to design and execute real world clinical trials.

The CLINTOS approach takes into consideration the divergent perspectives of each of the key stakeholders, namely, Citizens (Study Subjects), Study Sponsors (pharma industry), CROs (Clinical Research Organizations) and Data. The consortium has been carefully assembled to confirm the required and complementary expertise, and consists of Universities leading the key legal, technological and commercialization objectives and providing Intellectual Property (IP) from over x reference projects, as well as SMEs and Research Organizations , making project realization and subsequent commercialization highly feasible. The specific expertise and complementary skills of the partners to evidence a well-balanced consortium is depicted in 3.3.

Most importantly, the consortium includes at least 3 partners who are also participants of the original Trials@Home project, which is actually spearheading the European initiative for moving the traditional clinical trials away from the expensive and time consuming legacy systems that warrant multiple physical sites for conducting clinical trials, to the homes of study subjects. According to the ECSEL JU Trials@Home call Work Plan of 2020[57] this Trials@Home call is:

> *"timed and tuned to facilitate a close complementary activity between an existing medical consortium "Trials@Home" and a new to be formed ECS consortium working on the next generation of digital technologies for clinical trials. The specific requirements for this activity will be described in Annex 7. This third call will be in one and timing wise aligned with the ongoing IMI project."*

Three members of the EU funded *"existing medical consortium Trials@Home"* joining the CLINTOS project cannot be any less "*timing wise aligned with the ongoing IMI project*" and be more equitable to the primary ECSEL/IMI objective of *"complementary activity between Trials@Home"* and CLINTOS. Trials@Home is also EU's master project that takes the technology scan feed from projects like CLINTOS funded via this T@H call. As such the CLINTOS consortium tremendously benefits from the participation of the T@H partners whose valuable contribution will indeed align the CLINTOS platform architecture with T@H principles on one hand, and bring the tremendous stakeholder knowledge they acquired through their T@H participation. Moreover, their involvement makes the public/societal engagement a lot easier through their larger network.

Finally, the collective development of the proposal and its brief across all partners ensures that the consortium can work as a team from day 1.

1.3a)9. Project Positioning:

The two major components of the CLINTOS ecosystem, viz. PSIaaS and Wearable RDCT SmartHub have been implemented in standalone methodological and functional validation tests. So we believe in terms of Technology Readiness Level (TRL), CLINTOS framework as whole is at TRL 3 - *Analytical and experimental critical function and/or characteristic proof of concept*, while each of its components, modules and subsystems are at ≥ TRL 4 - *Technology validation in laboratory environment.* But we also believe due to our previous experience with the component technologies, their adaption and integration to deliver the CLINTOS solution will progress much faster than expected. This will make our goal to reach TRL7 - *System prototype demonstration in an operational environment*

[57] ECSEL JU Work Plan for ECSEL US Calls of 2020. Ver 15, page 16. https://www.ecsel.eu/calls-2020-wp2020

– by the end of the project smooth and easy.

Since the architecture of CLINTOS is designed to be modular, its prototype development will be broken down into modules described in detail in section 1.3b). Hence, for project positioning of the CLINTOS platform as a whole, we consider TRLs (Technology Readiness Level) of its various modules and subsystems at time zero and than project TRLs at end of the project.

Table 1.3a)7: Start and end TRL for the major modules and sub-systems of the CLINTOS Platform

	CLINTOS Components & Subsystems	Start TRL	End TRL	Comments
1	Backend PSIaaS Decentralized Network (Middleware) - LIQUIDUS Server & PODs - Fog & Edge Nodes - End Nodes	3	7	PSIaaS architecture decentralizes the CLINTOS network without the disadvantages of economic cost and data handling capacity of blockchain / DLT. Our prior experience with PSIaaS coupled with cloud expertise in the consortium partners will accelerate the development to TRL7.
2	SmartHub Wearable device	4	6	The SmartHub device was original designed for the COVID project with lower RAM, ROM and sensors configuration, and it was at TRL5-6. CLINTOS warrants higher configuration so we lower the baseline TRL to 4, and achieve end TRL6.
3	Smart T Shirt (Respiratory rate and compliance sensing)	3	6	Leveraging proven commercial sensors, flexible PCB technology and BLE module integration into clothing will make TRL 6 a realistic and practical goal using IoT expertise of consortium partners.
3	Smart ID & Smart Contracts	4	7	We had built Smart ID & Smart Contracts earlier for another project. So we believe our baseline is TRL4, and we will achieve TRL7 by the project end.
4	BC5 Blockchain	3	6	We have the blue print of the next generation blockchain & early proof-of-concept, so TRL3 is our baseline and goal of reaching TRL6 is realistic.
5	End Node Installable Apps	3	7	Leveraging & adopting pre-existing technologies, ZEROV & expertise from within consortium and in open source, TRL7 can be realistically achieved.
	Web Frontend, services & UI	3	7	Leveraging & adopting pre-existing technologies from within the consortium and in open source TRL 7 can be achieved realistically.

1.3a)9. Innovation Activities Linked To CLINTOS:

As disclosed earlier the core technologies deployed in designing the RDCT infrastructure are closely linked to two H2020 funded experiments. However, pertaining broadly to the trans-disciplinary field involved in this project there are a bunch of research and innovation activities of the consortium partners that feed into the project. Those activities are summarized in the following table:

Participant name	Projects Linked & Feed Into CLINTOS	How They Complement
Blockchain 5.0 OU	**XENO** (funded under Fed4Fire+ H2020 programme)	**XENO** is Women's Safety IoT device that keeps the identity of the wearer private, anonymous, and yet broadcasts her location in distress to anonymous rescuers in most adverse connectivity conditions. RDCT's BLE5 mesh-network draws from XENO
	COVID (funded under Fed4Fire+ H2020 programme)	**COVID** is a wearable device that embeds sensor for real time monitoring of user's vital signs & mobility for containing Covid-19 pandemic, but draws on XENO's privacy, anonymity & always on connectivity. RDCT SmartHub draws on COVID
	PSIaaS (Pending H2020 proposal with 13 consortium partners)	PSIaaS feeds into the decentralized architecture of CLINTOS that secures the platform, ensures privacy and interoperability.
Universitatea	**MHMD** (H2020 funded project)	A novel FHE scheme, called *Hybrid MORE*

Transilvania Din Brasov		*encryption scheme* developed in the linked MHMD project will be deployed in CLINTOS' AI deployment by combining AI with HE (homomorphic encryption)
Abich srl	EURL ECVAM	The European Union Reference Laboratory for alternatives to animal testing and is an integral part of the Joint Research Centre (JRC). Its aim is to advance the Replacement, Reduction and Refinement (the Three Rs) of animal procedures
European Medical Association	**iProcureSecurity** deals with major EMS challenges across EU: https://project.iprocuresecurity.eu/ **GDPR4H** project tackles privacy in health data: https://gdpr4h-project.eu/	EMA's experience dealing with emergency medical services and health data feeds into the CLINTOS data privacy and regulatory compliance. Moreover, EMA's Europe wide association with clinical medicine practitioners complements CLINTOS efforts to exploit and disseminate the results.
Innovation Sprint SRL	PANACEA, SecureIoT, ExACT	DLT-based decentralized patient-empowered data ownership project feed CLINTOS decentralized CT PODs. IoT security and precision health network exchange projects of ISS also feeds into CLINTOS.

1.3a)10. Gender Issues

The consortium acknowledges the "gender issue" as stated in the EU regulation 1291/2013 as of 11th December 2013 establishing Horizon 2020 and supports the objectives of the framework programme on:

a) Gender balance in research teams,
b) Gender balance in decision-making, and,
c) Integrating gender/sex analysis in R&I content.

The consortium will use a number of tools to address sex, gender and equality issues and align with a gendered and inclusive approach to innovation.

Firstly, it will responsibly calibrate the numbers of women by ensuring that an adequate number are participating in the project both as project partners and as members of the project management team.

Secondly, entities involved in the project are committed to encouraging equal opportunities of career among women and men in their staff according to national and European laws and corporate ethical code. It will also ensure adequate numbers of women are participating in research activities, including requirements gathering, event planning and development and project evaluation.

Thirdly, ensure gender balance by organizing special "Young Women in Health" workshops as part of CLINTOS dissemination plan.

Fourthly, all actions will be evaluated by the project's General Assembly, which is in charge of monitoring the progress of the overall project. The General Assembly, will also have the task of: (i) Adopting the appropriate measures encouraging women participation in the management of the project, in order to achieve a balanced representation; (ii) Solving any gender-related issue within the research process; (iii) Supporting the implementation of relevant recommendations produced by the European Technology Assessment Network (ETAN) as well as by the "Helsinki Group" on the development and production of statistics and indicators, about the situation of women in scientific research.

1.3(b). Methodology

We will use agile product development strategy. Cross-functional collaboration between the consortium members will be the key in implementing the development methodology. Active participation of consortium partners will be crucial at every stage for achieving all the project objectives. Participation of the members of Trials@Home consortium will add momentum to CLINTOS development plan as their feedback will align CLINTOS development strategy with the principles of Trials@Home. The development, validation and dissemination of the CLINTOS following an **Agile Development Methodology** as described in detail in the next section, we "*demonstrate the technology in relevant environment*." Hence, we believe we are at an overall TRL-4, and expect to reach an over all TRL-7 by the end of this project.

1.3(b)1 The CLINTOS Agile Methodology & Innovation Cycle

A conceptual framing of the project methodology is depicted in Figure 1.3(b)1. The starting point (01) aims for a fundamental understanding of the Trials@Home initiative, its objectives, goals and associated policies and legislation in general and specifically pertaining to the 3 use cases we selected for validating the concept of CLINTOS for its first market replication. Particularly, how the system implements the 3 different types of representative clinical interventions we selected for testing and validation of CLINTOS infrastructure in meeting the T@H call objectives:

i) achieving accuracy (compared to clinical instruments),
ii) data integration (into the workflow of hospitals and pharma),
iii) user friendliness (should be straightforward for non-technical staff and elderly),
iv) data security and Privacy (most hospitals don't want to have data outside the hospital), and,
v) patch to patch communication to prevent latency.

The 3 use-cases, which are described in detail in section 1.3(b)3, (which are actual clinical trials) are as follows:

i) CT-1:Plug-n-Play operability of 3rd party apps;
ii) CT-2: Validation of 8 built-in vital signs (including HRV & therapy adherance) for RDCTs; and,
iii) CT-3: Validation of RDCT as tool for phase-IV dermal /cosmetic product trials.

The Innovation Cycle:

It is envisaged that different technical and regulatory implications will apply in each case, owing to the unique procedural differences in the nature of the use case, offering and context. The fundamental objective in **step (01)** is to both understand the technical and regulatory constraints as it applies to each of the 3 use cases, as well as understand the variability and parameters for RDCT implementation that would apply in each of the 3 use cases. **Step (02)** deals with translating the fundamental understanding achieved in (01) to clearly define the requirements and technical specifications for designing the technical architecture of the CLINTOS concept. Once again, it is envisaged that different technical, procedural and regulatory implications will imply different approaches in cases, owing to the heterogeneity in concept, capability and functionality of the 3 types of clinical studies we selected for field-testing the CLINTOS solution. The goal is to translate these into different modules that engage a user through a simple UI (and associated helper screens), to enable the user to methodologically set their preferences and navigate through the system. **Step (03)** then builds on these design decisions and produces a proof of concept (POC) that is field-tested and validate in 3 different use case scenarios in the next **step (04)**. The fifth and **final step (05)** provides the crucial feedback from the users of the CLINTOS ecosystem leading to further ideating the improvements to complete or repeat the innovation cycle. The combined assistance from the clinical, legal, ethical, and ICT expertise in the consortium will help navigate the project through the innovation cycle and deliver a robust solution.

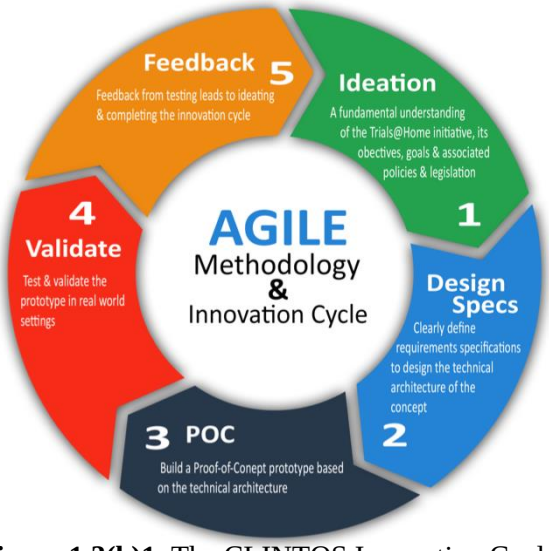


Figure 1.3(b)1. The CLINTOS Innovation Cycle

1.3(b)2. Development of CLINTOS Modular Infrastructure

The CLINTOS architecture is designed to be modular in two sets of modules. The first is the generic modular framework and the second is specific modules. The generic modular framework is designed to provide a holistic infrastructure that universally supports the diverse components of a clinical trial ecosystem. This will comprise a multitude of the tools and services required for enabling implementation of Trials@Home vision including third party products and services. The development of the generic modules of CLINTOS framework is divided into two broad categories: i) End Nodes, and ii) Network Nodes.

1.3(b)2.i CLINTOS End Nodes: There are four types of the end nodes or client devices that constitute the interfaces that users of the CLINTOS platform use to interact with the entire ecosystem, whether the generic CLINTOS framework, or the built in specific modules, or the third party applications, tools or accessories that can be plugged in to create an ecosystem that comprehensively services the pharmaceutical / CRO / health industry.

(a) The **CLINTOS SmartHub** wearable device, which hosts sensors for monitoring study subject's vital signs 24/7 in real time and broadcasts alets to the stakeholders involved in the RDCT. These sensors measure in real time 5 of the 7 vitals that the CLINTOS ecosystem is by design capable of monitoring 7 vital signs, which include SpO2, body temperature, heart rate, blood pressure, ECG, respiratory rate and additionally adherence to the therapeutic intervention (via an auxiliary Smart T Shirt). Please see section 1.3(a)3 for more details.

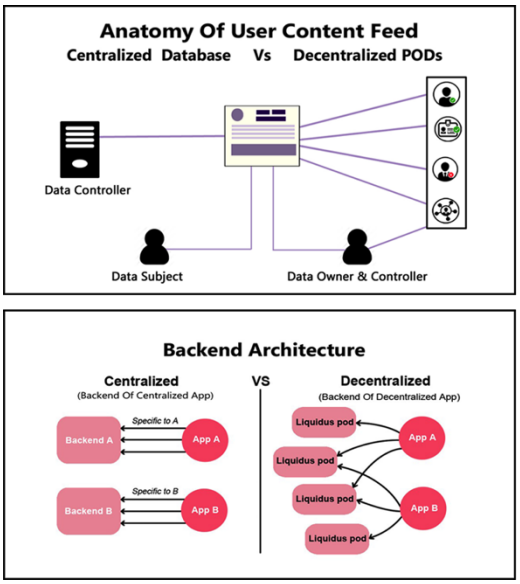
(b) **The CLINTOS companion device** application, which installs on study subject's mobile phone and complements the SmartHub in providing a more elaborate interface for user interaction.

(c) **The CLINTOS desktop application**, which installs on desktop, laptop or tablet computers. Mostly meant to serve the study subject, the administrator and the RDCT monitor, sponsor, etc. for coordinating and complying with the RDCT protocol procedures.

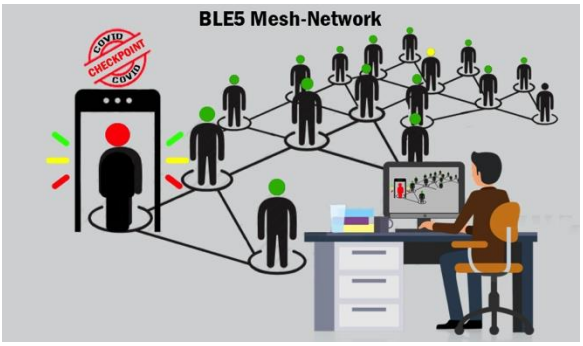
(d) **The Web Interface** services all stakeholders, requires no installation and can be accessed from anywhere using any Internet connected device.

1.3(b)2.ii CLINTOS Network Nodes: The CLINTOS network is based on decentralized network architecture, which is based on LIQUIDUS technology that embeds privacy, security & interoperability (PSI) into any cloud application. The decentralized network has two types of network nodes: a) PODs (Personal Online Data stores) and b) DLT (digital ledger technology) or blockchain nodes. While DLT is deployed only for user ID and limited interoperability authorizing smart contracts, PODs serve as units of storage of the user data in a decentralized manner. There will be several types of nodes hosting the PODs (LIQUIDUS) server depending on the location of the server, closest to the client node being the edge node, and furthest being the remote node and between them the, fog node.

The PODs: There is a major difference between the architecture of conventional databases and CLINTOS PODs. While in traditional centralized databases all content of users is stored in a single centralized server, PODs are created in a distributed manner for each unique user. Such PODs can be stored either locally at an Client Node or at any remote location of user's choice. The PODs can be linked to any application via APIs in such a way that the corresponding application interface does not exhibit any difference between the data retrieved from the application's own centralized server and the data served from the remote POD location. User data populates the application only if the user authorizes the access via API, and only to the extent and time period the user authorizes the data access.
The advantage of keeping the PODs at the client computer is that the data becomes available without latency only when the user is online. But the disadvantage is the inaccessibility of the linked data 24/7. The disadvantage may also be the permanent loss of data on account of any adverse event at the End Node. In CLINTOS implementation this is remediated by provisioning backup PODs in the cloud (Please see section 1.3a)6).



DLT Nodes: Because DLT / blockchain has latency, storage and cost issues DLT has a limited utility in the CLINTOS ecosystem. It is only deployed for authenticating ID where transactions of value are to be authorized e.g. sharing user data with third party provides such as EHR. The CLINTOS PODs thus allow interoperability and sharing information across diverse databases, disciplines and stakeholders without compromising privacy and security of the individuals, components and modules involved in the CLINTOS ecosystem.



1.3(b)2.iii Mesh-Networking: CLINTOS wearable device's

always-on connectivity feature uses a novel mesh-networking that deploys new Bluetooth Low Energy 5.0 (BLE5) mesh-networking protocol. The BLE5 mesh algorithm is designed to transmit the data by hopping on the nearby BLE 4+ devices until it reaches a device with Internet connectivity. This essentially means that a CLINTOS SmartHub device does not need an active Internet to transmit data allowing connectivity in most adverse situations.

1.3(b)2.iv AI Engine & Machine Learning Modules: CLINTOS generic architecture is powered with artificial intelligence, using machine learning (ML) modules to analyze the big data feed to the Input Matrix, learns from it, and delivers appropriate response options to caregivers and clinical trial monitors who can make treatment decisions remotely. The ML module also automates the triage decision in case of any emergency whether related to the RDCT itself or unrelated.

Some of the sensitive data warrant protection during computational processes. Homomorphic Encryption (HE) allows for computations to be run on encrypted data. HE schemes can be *Fully homomorphic encryption* (FHE) or *Partially homomorphic encryption* (PHE), depending on the type of operations to be performed and the execution time requirements. A more complex encryption strategy, that is homomorphic with respect to multiple operations, can be obtained by combining several PHE encryption schemes in a layered structure. By exploiting such encryption schemes one can train and employ an AI model which operates directly on homomorphically encrypted data, i.e. both input and output data is encrypted. A simplified overview of the proposed approach of combining HE and AI is illustrated in the following drawing:

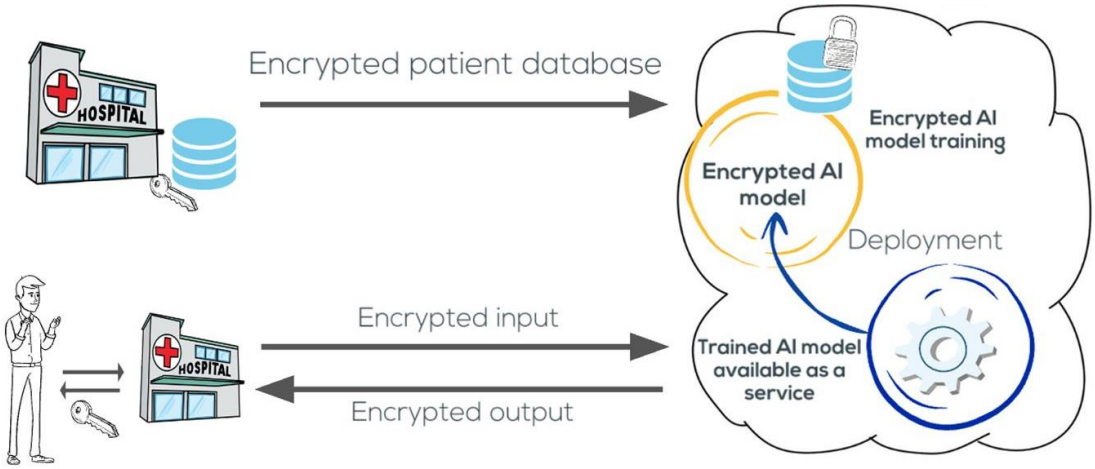


Fig 1.3(b)2.iv. Workflow of the proposed framework and solution

This solution implements a software framework for developing personalized clinical solutions based on homomorphically encrypted data and artificial intelligence (AI). The framework ensures that the data remains private, and the performance of the AI models is not affected by the encryption".

1.3(b)2.v Distributed / Federated Learning With Adversaries: Besides HE, federated learning can also be explored. When data (whether encrypted or not) are sent from nodes "centrally" towards the "cloud", the sent data may not be guaranteed to be truthful given that the single end-nodes may possess personal incentives to modify the inputs accordingly. The predictive system may, thus, be compromised and catastrophic repercussions may derive from such a tampering. This, in turn, implies that the AI model has to entail a set of design rules such that the end-nodes are disincentivized to report tampered information. The AI system also needs to be resilient to Denial of Service (DoS) attacks, whereby single and colluding end-nodes decide strategically not to send data centrally to the "cloud" so to prevent any type of complete statistical analysis and make the system abort or crash. This issue could be resolved or, at least, attenuated by a game theoretical study of the set of incentives raging through the decentralized network with techniques coming from algorithmic mechanism design or algorithmic contract theory. Another way this AI system could be designed is through the so-called Federated Learning approach, where, rather than data itself (whether encrypted or not), predictive model weight updates are sent to the "cloud" and the "cloud" sends back its updates in this multi-stage communication game. This model suffers from incentive-compatibility issues or potential DoS attacks just as much as the Distributed Learning one, but it is still "lighter" and more secure. The first adjective may be justified by the fact that sending the whole encrypted piece of data carries much more (possibly unnecessary) information than a single weight which is just a real number and whose bit representation is rather small. The second adjective comes from the fact that, even if an

adversary uncovers the encryption (which is utterly unlikely with HE or PHE), it is much more difficult to recover the original piece of data if the adversary has access to the weight update only. This model suffers from incentive-compatibility issues or potential DoS attacks just as much as the HE based one, but it is still "lighter" and more secure.

1.3(b)2.vi Specific Third-Party Plug-n-Play Modules: Our methodology to develop the generic CLINTOS architecture as modules makes it easy to add or delete any module according to the specific needs of the RDCT sponsor, CRO or caregiver. However, to validate a specific non-generic use case, our methodology also includes integration of specific third party use case modules, such as the CTMS/CDMS applications, such as an eClinical solution offered as a commercial service by one of CLINTOS partners, Innovation Sprint SPRL (ISS). ISS's Healthentia is an eClinical platform that collects Real-World Data (RWD) about the patients, either reported via questionnaires, or measured from wearable sensors and remote devices and provides an integrated data management cloud environment, where investigators, CROs and Pharma can monitor and support patients and make data-driven decisions of trial's objectives. In CLINTOS, Healthentia will act as one of the End Nodes of the PSIaaS layered architecture, connected to the Edge Layer.

Hence, our development methodology takes into account performance, scalability, responsiveness, and usability of the CLINTOS modules in cross-sector applicability of the CLINTOS ecosystem.

1.3(b)2.vii. CLINTOS Code QC

Software quality control[63] is a function that checks whether a software component or supporting artifact meets requirements, or is "fit for use". Software Quality Control is commonly referred to as Testing. While, BC5 team will accomplish much of the coding of CLINTOS infrastructure, one or two of the consortium members will take the responsibility of QC testing and validation studies.

1.3(b)2.viii. CLINTOS Code Review & Audit

A software code audit is a comprehensive analysis of source code in a programming project with the intent of discovering bugs, security breaches or violations of programming conventions. It is an integral part of the defensive programming[65] paradigm, which attempts to reduce errors before the software is released. Our methodology follows up QC checks with CLINTOS code review by another consortium member, followed up by a third party audit.

1.3(b)2.ix. CLINTOS Use Cases

A use case is a software and system engineering term that describes how a user uses a system to accomplish a particular goal. It is basically a list of actions or event steps typically defining the interactions between an actor and a system to achieve a goal. A use case acts as a software modeling technique that defines the features to be implemented and the resolution of any errors that may be encountered.

In software modeling literature there are basically two types of use cases depending on the user expectation and system performance:

i) Business Use Cases, and,

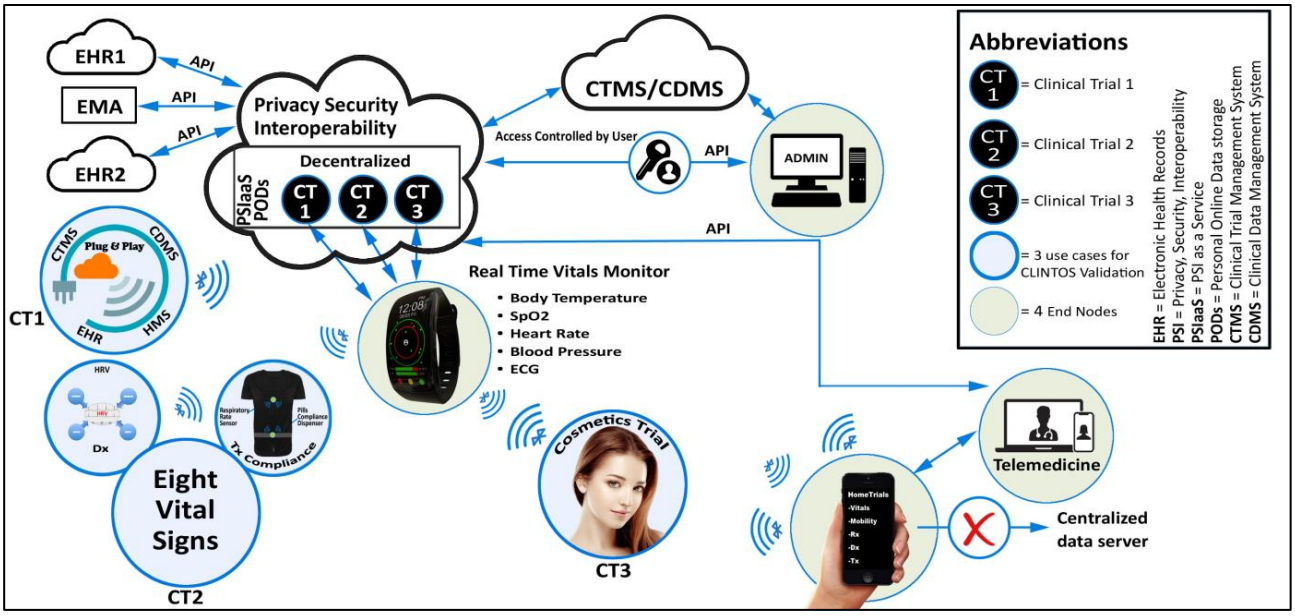
ii) System Use Cases.

Business Use Cases are more about what a user expects from a system while System Use Cases are more about what the system does. The CLINTOS SmartHub auxiliary T Shirt has a treatment adherence module. Hence CT-1:Plug-n-Play operability of 3rd party applications and 8 built-in vital signs (including HRV & therapy adherance) are system use cases; and, conducting a phase-IV dermal /cosmetic product trial is business use case.

1.3(b)3. CLINTOS Pilots & First Market Replication

Conducting pilot testing of software and hardware is a good practice to validate functionality of the system before going into production. In pilot testing group of users tries the software and hardware in totality, prior to its final launch or deployment. CLINTOS consortium will take the responsibility for piloting the CLINTOS ecosystem, at the end of which, the users will give feedback about the function, feel and response of the ecosystem as a whole. Based on the feedback received after the completion of the pilot, the software will be tweaked and bugs removed, if any, to meet the end user expectations.

Thus, we will ensure that from the end user viewpoint also, CLINTOS meets all expectations. We will take care of the user experience: how easy it is for them to use the product.



Bird's Eye View of CLINTOS Ecosystem & 3 CTs To Validate Its First Market Replication

CLINTOS will follow an integrated and agile approach (Figure 1.3(b)3) whereby results and lessons learned from the CTs influence the ecosystem development which in turn gets refined and redeployed for testing, constantly keeping CLINTOS users in the production loop.

The consortium includes partners with clinical experience of conducting pilot CTs in various hospital and homecare clinical settings. Assisted by other members of the consortium at least three of the partners (**MIA, ISS, ABI**) will lead the pilot studies to demonstrate first market replication of the CLINTOS infrastructure and its usability In the following three RDCT use cases:

- CT-1:Plug-n-Play operability of 3rd party apps;
- CT-2: Validation of 8 built-in vital signs (including HRV & therapy adherance) for RDCTs; and,
- CT-3: Validation of RDCT as tool for phase-IV dermal /cosmetic product trials.

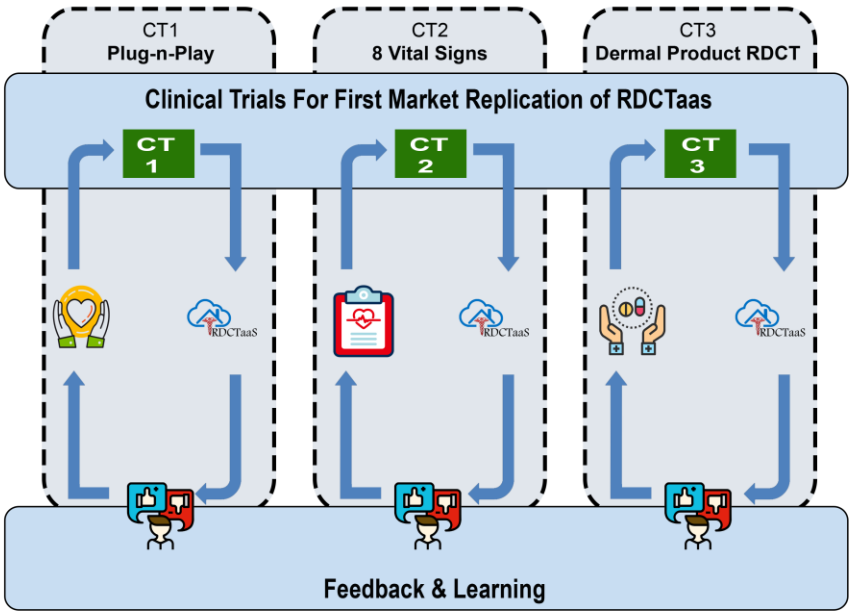


Figure 1.3(b)3 CLINTOS Use Cases & Their Validation: Integrated Deployment & Evaluation **Approach**

Although, the sponsors of this Trials@Home call have specifically clarified that the call does not entail full-fledged clinical trial, we are convinced that some form of real world clinical trial design, albeit very short duration, minimal complexity, completely non-invasive and falling in a category that already has an EMA/CE approved product on the market will do justice to the testing and validation of the CLINTOS ecosystem. We have identified these use cases and are also providing technical details and preliminary structure of the CTs, which in no case should be considered as final study protocol for clinical trial implementation. The consortium will design the final protocol in consultation with the Trials@Home after the CLINTOS proof-of-concept is ready in WP3, and its modules and their function are fully defined, tested and approved by appropriate regulatory agencies in WP4. The first two use-case scenarios can be tested and validated in a single clinical study that may be concluded in 6-8 weeks time period at multiple centers. The third use case is a phase IV trial of a commercially available dermal/cosmetic product. Detailed CT protocols of all the three CTs will be drafted and

approved by ethical committee in T4.8 and appropriate Institutional Review Board of the jurisdiction where the leader of the corresponding task is located.

CLINTOS CT-1: Validation of plug-n-play operability of third party CT/Health apps (Task 5.2, Partner MIA)

Actors & Stakeholders

The main actors and stakeholders of this CT in general are citizens, state, caregivers, payers, hospitals, HCP (health care professionals), clinicians, CROs and other CT service providers / vendors; and in particular Trials@Home center of excellence, CLINTOS CT sites, principal investigators (PIs), EHR, HMS, CTMS / CDMS vendors, partners ICS, SSS and ABI.

Primary Objective

CT-1 tests & validates CLINTOS as an operating system (OS) for seamlessly running and interoperating different kinds of third party software applications that constitute the healthcare ecosystem. Led by partner ICS, CT-1 primarily strives to test and successfully validate the successful integration of all the features of CLINTOS platform into the third party apps to enable seamless flow of data within the ecosystem for remote clinical monitoring of CT subjects in universal compliance to regulatory requirements. CT-1 also specifically validates the capability of the CLINTOS PSIaaS layered architecture in integrating a 3rd-party eClinical platform, Healthentia that captures patients' real world data, especially those reported by the patients via questionnaires. This way subjective patients' reports will complement CLINTOS objective measurements in capturing patients' outcomes.

As reasons therefore, the CT-1 is designed to provide measurable outcomes not only pertaining to the operations of the CLINTOS ecosystem as a whole, but also the outcomes on the safety of the wearable SmartHub device. It will also validate CLINTOS as an operating system (OS) for running all third party Trials@Home RDCTs. The task will be carried out by partner ICS in association with ISS and ABI in the facilities of ICS.

Main questions to be solved through the evaluation are:

- Is the technical stability of CLINTOS sufficient as an RDCT OS for operating a third party CTMS/CDMS/EHR/HMS application?
- Is the vital data collected by wearable sensors of the CLINTOS platorm is seamlesslessly transfering to a third party plug-and-play module - the eClinical platform Healthentia?

Anticipated Improvements - KPIs

Anticipated KPI goals include:

- 90% of the volunteers qualified for CT-2 participation were able to sign up and complete the evaluation remotely.
- The CLINTOS infrastructure recorded all the vital data in real time and delivered to the admin/study monitor in 100% of the attempts in real time.
- Achieve100% integrity of third party CT / health apps installation and operations.

2. CLINTOS CT-2: Validation of 8 built-in vital signs (including HRV) for RDCTs (Task 5.2, Partner ISS)

Actors & Stakeholders

Same as in CT-1 and CT-3. CT-2 can be conducted with the same subjects shortlisted for CT3 and hence doesn't need any separate recruitment process.

Primary Objective

CT-2 is designed to test and validate the integrity and performance of 8 vital signs that CLINTOS platform can record and transmit in real time. These vital signs include 6 traditional ones (body temperature, heart rate, blood pressure, Sp02, ECG & respiratory rate) and 2 new ones (HRV & medication adherence) that we propose as technologically recordable clinical parameters within the CLINTOS ecosystem.

Heart rate variability (HRV) is the fluctuation in the time intervals between adjacent heartbeats.[58] HRV reflects regulation of autonomic balance, blood pressure (BP), gas exchange, gut, heart, and vascular tone, which refers to the diameter of the blood vessels that regulate BP, and possibly facial muscles.[59] Of several HRV metrics,[60]

[58] McCraty R, Shaffer F. Heart rate variability: new perspectives on physiological mechanisms, assessment of self-regulatory capacity, and health risk. Glob Adv Health Med (2015) 4:46–61.10.7453/gahmj.2014.073.

[59] Gevirtz RN, Lehrer PM, Schwartz MS. Cardiorespiratory biofeedback. 4th ed In: Schwartz MS, Andrasik F,

SDNN (Standard Deviation of NN intervals) and RMSSD (Root mean square of successive RR interval differences) will be used as KPIs. HRV is fast emerging as a very important analytical tool for early ethical evaluation of cardiotoxicity and neurotoxicity of pharmaceutical agents in phase-1 and phase-2 clinical trials. It is also turning out to be a valuable marker in advance diagnosis of routine morbidities. As such HRV has potential to become a key analytical tool in clinical practice. CLINTOS offers HRV analysis by default to all RDCTs that use CLINTOS as their OS.

While HRV indeed has substantial diagnostic and prognostic value in countless of clinical situations, therapy adherence has been proposed as a new vital sign,[61] These 8 vital signs that CLINTOS offers to RDCTs are important in almost all types of clinical trials, and are not remotely measurable in state-of-the-art, thus establishing CLINTOS as an ideal Operating System (OS) for Trials@Home / RDCTs. CT-2 will be carried out by partner ISS in association with ABI and HBI.

Main questions to be solved through the evaluation are:

- Are HRV analysis & medication adherence monitoring features built into the CLINTOS operating system as additional vital signs delivering additional value to the CT sponsor and providing additional benefits in conducting RDCTs?
- Can HRV analysis be used as a diagnostic tool for cardio & neurotoxicity in evaluating safety of investigation new drug (IND) RDCTs in phase-1 and phase-2 clinical trials?
- Is HRV analysis a good marker of overall health and wellness?
- Is medication adherence monitoring feature built into the CLINTOS Smart T-shirt user friendly?

Anticipated Improvements - KPIs

Anticipated KPI goals include:

- All 8 vital signs of remotely recorded in 80% of the study subject
- Statistically significant therapy adherence rate compared to the historical data from case studies.
- HRV analysis pre and post CT-3 therapy compared with historical data on HRV in various physiological stress or toxicity situations.

CLINTOS CT-3: Validation of RDCT as tool for dermal/cosmetic product trials (Task 5.4, Partner ABI)

Actors & Stakeholders

The main actors and stakeholders of this CT in general are citizens, producers / vendors of consumer products, producers / vendors of ingredients, dermatologists, CROs and other CT service providers / vendors; and in particular Trials@Home project, CLINTOS CT sites, principal investigators (PIs), and of course the male and female trial participants aged between 18 to 60 years with following pre-qualification:

1. Subjects with healthy skin not taking any treatment (e.g. for acne or atopic dermatitis).

2. Subjects prone to have skin problems (e.g. irritation, rosacea, rashes, eczema, resurgence of acne and adult acne) due to skin microbial dysbiosis.

- *Subjects who are willing to refrain from any probiotic and other cosmetics supplement during the study period*
- *Subject we will undergo the trial procedure following the classical scheme.*
- *Subjects who understand the study procedures & willing to digitally enroll and provide informed consent to participate in the study and authorize release of the clinical data to the study investigators.*

Primary Objective

With regular findings suggesting various personal care applications, it is likely that consumers, product developers and marketers alike will have their eyes on the skin's bacterial communities for future cosmetics, skin and body care innovations. Like the gut, the skin has its own unique ecosystem consisting of millions of bacteria, fungi, and viruses which make up the skin microbiota. We have long known about the health benefits of maintaining balance in the gut microbiome but when it comes to skin care, bacteria have generally been perceived as something we need to remove. This narrative is beginning to change in scientific circles. Today, the skin microbiome is increasingly thought to be the key to enhancing skin appearance – addressing the causes of skin conditions rather than just the symptoms.

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editors. Biofeedback: A Practitioner's Guide. New York: The Guilford Press; (2016). p. 196–213.

[60] Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. Front. Public Health. 2017;5:258. doi: 10.3389/fpubh.2017.00258. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5624990/#B2

[61] Delamater AM. Improving patient adherence. *Clin Diabetes* 2006;24:71-7.

CT-3 tests & validates CLINTOS for evaluating the efficacy of probiotics / microbiome modulator cosmeceuticals in human volunteers under the overall supervision of consortium partner Abich. Because the partner acts as CRO the final aim is to validate the integration of the CLINTOS system in current trials' methodology.
The study protocol intends to use commercially available probiotics / microbiota modulators (e.g. OXY 229 PF, SYN-UP®, and ALPAFLOR® ALP®-SEBUM) as cases studies for CLINTOS field trial validation, and its first market replication.

Main questions to be solved through the evaluation are:
- Is the CLINTOS useful for cosmetics and personal care products evaluation?
- Can personal care produces embed CLINTOS in their clinical studies ecosystem?

Anticipated Improvements - KPIs
Anticipated KPI goals include:
- 90% of the study subjects qualified for RDCT participation were able to sign up and complete the study remotely.
- Admin and doctors are able to access and perform data analysis on CLINTOS with 100% success rate.
- The values of markers obtained from the RDCT volunteer match with classic trials volunteers with a degree of > 90%.

1.4 Ambition

Most radically new concepts in science & technology face significant uncertainties in terms of cultural and sociopolitical acceptability in addition to the inherent risks involved with technology itself. Our long-term vision and CLINTOS strategy are built around real world uncertainties of such an ambitious undertaking. CLINTOS objectives are realistic & conducive to the strategy our market positioning approach adopts for long-term sustainability against the brunt of risks & commercial plausibility.

As we've seen in the preceding paragraphs, CLINTOS infrastructure can deliver ground-breaking concepts that homogenizes the diverse clinical trial tools into a seamless platform that implements RDCT without study subjects having to leave their homes for frequent follow up monitoring. We've also demonstrated that CLINTOS virtually functions as an operating system (OS) for future clinical trials or RDCTs, and the common concepts of a traditional OS apply to the use of CLINTOS as an OS for the network nodes executing processes to implement RDCT in a smooth and clutter-free manner. Since all the benefits of CLINTOS are available to RDCTs of any type, **CLINTOS** project lays down the foundation of:

"a networking architecture that has the potential to change the very fabric of our existing Clinical Trials infrastructure and potentially become standard Operating System (OS) for future RDCTs."

Accordingly, its innovation potential can be steered to become a leading market solution with distinctive set of Unique Value Propositions (UVPs) that are explained below:

UVP1: Privacy by Design tools for citizens- To-date citizens / study subjects have only limited/passive roles in stating and managing their privacy preferences. CLINTOS changes this in multiple and substantive ways, putting the citizens in control of their own private health data stored in their PODs. This is accomplished in a convenient and user-friendly manner.

UVP2: Real Time Monitoring Of Vital Signs – User's real time remote surveillance of vital signs monitoring of health status via optical sensor that measure blood pressure, pulse rate, ECG, SpO2 (blood oxygen level), thermal sensor that monitors body temperature, and differential pressure sensor that monitor respiratory rate and treatment compliance, provides valuable data in real time that's impossible in the traditional clinical trials. Thus it,
i) Firstly, CLINTOS increases the number of vital signs that can be used to make clinical assessments to 7.
ii) Secondly, it automatically monitors all those 7 signs in real time.
iii) Thirdly, it alerts the stakeholders suggesting appropriate follow up decision options.

UVP3: HRV – A New Marker For Clinical Trials - In the past couple of decades HRV is fast evolving as a diagnostic aid in a large number of acute and chronic diseases, and particular as a very sensitive marker of cardiotoxic and neurotoxic effects of a new investigational drug. Providing HRV analysis in real time as a core feature of CLINTOS is a huge advantage.

UVP4: Option to eliminate or minimizing data silos & improving data exchange (EHR Interoperability) – Today's EHRs (electronic health records) more or less operate as data silos affording little or no data interoperability. The decentralized data structured as PODs introduces data interoperability and breaks the data silos.

UVP5: Protects Sponsor & State Interest: While empowering study subjects with control over their personal data, CLINTOS ensures that such empowerment of study subjects does not weaken sponsor / state interest in the research data.

UVP6: Always on BLE5 mesh networking – Most communication systems cannot tackle last mile connectivity issues in adverse scenarios. CLINTOS' always-on BLE5 mesh-network ensures mitigates those issues.

UVP7: New cloud development tools for developers of CTMS/CDMS Modules & Components – CLINTOS cloud networking tools to developers of RDCT technologies that are easy to use in diverse development scenarios ranging from coding a new clinical trial cloud application ground up, updating an existing product or building a multi-cloud CLINTOS ecosystem.

UVP8: Explicit, clear and transparent consent management to eliminate corporate liability– RDCT's decentralized PODs eliminates any ambiguity in consent management, because study subject's PODs will not serve content unless, study subject explicitly authorize the relevant APIs.

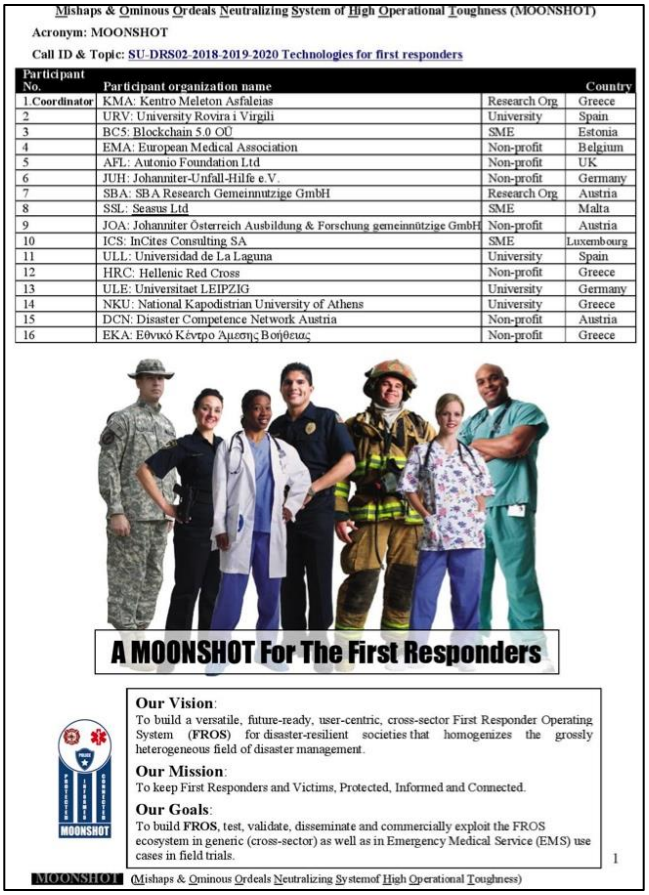
UVP9: Cost saving on GDPR compliance – As explained earlier businesses spend a considerable amount on having dedicated staff for manually implementing GDPR compliance. CLINTOS achieves compliance automatically.

UVP10: Additional corporate savings on cybersecurity–Segregating user data away from centralized servers considerably reduce the cost of deploying sophisticated cybersecurity monitoring tools and protocols.

UVP11: Improved Latency of CLINTOS- powered Clinical Trial applications- Latency has been one of the principal driving forces behind innovations created in developing fog and edge nodes to redistribute cloud resources closer to the user. CLINTOS uses PSIaaS to extend such distribution of cloud resources all the way to the End Node, thus making the cloud infrastructure considerably efficient and faster.

UVP12: Universal Compliance-by-Design (UCbD) & Ethics - Ethical impact assessment runs along the design and development phases of the CLINTOS infrastructure, and as a way of ensuring that, universal compliance-by-design is embedded in the technology. The CLINTOS PODs are user owned and controlled units of decentralized database that by default implement Universal Compliance by Design (UCbD) ensuring privacy, security & interoperability of stored personal data making it available to any app that needs it via an API at the user's behest. This essentially means that PODs can exchange data with EHRs, CDMSs, HSMs and seamlessly connect using just a single API. Since almost all regulatory regimes focus on securing patient's interest in their personal data, once CLINTOS vests full ownership and control in patients, all national or international regulatory regimes such as GDPR/CTR/GCP/ICH so on and so forth, UCbD will be potentially achieved by default. Conversely, legacy systems' protocol / rule-based compliance is cumbersome and resource consuming, and most importantly will only offer a palliative solution, keeping the problem of returning clinical data perpetually alive forever. This firstly, induces respect for GDPR, CTR and other country-specific regulatory practices and principles from the outset, secondly, disincentivizes cybercriminals by decentralizing citizen data away from central servers, which have traditionally been their key targets, and thirdly, provides an option to the CTMS, CDMS, HMS, EHR, providers to break their silos for enabling data interoperability.

UVP13: CLINTOS Framework Components Can Also Enable First Responder ICT Infrastructure - Using some of the components of the CLINTOS ecosystem, we recently collaborated with 15 other European entities to build a MOONSHOT consortium for bidding for a Horizon 2020 SUDRS02-2018-2019-2020 call for Technologies for first responders. The MOONSHOT first responder system also uses the wearable sensors and decentralized network to transmit vital signs in real time to create a new first responder concept of **"Transmit then Transfer"** for saving lives with improved pre-hospital life support and reducing the hospital triage time to zero.



UVP14: Finally, the RDCT SmartHub wearable device can be evolved to build a futuristic concept of worldwide passport standard to regulate human mobility in the post-Covid-19 world. The inter-border travel passport[62] was first created by the League of Nations (UN predecessor) in the aftermath of Spanish flu pandemic, a century ago in 1920. The double whammy of World War-I and Spanish Flu created enormous geopolitical shakeup triggering massive cross-border movement of populations. Travel passports were invented to regulate the huge influx of immigrants. Since then passport has become an essential document for cross-border mobility of citizens. The aftermath of Covid-19 pandemic is poised to create a new mobility standard for saving the world from the wrath of pathogens like or more virulent than Covid-19. **COVID** (Containment of Outbreaks of Virulent Infectious Diseases) project's ambition was to become that standard. CLINTOS' vision furthers that ambition.

2. Impact

2.1 Expected impacts

The nature of impact of a new technology is largely dependent on societal awareness of the perceived usefulness and perceived ease of use of the technology. The higher the societal awareness of these perceived values, the higher is the impact. Globalization, with increased global integration and travel, urbanization, deforestation and greater exploitation of the natural environment, has led to climate change resulting increased frequency of natural disasters including rapid spread of pathogens in pandemics, COVID-19 being deadliest of all natural disasters witnessed in our lifetimes thus far. The worldwide societal awareness of this catastrophe is the highest of any event in recent history. A solution that addresses such an emergency and the most frequent cause of sudden death, will obviously not only carry high awareness but high-perceived usefulness. Since CLINTOS is a non-intrusive wearable device in the form of an everyday gadget like a wristwatch, its perceived ease of use is also expected to be high.

Success breeds complacency, and complacency is the enemy of knowledge that invites failure. It is a double-edged sword, one edge kills success and the other decimates future. The technological successes made us so much intoxicated with the spoils of knowledge that we ignored threats to humanity from natural as well as man made calamities. The magnitude of Covid-19 pandemic has taught us not to be complacent anymore to impending disasters waiting to strike. Not to let such nano-sized enemies alleviate our successes and ruin our

[62] https://www.nationalgeographic.com/travel/features/a-history-of-the-passport/

future glory. Not to let emergencies take its toll when there exist technological possibilities to avert them or mitigate them.

The impact of CLINTOS innovation on humanity in general will be significant in saving lives across all sectors, and improving health of citizens. Its impact on the consortium partners will also be remarkable in enhancing the innovation capacity of all the consortium partners. While the academic partners of the CLINTOS consortium will gain from the new knowledge and build up their privacy, cybersecurity and particularly epidemiological and public health research capacities, the industry partners will benefit from an enhanced capacity in building profitable innovative solutions that deploy wearables, IoT devices that avert or mitigate emergencies and crises.

2.1a) Expected impacts set out in the Work Programme

CLINTOS will directly contribute to the expected impacts set out in the ECSEL-2020-3-IMI-ECSEL Joint Activity Trials@Home[63] Work Programme. The consortium is fully aware of the challenges the clinical trial industry faces. The costs of drug development have increased exponentially over the years, while clinical trial participation and retention have decreased. To that end, CLINTOS integrates sensors, wearable devices into a decentralized network of cloud computing resources that implement data security, data privacy and data interoperability as social and ethical values guiding the objectives of the Trials@Home work programme. The principal impact of the project will be the development of an ecosystem and testbeds, as well as new cloud-based services and infrastructures, new opportunities for the healthcare industry in general and pharmaceutical, clinical research, drug regulators and clinical trial subjects in particular. The impact of this project will enable new "technologies to implement a suite of processes in drug development.*"* The project will impact in building "the next generation digit technologies for clinical trials at home" by bringing together "all the scattered activities, technologies, platforms to a higher TRL level by addressing the technical, regulatory, compatibility and acceptability issues that at the moment block endorsement by pharma and hospitals"

Apart from its overall impact on the management of, and enhancing innovation capacities of the CLINTOS consortium partners in building their privacy, cybersecurity, and particularly CT and public health research capabilities in deploying wearables and IoT devices that enable remote decentralized clinical trials, CLINTOS directly has following expected impacts specifically set out in ECSEL-2020-3-IMI-ECSEL call. Accordingly, the extent to which the outputs of CLINTOS project will contribute at the European and/or International level include:

a. The creation and exploitation of market potential and the gain of a competitive technology advantage (Impact from participant perspective)
Over the decades all round technological advances in IoT, wearable sensors and cloud computing has made it possible to build a robust ICT infrastructure that can facilitate conducting the expensive clinical trials remotely affording substantial savings for the pharmaceutical industry on one hand, and make it convenient for the clinical trial participants on the other. Although several encouraging efforts have been made over the years, a comprehensive holistic solution is eluding, and warrants concentrated collective efforts to change the status quo in the global clinical trials scene. There is a substantial opportunity to create and exploit the potential market for Trials@Home technologies. Just as the advent of computers several decades ago created opportunities for building a diverse range software applications, which was basically jumpstarted by development of computer operating system (OS), the Trials@Home revolution needs a versatile OS to support the diverse clinical trial tools and applications. CLINTOS consortium creates and exploits that potential market to jumpstart a new health/pharma economy that builds on RDCTs. Given that Trials@Home is the future of drug development process, CLINTOS consortium positions their deliverables as the OS of the future clinical trials. This will give a significant technological advantage over a spectrum of competing products currently in development. This competitive advantage will not just be technological but will also be business as CLINTOS will be positioned in a "Complement not Compete" business model, which compliments all competing technologies as a Trials@Home operating system that supports all RDCT enabling technologies. CLINTOS architecture delivers an ecosystem that can support any cross-sector RDCT application and its components with the wearable SmartHub as its hub and decentralized backend for privacy, security and interoperability (PSI) of the network. CLINTOS' generic modular architecture allows any third party RDCT component or tool to be integrated into the CLINTOS ecosystem and by default benefit from the GDPR compliant PSI features of the CLINTOS architecture. CLINTOS is an application-agnostic OS for RDCTs.

[63] ECSEL Joint Undertaking, Work Plan 2020, page 62

For all the above reasons CLINTOS offers the consortium partners a substantial competitive technology advantage over competition, and presents an opportunity to exploit this new industry that's ready to be born.

b. Enhancing innovation capacity and integration of new knowledge (Impact from participant perspective);

The project will generate new knowledge on field validation of multiple novel use cases of the CLINTOS ecosystem. This new knowledge includes:

i) Field validation (CT-1) of CLINTOS as operating system for RDCTs with just plug-n-play convenience. It will establish that that platform will seamlessly integrate any third party CT / healthcare applications to facilitate remotely implemented RDCTs using CLINTOS ecosystem. The execution of such a clinical trial is as easy as installing a new software application on a computer OS. The RDCT sponsor just have to do the initial installation of the app (CTMS/CDMS etc) on the easy to use interfaces of the CLINTOS ecosystem, and all the necessary supporting services in the testing, validating and regulatory approval are automatically provisioned within the ecosystem.

ii) The field validation (CT-2) tests and validates 8 vital signs that the CLINTOS platform makes available to future RDCTs via a built-in real time vital signs monitoring system. Most new drugs are required to perform mandatory cardiotoxicity / neurotoxicity effects of the pharmaceutical agent. Heart Rate Variability (HRV) has emerged over the years as a very valuable marker of cardiotoxic / neurotoxic effects of drugs. The CLINTOS platform provides real time monitoring of HRV, picking up the earliest indications of any adverse effects on heart and brain. Hence CLINTOS has built in highly sensitive toxicity testing facility. It's built-in feature also ensures trial subject's adherence to the drug under trial. The CLINTOS SmartHub has ancillary wearable clothing that's powered with a Bluetooth and an electronic pill dispenser, which alerts the trial subject when the medication is due. If the trial subject misses the dose, it broadcasts the alert to the CLINTOS ecosystem and trial monitor / CRO / sponsor, who can respond appropriately.

iii) The field validation of the third CLINTOS (CT-3) use case is also a built-in frame feature that ensure volunteer adherence to cosmetics testing procedure. With more than 40.000 new cosmetic products released on the market every year the pressure for timely tests is increasing for CROs active in the field. The implementation of a RDCT system with a user friendly interface can guarantee faster product testing while ensuring adherence of volunteers to the trial boundary.

The new knowledge gained in the above validation studies will enhance the innovation capacity of the consortium participants, and encourage them to integrate the new knowledge into their area of expertise.

c. Strengthening Europe (by future employment and industrial investment) and the competitiveness and growth of companies by developing innovations meeting the needs of European and global markets; and, where relevant, by delivering such innovations to the markets or introducing new technologies into the industry (Impact from EU perspective);

In addition to the RDCT enabling features, two unique features of CLINTOS architecture – decentralized Personal Online Data stores (PODs) that ensure PSI (privacy, security, interoperability) of the data of the study subjects, and multi-cloud integration, make it easy for any size business to integrate GDPR/CTR compliance into any legacy CTMS / CDMS or any such clinical trial or patient data management tools / applications such as EHRs or HMSs (hospital management system). This not only disrupts the potential Trials@Home market, but also impacts the entire healthcare industry that deals with patient's personal data, creating new opportunities for European businesses, SMEs & developers to offer cloud based GDPR compliance by design, or cybersecurity enhancing services to not only the pharma industry, but also to the entire healthcare industry. CLINTOS thus increases the capacity of the European software industry to enhance EU's capabilities to exploit its own software infrastructures beyond just clinical trial industry, changing the way the world handles users' personal data in more ways than GDPR is already impacting the world in terms of privacy of the citizens.

The CLINTOS SmartHub comprising of sensors embedded in everyday wearables like a wristwatch and a smart T-shirt also have the potential to revolutionize the wearable industry in Europe and invite new investments in the wearable sector. The participation of one of Europe's leading textile brand Ozanteks in the consortium to produce a smart T-shirt itself is a testimony to the potential of the innovations that CLINTOS consortium is capable of bringing forth and creating future employment as well as industrial investments. This new innovation potential may trigger advanced technological/medical textile initiatives in the form of new spinoff companies. Comfortable, sustainable and technologically advanced smart t-shirt to be developed in the project may also generate an indirect market targeting individuals to be connected to a network not only for

health reasons but also for sports and/or leisure.

All of the above will create new employment opportunities, attract industrial investment in future and strengthen Europe, its competitiveness and growth of European businesses in the global markets.

d. The exploitation of project results per participant and, where relevant, at project level; management of IPR and where relevant management of the research data (for proposals that do not opt out of the pilot on open research data).

CLINTOS builds on leveraging several EU-funded research and innovation projects via the participation of 11 partners as consortium participants and 3 as Special Trials@Home Advisory Board, who bring their diverse experience gained in those Horizon 2020 projects. The research that this project undertakes in building CLINTOS infrastructure can be further leveraged to support the development and deployment of next generation applications and services in the ICT sector in general and healthcare sector in particular.

The CLINTOS consortium has participants from academia as well as industry. A mix of academia and industry make the consortium a very balanced one. CLINTOS technology ecosystem is so broad that there is room for every partner to exploit various aspects of the opportunities it offers. To maximize impact, it will be crucial to demonstrate the ROI in the proposed technology, but also to foster and manage the innovation potential resident in the CLINTOS IPR. This project begins with background IPR and also envisages foreground IPR resulting from the research undertaken by the consortium. Considering a substantial economic and social implication of CLINTOS, the consortium foresees a robust strategy to exploit the results per participant. IPR covering the novel CLINTOS architecture is already in place. Such IP will be treated as background IPR. The consortium will appoint appropriate IP firm to undertake "freedom to operate" analysis, and file and prosecute worldwide patents to ensure full IP protection to the novelty of CLINTOS wearable device and network architecture as child patents of the background IP or as foreground IP based on the extent of co-creation. An agreement between the consortium partners will define such IPR. All regulatory approvals will be sought for CLINTOS wearable devices. Such exploitation intent of some participant is categorically expressed in section 2.2(c)ii on **Exploitation**.

Further exploitation of the results of the research will be according to a robust data management plan (DMP) design in line with the principles of open research data as part of the pilot on open research data.

e. The dissemination of project results, the communication of the project; the development of standards, where appropriate.

The CLINTOS communication and dissemination activities are dealt with in **WP6** in detail. Building on the goals set by the dissemination strategy, the consortium will rollout a communications plan targeting different stakeholder groups and audiences. All activities will be organized in communication campaigns using a set of modern communication and knowledge management tools along with social media platforms to develop new communities of support and dissemination for the CLINTOS solution. CLINTOS consortium aims to involve in its activities the general public, pharma industry, health and clinical research management companies, healthcare, ICT sectors, and decision makers on public health and socioeconomic matters. A communication plan will be prepared (**WP6**) with the aim to present to a wide audience a realistic pathway to health / disaster management and to engage from the very early stage of design both the industrial and the academic sectors and governments in order to obtain important external input on this technological and political challenge. The communication plan will also identify the proper channels to maximize the impact of dissemination, also using the social media to build community awareness.

Successful dissemination will only occur if the market is receptive to the outcomes developed in the project and standards are a critical part of a functioning marketplace. Considering existing standards will guarantee that the project's results respect established practices, enhance interoperability and reach a better market application. Promoting the research results and to include them into future standards (protocols, guidelines, etc.) will facilitate the market uptake of the innovations. Standardization activities in CLINTOS are considered for this reason as a valuable tool for supporting dissemination of the project outcomes, by facilitating future reproducibility and widest use and raising market acceptance.

2.1b) Additional Impacts Over & Above The Call Text

2.1.(b)i. The Clinical Trial Operating System (CLINTOS):

The CLINTOS platform in general facilitates operation of all the diverse third party CT applications allowing them to operate seamlessly with other modules, components and tools in a plug-n-play fashion. Hence, it essentially functions as an operating system for all the CT applications, while introducing a few of its own.

2.1(b)ii. Interoperability With Electronic Health Records (EHR), EMS, etc:

Interoperability refers to the basic ability of computerized systems to connect and communicate with one another readily, even if they were developed by widely different manufacturers and supplied by different vendors. As much as EHR interoperability is desired for freer flow of information between different providers and systems, it is seriously lacking. Hospitals, clinics and doctor's offices, insurance providers, health networks, digital health devices, over thousand EHR vendors silo their data. To the beneficiary's disadvantage, they don't share. CLINTOS data saved in personal online data stores (PODs) stays in user's full control and can interact with any number of applications using a single API. Thus CLINTOS' decentralized PODs achieve interoperability by keeping user privacy intact, and without getting lost in the maze of disparate centralized servers of the legacy systems.

2.1.(b)iii. Life Beyond Covid-19:

The call text focuses on "Trials@Home" in general terms. However, Covid-19 pandemic is changing lives forever, and perhaps the ways CT practice will change in the future. Although Trials@Home concept precedes the Covid-19 pandemic, but the new normal that the pandemic is introducing will only accelerate uptake of RDCTs by pharma industry and CROs. The possibility of a more virulent pathogen posing existential threat to mankind is real, and we don't have any sustainable defense against such future catastrophes. If adapted universally, CLINTOS SmartHub device fills that void, and protects mankind from such life-disrupting pandemics in future.

2.1(b)iv. Mobility Check Points (MCPs):

AI-powered decentralized privacy-preserving CLINTOS device enable states to autonomously/ anonymously monitor and detect earliest signs of an outbreak or threat biological warfare threat, and implement privacy-preserving containment measures via screening, contact tracing, quarantine, social-distancing, mobility restrictions, etc. With an ultimate aim to become an autonomous health passport to seamlessly authorize safe human mobility across high footfall areas via Mobility Check Points (MCP). MCPs are non-intrusive walkthroughs that autonomously and seamlessly screen citizenry for any morbidity risk at entry point to spaces housing significant human congregation, like airports, malls, cinema halls, trains, buses, cross-border travels, etc.

2.1(b)v. Health Passport:

The currently omnipresent worldwide passport standard[64] was created in the aftermath of Spanish flu pandemic in 1920. One way the aftermath of Covid-19 pandemic will change our lives is restrictions on mobility. The world is perhaps a thousand fold more mobile than a century ago. In the current state-of-the-art regulating the movement of 7.8 billion people is conceptually impossible. A Digital Health Passport can create a new mobility standard for saving the world from the wrath of pathogens like Covid-19 and other catastrophe. As illustrated in the previous paragraph MCPs can seamlessly screen and authorize individuals' entry into any densely populated area or authenticate entry / exit at cross-border transfer points, such as traveling from one country to another.

[64] https://www.nationalgeographic.com/travel/features/a-history-of-the-passport/

2.1(b)vi. Digital Passport Holder:

A lot of jurisdictions are already implementing paperless entry/exit for International passengers. All paper passports will eventually become digital in future. Keeping them in mobile phone apps remains vulnerable to hacking. As compared to mobile phones, IoT devices with restricted applications are easier to secure (deploying ZEROV tech) compared to devices with application downloadability. CLINTOS security is strong enough to become a preferred device to hold citizen's passport securely. It will deploy ZEROV (Zero vulnerability) technology to make it unhackable.

2.1c) Potential barriers to impact & counter measures to deal with them

As a rule, every change, whether political or socio-economical, or technological, faces resistance either from existing stakeholders or from potential competing interests who prefer status quo. In case of CLINTOS, pharma industry is the major beneficiary and citizens as clinical trial subjects are the end users of the system.

Barriers	Contingency plan and counter measures
Citizens may not wish to use CLINTOS SmartHub wearable device	CLINTOS aims to not only provide clinical trial participants the convenience of remote participation from home, but also gives them total ownership control over their personal data to monitor & track where their data is sent & processed, and all in a wearable format that they are already used to. So CLINTOS awareness will remove this barrier.
CT sponsor, CROs & other CT vendors maintain status quo and do not wish to adopt the CLINTOS Platform perceived as competition	Participation of industry in the consortium is crucial for uptake of CLINTOS. The consortium plans briefings & demonstrations at multiple locations emphasizing that CLINTOS business model "**complement not compete**" and delivers higher ROI compared to the legacy CT systems that are in use today.
Competing systems may introduce different standards or interfaces that can also allow RDCTs to be implemented.	CLINTOS will review the competition for any IP infringement. Besides, technical partners are involved in multiple technical, privacy, security & CT related domains (See sec 4). They will use these networks to: i) stay informed about standards development, ii) influence agreed standards or recommend standards for consideration, iii) guarantee compatibility with third party systems.
Targeted CLINTOS users may perceive decentralization of private data as limitation for performance / scalability issue to enterprise production readiness	CLINTOS unique architecture cures the known performance and scalability problems of decentralization technologies, and also improves latency with exploitation of cloud continuum resources. Vertical and horizontal scalability can be easily achieved by adding additional server nodes at fog and edge level.
Legacy systems may find their backend databases difficult to sync with CLINTOS PODs	CLINTOS APIs can feed the frontend of any web application with POD data bypassing the legacy database fields serving user's personal data.
Interpretation of Articles of the GDPR may evolve as implementation of the GDPR matures	CLINTOS' compliance with GDPR is not rule-based implementation as other solutions are. Even if GDPR principles are judicially re-interpreted CLINTOS architecture transfers complete ownership & control to the users extinguishing any service provider liability

2.1d) European Added Value: A core principle of EU policy-making is the concept of "**European Added Value**". European Commission introduced the concept of the European added value (EAV) when it released its EU budget proposal for 2014 to 2020. According to the EC, the added value "is best defined as the value resulting from an EU intervention which is additional to the value that would have been otherwise created by member states alone".

The assumption is that "*a euro spent at EU level brings more benefits than if spent at national or regional level.*" According to this concept, EU's SOS funding will satisfy "**European Added Value"**.

2.1e) Impact Monitoring Framework

From the field trials of three use cases (CT-1, CT-2 and CT-3, key *performance indicators (s)* will be fed and

monitored during the project progress, applying the Impact mapping technique[65], thus constituting the main driver for CLINTOS. In this respect, the Impact Analysis and Monitoring Framework will be applied for collecting and analyzing data using the assigned KPIs. Each assigned partner will implement a context-driven combination of innovations. The resulting outcome will be evaluated using the initial KPIs and measurement system. It should be noted that the initial estimate of potential improvements is substantial, indicating the real need for the proposed work and innovations. At each level of targeted outcome KPI measurements will be recorded and will be compared to the target as indicated in the following table:

Outcome	KPIs
Objective: Minimum time on boarding customers take to realize value from CLINTOS solution. Estimating Time to Value (TTV) **(PERFORMANCE)**	
Developer time to customize, configure, test and deploy CLINTOS to specific business needs	• 1 day for experienced developers • 2 days for new / less experienced developers
Time to business impact in terms of months required for ROI	• CT/EHR/HMS related interests are immediate, increased visibility & control improves quickly over time, within 3 months business has full end to end visibility • 100% ROI in 6 months (breakeven)
Time to download, install, set up & deploy the CLINTOS solution (1,000 end-users)	• 10-15 minutes for 80% end-users • 15-30 minutes for novice end-users
Ease of use & Intuitiveness (1000 end-user survey rating 1-5 stars)	• 50% of users rating the product 5 stars for ease of use, usability, and intuitiveness, demonstrated through user feedback questionnaires
Time to configure Personal Online Data stores (PODs)	• 10-15 minutes for 80% end-users • 15-30 minutes for novice end-users
Always-on 24/7 vital signs monitoring in real time	• 100% CLINTOS SmartHub devices transmit victim's vital signs to remote server in real time
Plug-n-Play installation of third party CT apps on CLINTOS platform to establish it as an OS	• All 3 CTs report 100% integrity of third party CT apps installation and operations
Objective: End users are equipped with the CLINTOS to embed privacy, security & interoperability by default in their CT applications (OPERATION)	
CLINTOS platform is capable of automatically implementing privacy and interoperability by default.	• 100% cases in the 3 CTs pass GDPR criteria for privacy & interoperability test with at least one EHR
CLINTOS tools are easy to use and understand by developers, non-savvy businesses and end-users.	• >85% of pilot participants report "satisfied" or "very satisfied" in ease of use.
CLINTOS resources, tools can be used by a wide range of stakeholders (businesses, data managers, developers)	• Usability score of 300 users within 95% confidence limit, statistically insignificant difference in the usability reports when disaggregating by type of entities involved in the field tests.
Objective: CLINTOS platform used by businesses & developers in the long term **(EXPLOITATION)**	
CLINTOS achieves a TRL7 by the project end.	• CLINTOS platform available in 3 languages and 2 operating systems
CLINTOS backend PODs "public and free service" exploitation model available in English, German & Spanish through AFL, SS SST & UB respectively	• >200 businesses/developers test the platform • >100 German/Spanish stakeholders test the platform • 3 CT vendors interested in adapting the CLINTOS as generic RDCT ecosystem option.
CLINTOS commercial service to businesses / developers to be used across the EU as a standalone service or federated with existing service	• >10 of SMEs/developers test the platform and participate in market assessment. • At least 1 CT application vendor tests the platform
CLINTOS CT advisory, consultancy, training skills amongst consortium partners	• At least one of the partners becomes a CLINTOS CT advisory to promote it within the healthcare industry.

[65]Adzic, G., (2012), Impact Mapping: Making a big impact with software products and projects. Provoking Thoughts.

Outcome	KPIs
Accelerate the process of building a CLINTOS ecosystem within Europe	• By the end of year 1, at least 3,000 more people knowing about the CLINTOS ecosystem • By the end of the 3rd year, collaborating with at least 3 European business or projects

2.2 Measures to Maximize Impact

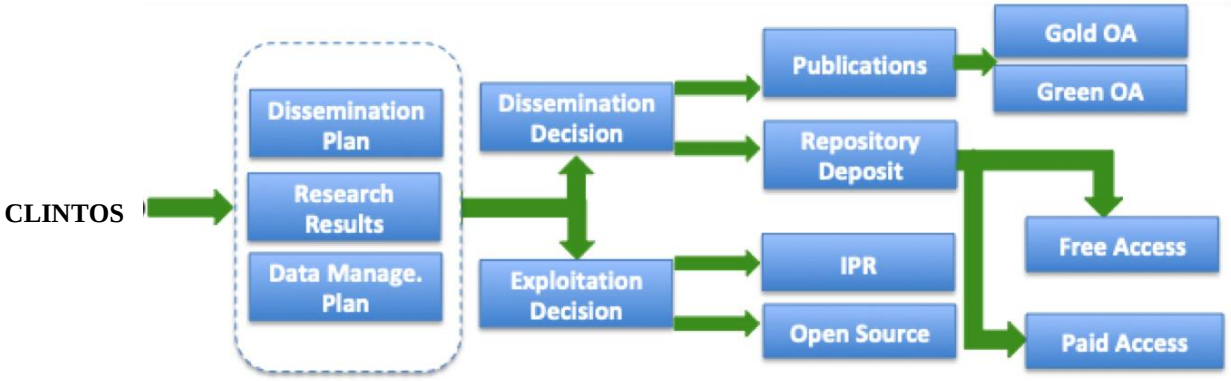
Adoption of a new technology by individuals can be explained by the "Technology acceptance model (TAM)[66]," which establishes a connection between how the ease-of-use and usefulness of a technology is perceived, in addition to social influences. If the technology is supported by an organization or consortium, then it is more likely to be seen as useful as well as credible to an extent. People are more likely to successfully adopt a technology if the management provides enough supporting resources to reduce the friction while transitioning to a new system.

Assuming that CLINTOS project deliverables satisfy the TAM criteria of mass acceptability, the project results exploitation & dissemination measures will include participation in conferences, workshops, forums, research activities, commercial activities, standardization, skills and educational training, social media marketing, lobbying policy makers and implementers, etc., for reaching out to potential end-users and stakeholders.

2.2(a) Overall CLINTOS Dissemination and Exploitation Capability and Approach

To maximize impact, it will be crucial to demonstrate the ROI in the proposed technology, but also to foster the innovation potential resident in the background IPR but also resulting foreground IPR. Considering a substantial economic and social implication of CLINTOS, we envisage a robust strategy to disseminate and exploit the results.

The CLINTOS partners have extensive experience in the area of safety, security, privacy and health of citizens including crisis and disaster management, as well as cloud computing, IoT and ICT perspective accumulated through collaborative participation in multiple CT related projects in addition to their own in-house ICT activities. The consortium partners are therefore well placed to jointly raise targeted awareness regarding CLINTOS among beneficiaries and stakeholders, reaching a wide cross-sector acceptance of the offered



Dissemination and exploitation approach

technological opportunities. Accordingly, each partner in WP6 has a dedicated dissemination expert that specializes in the dissemination of project outcomes and is experienced in leading targeted dissemination activities.

Exploitation and dissemination activities serve to create awareness in support of commercialization objectives but also to contribute in building the collective EU knowledge and EU innovation capacity in advancing towards a smart RDCT ecosystem that's by default compliant with privacy and security regulations and protocols. Exploitation of the technologies developed in this project culminates in a consensus commercialization strategy. From an exploitation perspective, the consortium consists of three main groups, each having a different role in the exploitation of the innovative CLINTOS consultancy and technology service. Organizations that need assistance in upgrading their clinical trial services to RDCT, fall in these three groups:

i) Pharmaceutical companies as sponsors of clinical trials

[66] https://pdfs.semanticscholar.org/dfb8/4d8c2c81fb67355f4af3bc361b79c45fb017.pdf

ii) CROs
iii) CTMS/CDMS and other CT vendors.

The development of the proposed CLINTOS ecosystem is considered a key capacity business growth. It allows for advancement of dialogue with stakeholders regarding the performance of advanced digital technologies for the clinical trials of the future in the context of their overall economic viability and long-term sustainability. It also contributes to making the European industrial context more attractive to foreign investors. New products and processes, as well as cost and time savings due to an increased efficiency of RDCTs facilitating not only the management of Trials@Home, but also the possibility of deploying CLINTOS as a comprehensive Operating System (OS) to run any CT vendor application, tool seamlessly. The overall approach to dissemination and exploitation of CLINTOS results is summarized in the following diagram:

2.2(a)i. CLINTOS end-users:
The final end users of the CLINTOS devices are the citizens that will be initially reached as User Groups through the partner organizations (in sectors outlined above). A B2C business strategy will reach out directly to the citizens and CT/privacy activists, while a B2B strategy will offer the tech to pharma industry, hospitals, CROs, CT vendors and NGOs directly or via WHO or other healthcare agencies.

2.2(a)ii. Commercial services and technology suppliers / developers:
These suppliers are represented in the consortium by 4 SMEs and 1 large enterprise viz. BC5, ISS, ABI & MIA as SMEs and OT as a large enterprise each specializing in different aspects of the CLINTOS offering (see section 3.3). These SMEs companies have a broad and credible experience in commercializing and supplying innovative services and technologies.

2.2(a)iii. Research organizations:
The research organizations are adequately represented by 2 universities (1 as consortium partner and coordinator and 1 as advisory board member), 2 research organizations (via Trials@Home advisory board) and 1 non-profit, out of which CERTH and MLC are carrying out leading research in the area of RDCTs, patient data, cloud computing, data privacy, security and interoperability and will lead the CLINTOS innovation stream along with BC5, the originator of the wearable SmartHub technology.

2.2.(a)iv. Stakeholders:
Our focus will be pharmaceutical companies, governments, caregivers, payers, NGOs and frontline activists. Since Covid-19 pandemic became a global health & economic catastrophe with no precedence in living memory, and no community or country spared, every citizen, neighborhood, city, country and their governments, health and economic regulators have woken up to the need for conducting clinical trials remotely making them stakeholders.

2.2(a)v. The CLINTOS Consortium Website:
Creating a website for the consortium will be one of the very first steps towards building an outlet for communicating with the end users, stakeholders and public in general. A domain such as www.theCLINTOS.eu will be acquired.

2.2(a)vi. Knowledge Management:
The publications resulting from the results of the project will be published in peer-reviewed scientific journals as well as other online forums providing free online access in compliance with the principles of Open Access Gold model. A repository of the open source component of the ecosystem will also be created at GitHub for facilitating the code access to the consortium partners and the developer community.

2.2(a)vii. Open Access and Data Management Plan
Research Data: The Consortium will adopt a policy of open access to all research data generated from the project, and appoint a member to manage the results of the research and create a knowledge management and protection strategy that will make the data findable, accessible, interoperable and reusable (FAIR). CLINTOS will not publish confidential or restricted results under Open Access, regarding all scientific publications produced along the project lifecycle. Specifically, special attention is being given to the information and data characterized as EU CONFIDENTIAL, for which access will be granted only to authorize project participants.

Business / Marketing Data: Since CLINTOS will be developed as a commercially viable business, the results of the field trials will be quickly analyzed to create marketing data, and will be promptly disseminated by consortium partners via social media channels, conferences and workshops during the course of the project.

For any other project outcome with public level of dissemination, wider distribution will be considered and examined in the Data Management Plan (DMP). With respect to data exploitation, the DMP will determine how

other stakeholders might exploit the data and how the data can be verified after it has been deposited. The project will use established standards and non-proprietary formats for data collection, as far as possible to support future exploitation of the data either by project partners or by external entities where open access is implemented.

With respect to publications, although it is preferable to publish in online publications free of charge, when it is not possible it will be up to the partner who will cover the associated costs. Two ways of publishing will be evaluated: ***Gold Open Access***, which grants immediate access through a publisher, and ***Green Open Access***, that will be considered as a second option. This strategy is directly related to the "Open" paradigm that will be used for publishing project results. The initial version of the DMP will be delivered by M8, and will evolve during the lifetime of the project. The final version will be delivered at the end of the project.

2.2(a)viii. IPR Management & Regulatory Issues:

A provisional patent application covering the novel CLINTOS architecture is already in place. Such IP will be treated as background IP. The consortium will appoint appropriate IP firm to undertake "freedom to operate" analysis, and file and prosecute worldwide patents to ensure full IP protection to the novelty of CLINTOS wearable device and network architecture as child patents of the background IP or as foreground IP based on the extent of co-creation. An agreement between the consortium partners will define such IPR. All regulatory approvals will be sought for CLINTOS wearable devices.

2.2(a)ix. Standardization Activities and Regulation:

Successful exploitation will only occur if the market is receptive to the outcomes developed in the project and standards are a critical part of a functioning marketplace. Considering existing standards will guarantee that the project's results respect established practices, enhance interoperability and reach a better market application. Moreover, promoting the research results and to include them into future standards (protocols, guidelines, etc.) will facilitate the market uptake of the innovations. Standardization activities in CLINTOS are considered for this reason as a valuable tool for supporting the exploitation and the dissemination of the project outcomes, by facilitating future replicability and widest use and raising market acceptance.

Relevant standardization is being developed in European and international standardization committees: CEN/CLC/JTC 13 is responsible or *Cybersecurity and Data Protection* in the European environment and ISO/IEC JTC 1 *Information technology* with its many subcommittees, among them, e.g., SC 27 *Information security, cybersecurity and privacy protection*, SC 32 *Data management and interchange* and SC 38 *Cloud Computing and Distributed Platforms*, is responsible for the activities on international level. Furthermore, IEEE has several communities, like the *Cloud Computing* or the *Cybersecurity Community*, and standardization activities with relevance for CLINTOS. A short list of standards that will be considered is given in the following table.

Standard	Impact on CLINTOS
ISO/IEC 29100 *Information technology — Security techniques — Privacy framework*	Provides a privacy framework with a common privacy terminology. It defines the actors and their roles in processing personally identifiable information (PII), describes privacy safeguarding considerations and provides references to known privacy principles for information technology.
ISO/IEC TR 27550 *Information technology — Security techniques — Privacy engineering for system life cycle processes*	Provides with a privacy engineering approach from a system life cycle process vision.
ISO 2054 *Information technology — Big data reference architecture*	The ISO/IEC 20547 series provides reference architecture, with use cases and derived requirements, a framework for this and an application process as well as security and privacy specifications.
ISO/IEC 27018 *Information technology — Security techniques — Code of practice for protection of personally identifiable information (PII) in public clouds acting as PII processors*	Provides commonly accepted control objectives, controls and guidelines for implementing measures to protect Personally Identifiable Information (PII) in accordance with the privacy principles in the public cloud-computing environment.
ISO/IEC 29100 *Information technology — Security techniques — Privacy framework*	Specifies a privacy framework which specifies a common privacy terminology, defines the actors and their roles in processing personally identifiable information (PII), describes privacy safeguarding considerations, and provides references to known privacy principles for information technology
IEEE SA P1912 *Standard for Privacy and Security Framework for Consumer Wireless Devices*	Defines a privacy scale that shall be applied to data that is defined as personal identifiable information that is being collected, retained, processed or shared by or among applications

	implemented on networked edge, fog, or cloud computing devices. This privacy scale data provides input to assessment tools that developers or users of these applications use to develop, discover, recognize, or implement appropriate privacy settings for types or levels of personal data resident on these devices.
IEEE SA P7002 *Data Privacy Process*	Provides an overall methodological approach that specifies practices to manage privacy issues within the systems/software engineering life cycle processes.
IEEE 11073 Service-oriented Device Connectivity	Allows for plug-and-play interconnectivity of medical devices and data exchange with the CLINTOS system, as well as getting access to specific functionalities of the devices and exchanging control signals

In addition, CLINTOS will comply with the GDPR, which will also be referenced in the CLINTOS Knowledge Base Observatory. The activities of European regulatory institutions will be followed up and relevant future regulations will be considered.

2.2(a)x. CLINTOS future commercialization strategy

The CLINTOS product consists of the components produced in WP2, WP3 & WP4, and their integration into solutions produced for the testing and validation in WP5, and dissemination and exploitation in WP6. No exploitation or dissemination plan to maximize the impact of a technology is complete without a follow up strategy in place. Without a follow up strategy to scale the technology and fund its commercialization, the investments made in its R&D remain at high risk. Our follow up strategy is aimed at achieving positive ROI within 12-24 months after the completion of the present phase of the CLINTOS project & and expanding beyond Europe.

2.2(a)xi. Addressing barriers that impede successful commercialization

CLINTOS, from the outset, has identified and put in place pre-emptive remediation steps to circumvent the conventional barriers that impede successful commercialization as summarized in table below:

Barriers	Contingency plan and counter measures
A commercialization endeavor tends to have a relatively low probability of success if the commercializing entities have not been named/agreed in advance of the project start.	The consortium collectively supports Blockchain 5.0 on a path to commercializing the technology
The absence of IP protection strategy	The first CLINTOS patent is already in process & additional expected as the project progresses. Where possible, all avenues towards exploitation of open source & open platform will also be explored as a basis for IP.
The absence of a commercialization business plan at the end of the project stalls or stagnates commercial exploitation	A Business Plan will be completed with a view to being "investment ready" by the end of year 3

2.2.(b) Social Impact Plan (SIP).

The EC research strategy indicates the importance that European projects achieve social impact. Starting from this demand, the consortium will design a specific Social Impact Plan (SIP) during the first month of the project. The SIP will include concrete strategies to consider during the project lifespan to achieve social impact. This strategy will be based on fulfilling a set of indicators (short-term, mid-term, and long-term) to measure and monitor the social impact during and after the implementation of the project. In addition, SIP will incorporate the shaping of a set of evaluation instruments in order to collect data on regards of the CLINTOS Social Impact.

The following table will be developed in advance to monitor the social impact of the project throughout its duration. The table is designed on the basis of the EC document *Monitoring the impact of EU Framework Programmes.*[67]

Project's contribution to the expected impact in relation to the Key Impact Pathways

Call´s expected impact:
1) **The creation and exploitation of market potential and the gain of a competitive technology advantage (Impact from participant perspective)**

[67] https://op.europa.eu/en/publication-detail/-/publication/cbb7ce39-d66d-11e8-9424-01aa75ed71a1

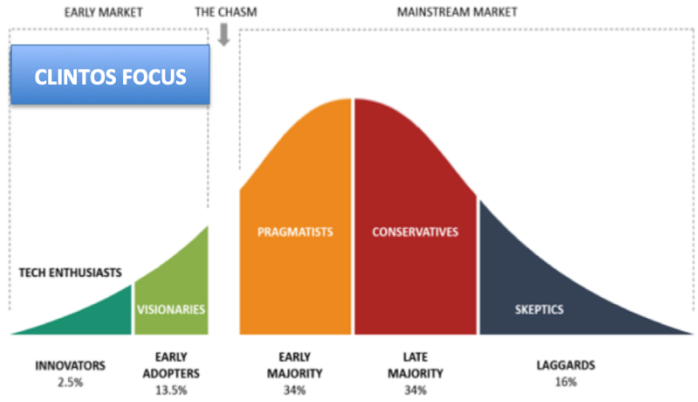
Key-Impact Pathway	Short-term indicators	Mid-term indicators	Long-term indicators
Addressing global challenges	Knowledge	Transference	Social impact
Engaging EU Citizen	Citizen engagement within the project's activities	Citizen engagement beyond the project	Quantitative and qualitative evidence of engagement, up-taking the project results
Supporting policy-making	Outputs relevant for EU policies	Number of interactions with policy-makers concerning the policy outputs	Number of policies including evidence of social impact based on the project's outputs
Call´s expected impact: ***2)*** **Enhancing innovation capacity and integration of new knowledge (Impact from participant perspective)**			
Key-Impact Pathway	**Short-term indicators**	**Mid-term indicators**	**Long-term indicators**
Addressing global challenges	Knowledge	Transference	Social impact
Engaging EU Citizen	Citizen engagement within the project's activities	Citizen engagement beyond the project	Quantitative and qualitative evidence of engagement, up-taking the project results
Supporting policy-making	Outputs relevant for EU policies	Number of interactions with policy-makers concerning the policy outputs	Number of policies including evidence of social impact based on the project's outputs
Call´s expected impact: ***3)*** **Strengthening Europe (by future employment and industrial investment) and the competitiveness and growth of companies by developing innovations meeting the needs of European and global markets; and, where relevant, by delivering such innovations to the markets or introducing new technologies into the industry (Impact from EU perspective);**			
Key-Impact Pathway	**Short-term indicators**	**Mid-term indicators**	**Long-term indicators**
Addressing global challenges	Knowledge	Transference	Social impact
Engaging EU Citizen	Citizen engagement within the project's activities	Citizen engagement beyond the project	Quantitative and qualitative evidence of engagement, up-taking the project results
Supporting policy-making	Outputs relevant for EU policies	Number of interactions with policy-makers concerning the policy outputs	Number of policies including evidence of social impact based on the project's outputs
Call´s expected impact: ***4)*** **The exploitation of project results per participant and, where relevant, at project level; management of IPR and where relevant management of the research data (for proposals that do not opt out of the pilot on open research data).**			
Key-Impact Pathway	**Short-term indicators**	**Mid-term indicators**	**Long-term indicators**
Addressing global challenges	Knowledge	Transference	Social impact
Engaging EU Citizen	Citizen engagement within the project's activities	Citizen engagement beyond the project	Quantitative and qualitative evidence of engagement, up-taking the project results
Supporting policy-making	Outputs relevant for EU policies	Number of interactions with policy-makers concerning the policy outputs	Number of policies including evidence of social impact based on the project's outputs
Call´s expected impact: ***5)*** **The dissemination of project results, the communication of the project; the development of standards, where appropriate**			
Key-Impact Pathway	**Short-term indicators**	**Mid-term indicators**	**Long-term indicators**
Addressing global challenges	Knowledge	Transference	Social impact

Engaging EU Citizen	Citizen engagement within the project's activities	Citizen engagement beyond the project	Quantitative and qualitative evidence of engagement, up-taking the project results
Supporting policy-making	Outputs relevant for EU policies	Number of interactions with policy-makers concerning the policy outputs	Number of policies including evidence of social impact based on the project's outputs

2.2(c) CLINTOS Adoption, Scale up, Offering and Engagement Strategy:

The project provides a range of activities and supporting tools addressing all functions of RDCTs - Development - Deployment - Operation - Learning life cycle of the CLINTOS offering. An inclusive stakeholder engagement strategy, will be adopted, through the CLINTOS Forum including Experts and Users Group and reaching out to the EU pharmaceutical industry / CT sponsors, CROs, CT vendors and state agencies who are placed in the driving seat in creating the trust environment that innovators and early adaptors need to facilitate CLINTOS' early market entry.

As proposed by Everett M Rogers in his **Diffusion of Innovations**,[68] every new technology dissemination goes through 5 stages. Such Technology Adoption Life Cycle has a bell curve and the divisions in the curve are roughly equivalent to where standard deviations would fall. This means that Innovators make up about 2.5% of the total population, the Early Adopters about 13.5%, the Early Majority and the Late Majority both 34% and the Laggards the remaining 16%. Each group represents a unique psychographic profile (i.e. a combination of psychological and demographic traits) that makes its marketing responses different from those of the other groups.



CLINTOS Engagement Strategy & Technology Adoption Life Cycle

Innovators and visionaries (early adapters) are the first groups of people that are likely to invest in new technology such as CLINTOS. Since they are more likely to pursue new technology products aggressively, they constitute the major focus of CLINTOS dissemination strategy. Although they are only a tiny segment of the target market, winning them over is important, because their endorsement reassures the other consumers in the marketplace that the product could in fact work. Furthermore, these Tech Enthusiasts can serve well as a test group in order to make the necessary modifications before targeting the mainstream. Early Adopters, like Innovators, buy into a new product concept very early in its life cycle and because they are good at alerting the rest of the population, they are of upmost importance to win over. And, moreover, because there is a big chasm before reaching out to the next group in the technology adoption life cycle, it is the most appropriate strategy for a new technology at the stage that CLINTOS is, to focus on the left side of the chasm. Hence CLINTOS engagement strategy focuses innovators and early adopters.

2.2(c)i Dissemination goals and strategies

The detailed aims of the CLINTOS dissemination plan are fourfold:

1. *Providing information to the research community about the general aims and progress of the project*. The intention is to ensure that interested parties are alerted as to the intent and general achievement of the project so that they can make contact with project members about areas of common interest and to minimize unnecessary duplication of effort in related projects. The primary method of achieving this goal will be through the development of a dedicated web site and targeted journal / conference papers. The CLINTOS *web site* will be the primary interface for project researchers and the intent is to give a concise summary of the open aspects of the project aims, work and achievement with the ability to drill down into publicly available detail. Key aspects of the site will be clarity, liveliness, debate and the ability to elicit appropriate and timely response from project team members when readers desire further information than is presented on the site. Targeted journal articles and presentation of project papers at selected conferences and seminars also support this aspect of the dissemination activity. Here the intent is to raise awareness of the project and its aims with relevant researchers and allow them to follow up on areas of common interest.

[68] STEPHEN F. MOSELEY (2004) Everett Rogers' Diffusion of Innovations Theory: Its Utility and Value in Public Health, Journal of Health Communication, 9:sup1, 149-151, DOI: 10.1080/10810730490271601

2. *Developing dialogue with researchers and developers* working in contiguous or overlapping areas to that of the project. The intent here is to open up a two-way dialogue to the benefit of both the project and external researchers. The primary tool for this will be a series of workshops discussing the project's achievements and needs. The benefit in doing this has two aspects. First, the project can benefit from being able to adopt common practices with groups in the wider research community, e.g. in the development of the widely accepted metrics. Second, the future exploitation potential of the results will be enhanced if outside groups adopt similar development methodologies or, at least, aspects of the project's methodology.

Although *workshops* will be the primary method of achieving this second aim, interactive methods such as communities, blogs and wikis will be used for their potential to involve a much wider target group than can be accommodated within a workshop, and for developing a continuous dialogue model. Increasingly all communications can be connected with each channel and platform (social media, blogs, micro media, mainstream news, Facebook, Youtube, Twitter) influencing one another.

3. *Communications program for raising the awareness of the potential benefits of the project results with commercial developers and commercial end-users*. These represent groups that could benefit both from the adoption of the general methodologies of the project and also the specific IP generated within the project. The primary method used to achieve this aim is essentially *targeted marketing of key results and messages*. This marketing will take the form of both directly delivered information and tailored presentations to individuals and / or single companies. A mailing/distribution list will be established which can raise awareness and allow regular contact (*e-newsletter*). Consideration will also be given to presentation of the project at relevant trade shows and exhibitions. The intent of this action is to assure that the expected outputs of the project are considered within the long-term development plans of the organizations concerned. This is particularly important where the targeted organization is a public body that may be responsible for future development programmes that could benefit from the project's outputs. The initial Communication Plan (Dissemination Matrix) is detailed in paragraph **2.2(a)**.

4. *Enacting a Public relations program* is to raise awareness of the benefits of the project in terms of future capability and cost effectiveness with both the general public and the press. The primary method used in this area will be press releases and selected media appearances backed up by a public friendly area of the web site and web hosted resources for the press.

2.2(c)ii Exploitation

Commercialization principles agreed by the consortium partners

The Consortium's stated intention is to commercialize the results and outputs from the CLINTOS Project with a view to large-scale adoption, initially targeting the EU market and, subsequently, North America, and beyond. To place the project on a viable commercialization path from the outset, the consortium recognizes that CLINTOS represents "*Industry led Innovation and Commercialization*" with specific contributions from partners, and has structured purpose, objective and approach accordingly. Commercialization will be governed by the Intellectual Property Agreements between the partners, which will be detailed within the Consortium Agreement. Nothing within the commercialization plan will restrict a partner's ability to act in his or her own interests in individually exploiting rights granted to them under the Consortium Agreement. However, it is intended that the commercialization plan should assist partners in their individual efforts and provide a common platform for maximally exploiting the opportunities presented by the project outcomes.

The shared commercial exploitation principles include:

- Share of the foreground IPR on the developed system between the partners.
- Shared further development and commercial exploitation of the developed CLINTOS system.
- Trials to get data on the commercial advantages of the system
- Demonstration to potential customers of the CLINTOS research and innovation to European industry and public bodies about the significance of this technological development.

Initial exploitation intentions of consortium partners

Participation in CLINTOS aims to allow the commercial partners to acquire significant expertise and know-how in state-of-the-art pertaining to RDCT tools and services. Commercial prospects are enhanced by virtue of steering the project and its work plan, from the very outset.

BC5	BC5 will lead the commercialization process and has strong interest in continued research and development of CLINTOS, its predecessor COVID and its decentralized PSIaaS ecosystem.
ISS	Extend the capabilities and functionalities of ISS existing portfolio of products catering to the cinical trials industry, improving models, front-end dashboards and user-friendly open standards APIs.

	Advance knowledge in privacy, security and interoperability (PSI)will extend the company's R&D activities in fields related to AI, Internet, Cloud and ICT. Will include user feedback from demonstrators and use cases as input for future improvements in user experience. Will support the common commercialization strategy and exploit project knowledge in regulatory compliance.
UTB	The University will support the common commercialization strategy and will use the results & findings to enrich the existing course program for students as well as security authorities officials in the areas of RDCT, cloud technologies, cloud forensics, cyber security & GDPR. Furthermore, it plans to use the knowledge and expertise gained for further research in the field of post quantum cryptography.
SST	Will exploit the results derived from its contribution to CLINTOS through academic research publications that will enhance its already reputed position in the ICT, health data, ethical and legal research arena. In addition, will look for incorporating the results of the project within its portfolio of legal and research services in the field of cyber security.
MIA	Will exploit tools and software libraries developed in the project in order to provide secure solutions to customers that are managing personal information within the companies existing portfolio of cloud services including their proprietary hospital information management system. MIA will extend its portfolio eHealth solutions to new RDCT service and will also improve its existing ICT services. It will contribute to the documentation with experience from ISO 27001 certification methodology.
OT	Will support the consortium with their knowledge they have accumulated since 1970s. The textile company will develop and test the wearable textile product, which is to be home for sensors and other data providing equipment to be made available by the other partners in the consortium. The company will design, produce and test the smart T-shirt to improve the goals of the project by providing a quality and comfortable product to increase the chance of data quality and duration of data flow from the patient for better diagnoses, treatments and/or rehabilitates. Therefore, with this aim, the company will determine and analyze yarn properties (antibacterial, thermal, thermo-regulative, conductive, etc.); design and manufacture T-shirt; optimize dyeing and finishing processes; evaluate comfort and performance properties and carry out all necessary final tests for the T-shirt. The company will contribute all relevant dissemination activities and carry out the indirect market analysis for the smart textile product.
ABI	ABI will support the common commercialization strategy by incorporating RDCT services within its cosmetic care specialty, testing and evaluating skin care products for clients as a specialized CRO. It will use the results & findings to enrich its existing knowledge base in dermatology.
HBI	HBI will support the common commercialization strategy by promoting the value HRV analysis in the context of RDCTs.

2.2(c)iii. Communication activities

Building on the goals set by the dissemination and exploitation strategy, the consortium will roll-out a communications plan targeting different stakeholder groups and audiences. All activities will be organized in communication campaigns. A set of modern communication and knowledge management tools will be used along with social media platforms to develop new communities of support and dissemination for the CLINTOS solutions

CLINTOS consortium aims to involve in its activities the general public, pharmaceutical companies / CT sponsors, CROs, CTMS / CDMS vendors, healthcare, ICT sectors, and decision makers on public health and socioeconomic matters. A communication plan will be prepared (**WP6**) with the aim to present to a wide audience a realistic pathway to health / disaster management and to engage from the very early stage of design both the industrial and the academic sectors and governments in order to obtain important external input on this technological and political challenge. The communication plan will also identify the proper channels to maximize the impact of dissemination, also using the social media to build community awareness.

A collaborative workspace for project members and a public website will be developed. Dedicated links on the public website will help sharing and enhancing knowledge of technical information, also in a non-specialized format. This will also help increase general awareness of the existential threats from pandemic and demonstrate the benefits of the project to policy makers. Policy makers will be informed about the costs and benefits of the solution, scientists will have a base for exchanging technical information, the general public will be exposed to data on which to base their informed judgment.

It is also important to carry out communication actions addressed to a wider public, because global crisis is of

public concern. For this reason, a series of factsheets explaining the benefits of this technology, will be prepared, periodically updated, made available on the website and also presented to selected audiences and newsgroups.

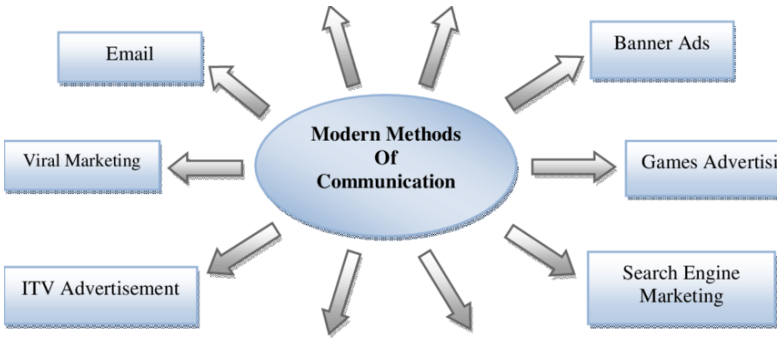
WP6 will organize the event "**Young Women in Healthcare**", with participation of professionals and PhD students, aiming to promote the role of women in computer science and to attract young scientists into this crucial field for the future of our civilization.

Developer Community Bootstrapping & Onboarding: Expectations, perceptions and feelings of developers with respect to onboarding on a new platform and participation, have to be taken into account in designing any bootstrapping strategy. The developers need incentives for entering the ecosystem as well as staying in it. They are motivated to participate in a software platform[69] for 1) improving technical knowledge, 2) obtaining new knowledge, 3) building successful applications, and 4) project visibility.

The motives that lead developers to initiate participation in open source[70] projects include, "software use value, status and recognition, learning, personal enjoyment, reciprocity, getting paid, sense of ownership and control, career advancement, free software ideology, and social identity".

The factors that affect developer experience and the reasons developers come to platform technology projects can be summarized as follows:

- Technology shows promise
- Visibility or popularity
- Job opportunities
- Interesting
- Ideology
- Recognition and identity



The reasons developers stay with projects are:

- Good developer experience
- Job opportunities
- Good developer community
- Growth in platform
- Incentives

Factors affecting developer experience:

- Quality of learning resources
- Activity in the community
- Quality and Quantity of tooling Stability of platform
- Technical capabilities and features of the project

Our strategy to engage the developer community will be based on these factors that incentivize their participation.

Policy Makers: Lawmakers play a key role in drafting regulations that concern safety, security and privacy of citizens. Engaging policy makers at the outset smoothens adaptation and implementation of technologies that impact citizens' safety. "Privacy By Design" has so far been more or less a concept of regulatory implementation of centralized databases, and not purely a technological implementation. CLINTOS is completely and entirely a technological "By Design" implementation that autonomously protects user privacy without any intervention from the business owner or the service provider. This is a major paradigm shift from the concepts that privacy policy makers relied on for enacting the GDPR. Establishing communication channels with the policy makers therefore serves the consortium objectives better**.**

Privacy Activists: Privacy activists all across Europe have played a very important role in drafting and enacting the GDPR. They also can play an important role if CLINTOS technology and infrastructure can ensure user privacy by default, without businesses having to fix loopholes in their current privacy-compromising centralized systems.

[69] https://ieeexplore.ieee.org/document/7961694

[70] https://www.researchgate.net/publication/220591474_Understanding_Sustained_Participation_in_Open_Source_Software_Projects

RDCT Forums: Projected to exceed $65 Billion,[71] clinical trials market is poised for poised for personalized medicine that suites the RDCTs. RDCT forums will be important targets for engaging innovators and early adopters.

Masses & Media: The most common platforms for reaching out to the masses are newspapers, magazines, radio, television, and the Internet. It's the primary means of communication used to reach the vast majority of the general public. Each type of media involves both content, and also a device or object through which that content is delivered. In the next section we will deal in detail with the content and appropriate devices or delivery vehicles for the content.

Investors & Business Plan: Communicating with the potential investors is as important as with any other stakeholder. Every business needs to have a written business plan that it uses to connect to investors. Whether it's to provide direction or attract investors, a business plan is vital for the success of a business. It is also a road map that provides directions so a business can plan its future and helps it avoid bumps in the road. Our business strategy models around "**complement not compete**" theme that connects with the current clinical trial industry incumbents as providers of a CLINTOS ecosystem that complements their cloud offerings by adding real time remote patient monitoring instead of directly competing their –cloud CT offerings.

2.2(c)iv Communication Materials & Learning Resources:

Stiller and LeBlanc's study in the effectiveness of "software engineering pedagogy[72]" is helpful in formulating some guidelines for producing learning resources that result in more successful transfer of knowledge to different target audiences. Such communication activities can be in the form of tutorials for target audience that range from developers, policy makers, pharma industry, CROs CT vendors and CT participants. Such tutorials may be scripted according to following guidelines:

- A tutorial should be fun.
- A tutorial should be accessible.
- A tutorial should be useful, and should lead to actual learning, not merely theoretical or conceptual.
- A tutorial should have a clear, consistent voice focused on characterizing the technology being taught.
- A good software technology tutorial has an actual application as an objective.
- A tutorial should be complete with links to additional materials and further reading supporting subsequent learning. An open-ended tutorial can leave readers confused.
- If the target audience is developer community the tutorial should include relevant code samples.

2.2(c)v. Communication Methods:

The standard methods of communication have always been speaking or writing by a communicator, and listening or reading by the receiver. Most conventional communication is oral, with one party speaking and others listening. However, technology has considerably evolved our means of communication. Modern methods of communication break all the barriers that ever existed connecting to humanity. There are now countless ways that one can connect with one's target audiences. They are so numerous that no infographic can do justice listing them all. Here is our best effort. Since our entire target audience and online privacy/security stakeholders are online and connected, our main thrust will be communication via social media channels.

The best way to exploit our business model and all possible online channels would be to divide various communication modalities into explicitly defined work packages, and appoint specific consortium partners to lead them. Accordingly we envisage the following dissemination / communication **WP6** tasks:

- Diffuse scientific and technological knowledge generated within the context of the project through a set of dissemination activities.
- Provide valuable feedback to relative standardization bodies and consortiums about the integration of the respective technologies, their applicability, their completeness, their optimization and their future development.

[71] https://www.businesswire.com/news/home/20190801005504/en/Global-Clinical-Trials-Market-Projected-Exceed-65
[72] https://www.researchgate.net/publication/234832323_Effective_software_engineering_pedagogy

- Raise awareness and attract potential supporters, end users and customers through a detailed communication strategy consisting of a bouquet of tools and channels, tailored to each target stakeholder.
- Understand the existing market, the potential client base for the proposed ecosystem, to identify the competitors and formulate a marketing strategy based on "Complement not Compete" for a feasible business plan.
- -Identify all exploitable components of the CLINTOS ecosystem, define the potential commercial products and commercial strategies for these results (target market, business model(s), distribution channels and promotional strategy) to reach the market.

2.2(c)vi. Dissemination matrix

CLINTOS is an enabling platform technology that has cross-sector applicability in a wide range of clinical trial scenarios. A communication plan will be prepared (**WP6**) with the aim to present to a wide audience a realistic pathway to disaster management and to engage from the very early stage both industrial & academic sectors in order to obtain important external input on the CLINTOS challenge. Moreover, "**Young Women in healthcare**" workshop that the CLINTOS consortium will organize, will promote women's role in CT and healthcare, attracting young scientists into this field. The overall dissemination matrix of the communication plan is presented here:

	Communication Tool	Type	Success Metrics	No.	Target Audience
1	CLINTOS Website	Online	SEO Metrics	1	>50,000
2	Research Publications	Peer Review	No. of articles	6	6000
3	GitHub Repository	Uploads	No of entries	20	4000
5	Webinars	Online	Participant nos.	6	600
6	TV /Web shows	Online	Viewers	2	>50,000
7	Socials: Facebook, Twitter, Youtube, LinkedIn	Online	No of users	3	>10,000
8	Project meetings, stakeholder roundtables	Events	No of events	8	>20
9	Dissemination & Validation Workshops (e.g. **Young Women in Health** & **Academia meets industry**)	Events	No of attendees	4	>150
10	Newsletters, Success Stories, Factsheets	Documentation	Publications nos.	4	>1500
11	Promotional Videos	Distribute Online	Views	2	> 2,000 views
12	Conferences	Events	No of events		6
13	Training modules	On request	No of Modules	1	>20
14	Press Releases, Policy Briefs etc.	Online	No of elements	8	8,000
15	CLINTOS Community	Online	No of members	1	>100
16	CLINTOS Global Hack Challenge To Hackers	Online	Winner	1	100

3. Implementation

3.1 Work plan – Work packages, deliverables

The project work will be organized in 6 Work Packages (WPs) that correspond to the project objectives 1 through

5, and are aligned with the project methodology (new research for MVP in **WP2-WP3**, testing and validation procedures in **WP4-WP5**) described in **1.3(b)**, and implemented in **WP2** through **WP5**. **WP6** implements the project's **plan for exploitation and dissemination of results (PEDR)**. **WP1** led by **UTB** links all the WPs that accomplish the 5 objectives together and ensures that the Consortium as a whole complies with the rules and regulations set by the European Commission, so that the coordination of the Consortium Partners results in success of the project in terms of accomplishing the timely delivery of the project deliverables and financial adherence.

The goals of **WP2** led by **SST** include analysis with assessment of legal and business practices and role of supporting technologies to create a reference framework for Trials@Home and detailed vision for the project. This detailed vision will take the form of a blueprint for a user-centric network architecture & specifications of the CLINTOS platform that revolutionizes the RDCT ecosystem with CLINTOS' novel "**Operating System**" concept for future RDCTs that provides a universally compliant ecosystem that supports all types of existing CT applications for diverse CT use cases such as CTMS, CDMS, EDS, eTMF, so on and so forth.

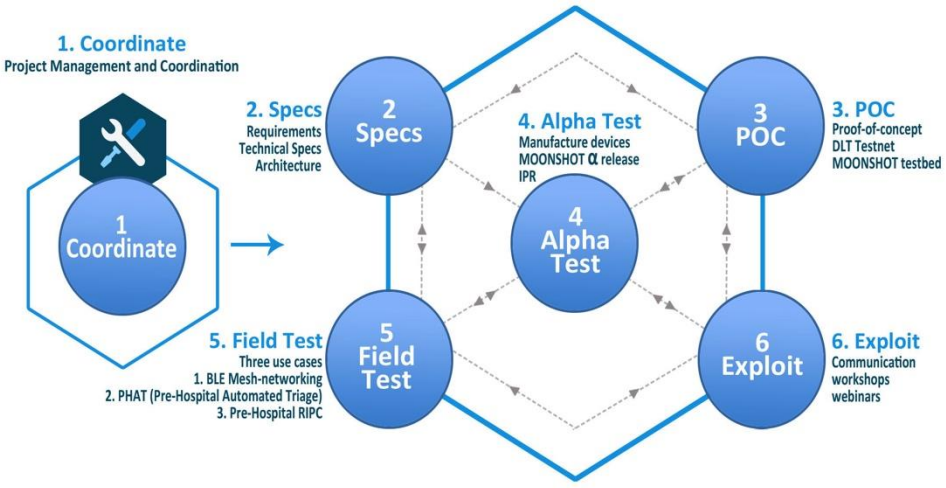
Deliverables of the **WP2** will guide research to build the components of the CLINTOS ecosystem as a modular infrastructure that can easily add different modules as needed in a plug-n-play fashion. The development and integration of these modules of the CLINTOS infrastructure as specified in section 1.3(b)1.i are accomplished to deliver a fully functional Minimum Viable Product (MVP) in **WP3**. While **SST** is leading **WP2** for development of full specifications and architecture of the technology – CLINTOS, **BC5**, as originator of the existing wearable devices and decentralized network, will lead the MVP / POC development in **WP3**. The deliverables of **WP3** are the CLINTOS MVP and CLINTOS testbed and DLT testnet. The CLINTOS POC hardware will be manufactured for testing and CE marking and releasing an alpha version of the CLINTOS platform prototype in **WP4** led by **AFL**. CLINTOS prototype manufacturing will be scaled up for real world usability testing in three pilot clinical trials for CLINTOS' first market replication.

The CLINTOS MVP will be tested and validated individually, collectively and in the real world user cases in the next two WPs, viz. **WP4** and **WP5**. While **WP4** focuses on testing each of the modules as components of the Trials@Home operating system network to deliver the alpha version of the complete CLINTOS software product that goes through first market replication pilot testing and trial in **WP5**, in at least three use-cases specified in sec **1.3(b)**. A detailed IPR review is also performed in **WP4** and appropriate patent applications are filed to protect the novelty of the CLINTOS software. **WP5** will be led by **ISS**. These use-cases are real world use-cases, and tested in different settings will offer different challenges, innovation opportunities, and future market segments for CLINTOS outputs. The three CTs (CT-1, CT-2 & CT-3) validated in **WP5** are deemed to offer different challenges, innovation opportunities, and future market segments for the CLINTOS first market replication outputs. Such market segments are focused toward a niche "**complement and not compete**" business model strategy. The **WP5** field-testing also completes a third party audit of the CLINTOS software code. After final bug fixes the CLINTOS code is qualified for a limited closed beta release and deposited in one of the code repositories such as GitHub. The CLINTOS product's limited release serves the specific objectives of exploitation and dissemination of results implemented in the sixth and last WP. The open source components of the ecosystem will be released as open source software under MIT license. **WP6** led by **EMA** shall execute **PEDR** (Plan for Exploitation & Dissemination of Results).

WP6 will introduce the CLINTOS ecosystem to the European ICT projects for defragmenting the roadmap to single digital market (SDM) for the benefit of European industry, the European research community and ultimately for the benefit of the European citizens. **WP6** will also educate, explain the novel **"Trials@Home Operating System"** concept of the CLINTOS ecosystem to potential beneficiaries, end-users, developers, policymakers, industry, scientific & standardization community. This will be done in a series of workshops (including "**Young Women in Health**" workshop), webinars and publications. **WP6** will also deliver a Business Plan to steer the project's innovation on an accelerated path to commercial adoption in a "**complement not compete**" business model that's non-intimidating to the current clinical trial industry incumbents by offering a comprehensive RDCT operating system that embeds Privacy-Security-Interoperability by default into their existing offerings instead of competing with their services.

WP6 will also build Pan-European CLINTOS awareness by engaging EC-fundedCT projects in inter-consortia alliances. As specified in section **1.3(a)9**, there are over a dozen related projects that are linked to the CLINTOS consortium through common partners. **WP6** will also build a community of developers, CT sponsors, CROs CT vendors, NGOs, DPAs (Data Protection Agencies), stakeholders at all levels of International / European cooperation.

As illustrated in detail in section **1.3(b)i a**n agile development methodology and innovation cycle will be adopted. This agile development strategy will be aided by a learning system, which is an integral part of the solutions in each CT and allows stakeholders to share knowledge, experiment and innovate. The Learning system incorporates the Privacy and Ethical Impact Assessment (P/EIA) of the CLINTOS Platform that supports knowledge development and commercialization readiness.



PERT Chart

A bird's eye view of the overall organization of WPs and their relational landscape is illustrated in the PERT Chart exhibited herein.

3.1(a) Timing of WPs and Components (Gantt Chart)

The time dimension of the project is displayed in the following Gantt Chart below. As the project follows an agile approach, there are number of iterations per work package and task. Milestones are represented with vertical red lines.

Work Plan Scheduling of WP Tasks & Milestones (Gantt chart)

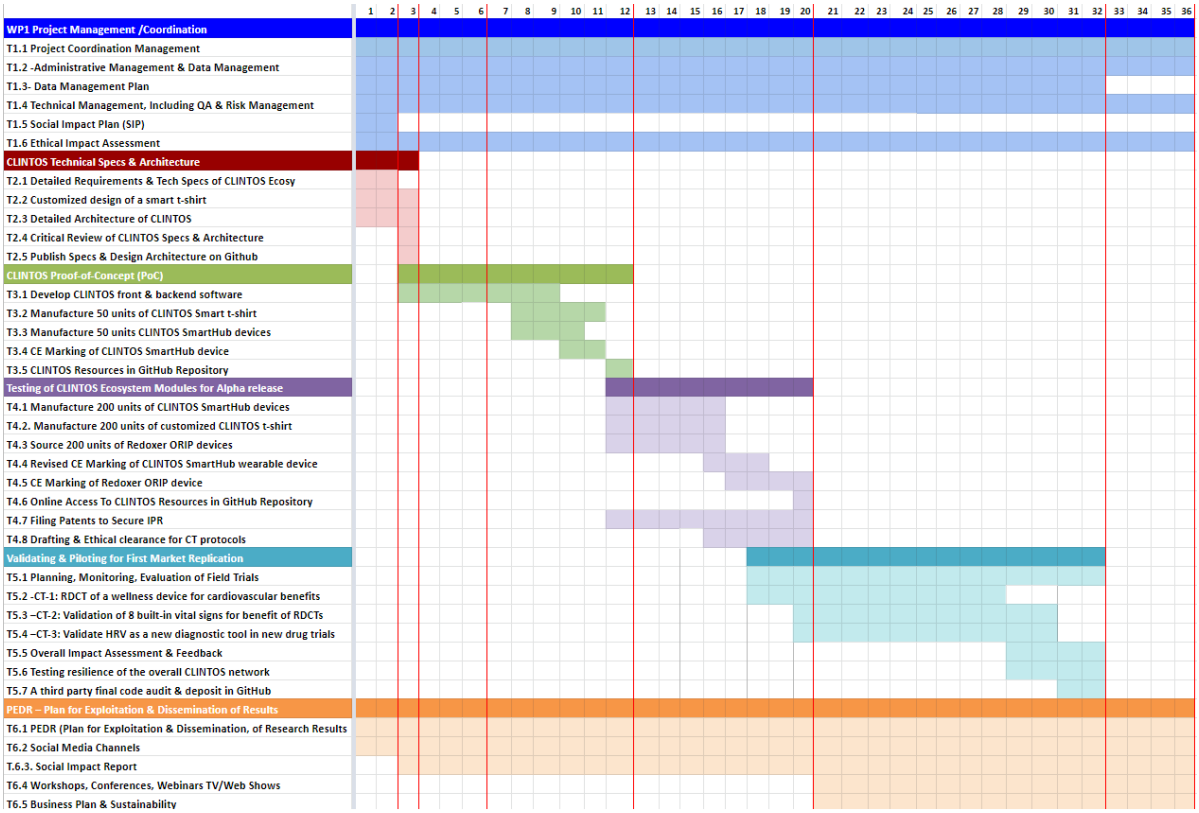


Table 3.1a: List of Work Packages

WP No.	WP Title	Leader No.	Leader S Name	Person Months	Start Month	End Month

1	Project Management / Coordination	1	UTB		1	36
2	Technical specifications and architecture	6	SST		1	3
3	Development of POC	2	BC5		3	12
4	Manufacture, test & alpha release	4	AFL		12	20
5	Field testing for 3 use cases	7	ISS		18	32
6	PEDR: Dissemination & Exploitation of Results	3	EMA		1	36
	Total Person Months					

3.1b: Work Package Description

WP No.	**1**			**Lead beneficiary**			UTB			
WP Title	Project Management /Coordination									
Participant. No.	1	2	3	4	5	6	7	8	9	10	11
Participant	UTB	BC5	EMA	AFL	OT	SST	ISS	ABI	MIA	SBA	HBI
PMs /participant	30	8	6	6	6	6	6	2	5	4	2
Start month	1					End	36				

Objectives*:* **WP1** led by UTB ensures the completion of all deliverables in time, within budget & to the required QA standard. The tasks of WP1 are divided into four groups: i) administrative aspects & data management, ii) technical, innovation & quality, iii) Social Impact, and iv) Research Ethics. It involves administrative, technical, innovation, quality, ethics, data management plan and social impact plan. For further discussion on operational details of this work package please refer to Section 3.2

Description of Work:
The task ensures that the project is managed according to the rules and regulations set by the European Commission. The coordination of the Consortium Partners, WPs and stakeholders involved are covered here.

T1.1 Project Coordination Management (Leader: UTB, Participants: All):
Management of all administrative, financial, contractual and legal aspects of the project, as well as other general societal, data management, ethical or security issues. The coordination of the Consortium Partners, WPs and stakeholders involved are covered here. The task ensures that the project is managed according to the rules & regulations set by the EC, and progress reports are timely submitted at M12, M18 and finally at the closing at M36. The task involves two subtasks:

T1.2 -Administrative Management & Data Management (Leader: UTB, Participants: All):
Overall legal, contractual, financial and administrative management of the project including resources allocation. Specifically: (a) Preparation of Progress Reports for the European Commission, (b) Management of the distribution of all required documents (deliverables, progress reports), (c) Budget controlling and accounting, (d) Organization of meetings and minutes keeping, (e) Monitoring of the progress according to the contractual schedule, (f) Ensuring that gender equality issues are addressed.
This task will produce a handbook on data management procedures to regulate the consortium's activities. The handbook will provide detailed guidelines and protocols that all project partners must follow when collecting, storing, using, analyzing and publishing data and results. All partners will sign a letter of compliance confirming their commitment to the outlined procedures.

T1.3- Data Management Plan (Leader: SST, Participants: All)
Involves partners developing a data management plan (DMP) for the project, the outline of which is presented in 2.2(a)vii. This DMP will finalize information related to the types of data the project will generate and collect (including personal data) during project activities, the standards that will be used to represent the data during the project and how partners might exploit the data resulting from the project. The task will ensure that the DMP is established in compliance with the applicable legal framework, particularly the GDPR. It will also determine the extent to which data resulting from the project might be suitable for open access provision at the close of the project. The plan will be initially produced at M8 and updated at Month M32, and as a result, SST will provide input into the interim and final review reports.

- Providing an internal platform for information exchange between project partners

T1.4 Technical Management, Including QA & Risk Management (Leader: UTB, Participants: All)

Overall technical management of the project including monitoring of the technical progress and deliverables of the project according to the contractual schedule, aligning technical direction with innovation and adoption strategies, ensuring that proactive measures are taken to mitigate risks which could jeopardize the planned outcomes.

T1.5 Social Impact Plan (SIP) (Leader: UTB, Participants: All)
The consortium will design a specific Social Impact Plan (SIP) during the first month of the project. The SIP will include concrete strategies to consider during the project lifespan achieving social impact. This strategy will be based on fulfilling a set of indicators (short-term, mid-term, and long-term) to measure and monitor the social impact during and after the implementation of the project. In addition, SIP will incorporate the shaping of a set of evaluation instruments in order to collect data on regards of the CLINTOS Social Impact.

T1.6 Ethical Impact Assessment (Leader: EMA, Participants: All): Deployment of technologies and procedures in the course of the project will be evaluated and assessed in terms of the ethical risks that may rise during the implementation of the CLINTOS device. The Ethical Risk Assessment (ERA) process will be used to identify, quantify and mitigate any ethical risks that may surface in the course of the development or deployment of emerging techniques and methodologies (ethical governance of the technology and/or value sensitive design approach).

During the lifetime of the project the ethical and legal regulations in Europe will be reviewed to identify the possible ways that the proposed and deployed tools and processes may be affected by these regulations. Furthermore, once the risks are identified, measures that will mitigate the impact will be designed and proposed in this task.

This task will produce a handbook on ethical research procedures to regulate the consortium's activities as well as processes for undertaking empirical research. All partners will sign a letter of compliance confirming their commitment to the outlined procedures. The handbook will be updated in M30 of the project. This task consists of the following activities:

- Liaising with the ethics advisory board: This task will involve all necessary actions to be taken by partners regarding communicating with the ethics advisory board to guarantee responsible ethical conduct throughout the duration of the project.

- Ethical monitoring and review: EMA will lead the ethical review of the project at months 6, 18 and 36 and will ask that the ethical protocol is scrutinized by the ethics board. JOA will use this information to provide input into the interim and final review reports.

Deliverables:

D1.1 Project Handbook - Quality Assurance Plan [UTB, M2]
Provides useful information for project partners including procedures and instructions for reporting and using the project management tools. Annual quality reports are included in the periodic project progress reports. It will set the day to day rules of the project: documents and deliverables handling, project planning and manpower, meeting organization, internal reporting and information management, external information management, list of personnel with corresponding responsibilities.. Finally, it will detail beyond the terms of the EC grant agreement and the Consortium Agreement, the internal project rules and guidelines concerning the daily management of foreground and IPR. It will also define the quality assurances and quality control rules and guidelines to follow, including documentation and information to provide and the different internal milestones in the R&D process, and change control procedures. It will also address Risk Management and will identify detailed risks that can arise during project time scale, provide detailed risk resolving and decision making procedures. Special attention will be turned to handle the relationship with the External Advisory Board.

D1.2 CLINTOS Data Management Plan (DMP) Handbook V1 [SST, M6]
A DMP for CLINTOS project activities will be initially produced at M6 and updated at M32 (D1.4). Partner SST will provide the initial inputs on the plan and the plan will be finalized once the data of all 3 use-case pilot studies are received.

D1.3 Midterm Project Progress Report [UTB, M18]
UTB will deliver the midterm project report entailing the progress and probable strategies to make the project go as per the desired plan.

D1.4 CLINTOS Data Management Plan (DMP) Handbook V2 [SST, M32]
Partner SST, depending on initial findings, will circulate the primary version of the DMP handbook. The suggestions from all the consortium members will be incorporated and the final version will be made available by the end of 32nd month.

D1.5 CLINTOS Social Impact Plan (SIP) Handbook [UTB, M2]
UTB will deliver a social impact plan handbook at M2. This SIP will include concrete strategies to consider during the project lifespan achieving social impacts as expected in the Trials@Home call.

D1.6 Final Project Progress Report [UTB, M36]
UTB will deliver the final project report entailing the project outcomes, learnings and future strategies at the end of the project tenure.

D1.7 Ethics Impact Assessment Report [EMA, M36]
Partner EMA will continuously review ethical and legal regulations in Europe throughout the life of the project and will deliver the final report on the Ethical Impacts by the end of the project.

Work Package 2:

WP No.	**2**			**Lead beneficiary**			SST				
WP Title	CLINTOS Technical Specs & Architecture										
Participant. No.	1	2	3	4	5	6	7	8	9	10	11
Participant	UTB	BC5	EMA	AFL	OT	SST	ISS	ABI	MIA	SBA	HBI
PMs /participant	6	14	4	8	12	16	4	1	2	8	3
Start month	1					End	3				

Objectives: WP2 led by SST will produce the project baseline and project vision. In particular, it will produce the overall technical requirements, specification and architecture of CLINTOS network and wearable SmartHub infrastructure based on enhancement over existing CE marked COVID smart wearable device. CLINTOS SmartHub is an IoT device with a lighter & simpler front-end human computer interface (HCI) that displays output from an AI-powered complex input matrix that includes body sensors that measure body vital signs to diagnose human morbid conditions such as hypertension, fever, pulmonary deficiencies, etc. The SmartHub also has an ancillary wearable subunit designed as a smart T-shirt, which hosts a pulmonary sensor and an integrated wireless therapy adherence (WTA) device. The integrated wearable components of the CLINTOS platform support 8 vial signs that we proposed for future RDCTs (see **sec 1.3(a)3**).

The decentralized CLINTOS network architecture adds privacy, security & interoperability (PSI) by design in a PSI-as-a-Service model, which also makes it easy to integrate third party CT/RDCT applications or services by federating a multi-cloud ecosystem. WP2 work is therefore aimed at providing:

- Detailed Technical Architecture specification of the CLINTOS Platform addressing both business/legislation and ICT perspectives and directing the subsequent implementation of components and their integration into a smart cloud based decentralized privacy-preserving RDCT infrastructure.

- Core CLINTOS Platform functionalities and fundamental infrastructure, covering the implementation of the data models as decentralized Personal Online Data stores (PODs) for the User Profiles, smart and intelligent client application at the End Node, additionally supplemented by AI-powered Edge & Fog Nodes to minimize the latency of CLINTOS components, including solutions based on ML and DL at the Cloud Edge that exploit *model compression approaches* (e.g., [CWZZ2017[73], BCN2006[74]), as well as the development of the workflow facilitation for businesses and testbeds for developers. In this context, a specific research and development line will concern with the design and development of LIQUIDUS-compliant software components able to guarantee the *privacy* of PODs during data analytics tasks (e.g., social network analysis) while ensuring their *security*. This research focus is recognized under the term "secure privacy-preserving data management" (e.g., [WJGYCL2020[75], CD2019[76]), and it finds Cloud and Multi-Cloud architectures as the "natural" humus for its

[73] Yu Cheng, Duo Wang, Pan Zhou, Tao Zhang, "A Survey of Model Compression and Acceleration for Deep Neural Networks". CoRR abs/1710.09282, 2017
[74] Cristian Bucila, Rich Caruana, Alexandru Niculescu-Mizil, "Model Compression". ACM KDD 2006, pp. 535-541, 2006
[75] Qianlong Wang, Tianxi Ji, Yifan Guo, Lixing Yu, Xuhui Chen, Pan Li, "TrafficChain: A Blockchain-Based Secure and Privacy--Preserving Traffic Map". IEEE Access 8, pp. 60598-60612, 2020
[76] Alfredo Cuzzocrea, Ernesto Damiani, "Making the Pedigree to Your Big Data Repository: Innovative Methods, Solutions, and Algorithms for Supporting Big Data Privacy in Distributed Settings via Data-Driven Paradigms". IEEE COMPSAC

explicitation (e.g., [AEW2012[77]). In addition to this, in order to further ensure high availability and consistency of PODs in this decentralized environment, *Optimistic Replication Algorithms* will be proposed, as an architectural component of the overall framework.

- Design of user-friendly interface for enabling users to define and distribute their personal profile data between several PODs to effectively manage level of data authorization to companies / service providers. APIs that link the personal user data to feed the service providers frontend interface with similar or better efficiency as in the legacy cloud systems.

- Design CLINTOS proof-of-concept as a backbone of a generic CT/RDCT ecosystem that can be integrated with the specialized external cloud computing systems (for diverse use cases) in a multi-cloud setting for testing to provide initial validation and verification using actual test data in the three identified use-cases.

This WP therefore entails producing requirements and technical specs of decentralized CLINTOS framework / ecosystem, which will be deployed in at least 3 use cases in WP5 field trials for CLINTOS' first market replication.

Description of Work

T2.1 Detailed Requirements & Tech Specs of CLINTOS Ecosystem (Leader: SST, Participants: SBA, BC5, HBI, UTB, OT, ISS, ABI)

Draw up detailed textual specifications of the overall architecture, comprising the hardware and software components, their responsibilities, platform-internal interfaces, and specify the precise role of foundational components of the CLINTOS platform, their interaction with each other. Additionally, the technical requirements (functional as well as non-functional) for all components will be defined in order to bootstrap the technology review process. The whole architectural design process will be steered by the compliance-by-design paradigm. The goal of this task is to specify the role-specific platform API's for the user and organizational components as well as the interaction mechanisms used by the data protection authorities and auditors. Different communication/interface technologies like SDC, HTTP, IPPFS, RESTful APIs (JSON, XML), WebSockets (STOMP) or message-based communication (MQTT) are considered, compared and selected based on the particular communication requirements (client/server, publish/subscribe or bi-directional). The hardware configuration of the SmartHub wearable device will be clearly specified in textual as well as visual forms.

T2.2 Customized design of a smart t-shirt (Leader: OT, Participants: BC5, ABI, ISS, AFL,SBA)

The task will be performed to determine technical and used requirements of t-shirt which is to be home for sensors and other data providing equipment to be made available by the other partners in the consortium. The requirements will be identified though meetings of focus group of related consortium partners. These requirements determined will be converted into design specifications using the Quality Function Deployment (QFD) approach and multi-criteria decision tools such as Analytic Network Process. In order to meet the design specs, an extensive theoretical and industrial research will be carried out to determine and analyze yarn properties (antibacterial, thermo-regulative, conductive, breathable, quick dry, soft-touch etc.) of t-shirt. Later designers will develop alternative t-shirt concepts and knitting processes considering the specs determined. Designers will try different types of knits on different parts of the shirt to provide comfort features. ASTM E2149-01 test for determination of antibacterial properties, AATCC 79 test for determination of hydrophilic properties, TS 3981 EN ISO 9237 test for determination of air permeability properties, and AATCC 195 MMT test for detection absorbency properties, FTTS-FA-004: Moisture Transfer and Quick Drying Requirements test of Textiles can be performed to determine the fast drying properties of T-shirts. After the test results and evaluation, an iterative approach will be used to make the t-shirt more comfortable.

T2.3 Detailed Architecture of CLINTOS (Leader: BC5, Participants: All)

This task will produce detailed design of the CLINTOS architecture & the architectural variations from the original COVID device as mandated for the CLINTOS wearable SmartHub device, covering the formal definition and description of the structure, functions and interactions of architectural components, as well as the main physical deployment options. A standard modeling language and methodology will be used, such as UML. The architectural design choices and activities will be based on the objectives defined in this WP, and address performance, privacy, security, interoperability and scalability issues. This task will produce the blueprint for implementing the core CLINTOS Platform, the client nodes, the remote, the fog and the edge servers, the APIs to link user data to service provider interfaces and to federate a multi-cloud ecosystem, by

2019, pp. 508-516, 2019

[77] Divyakant Agrawal, Amr El Abbadi, Shiyuan Wang, "Secure and Privacy-Preserving Data Services in the Cloud: A Data Centric View". Proceedings of the VLDB Endowment 5(12), pp. 2028-2029, 2012

also exploiting intelligent ML and DL techniques closer to the end node. The blueprint will also include architectural design details of the associated tools and services, such as the software components supporting secure privacy-preserving management of PODs (Personal Online Data stores). The topology of the decentralized network will also be decided and mapped. Advanced optimistic replication mechanisms will be adapted to the network in order to ensure high availability of PODs. BC5 and SST will participate in this Task in the design of the CLINTOS network architecture, focusing on the protection, detection, mitigation and response components and measures that satisfy the distributed resilience required by the CLINTOS ecosystem. ULE will contribute with regards to communication/interface technologies, in particular APIs. Partner SST will contribute with experience in UML modeling, and other languages, addressing privacy and security in the design of the architecture. BC5 will contribute with their IoT expertise.

T2.4 Critical Review of CLINTOS Specs & Architecture (Leader: SBA, Participants: All):
In this task CLINTOS wearable SmartHub device and architecture design specs will be reviewed by all the participants, and comments for revision posted on the consortium forum.

T2.5 Publish Specs & Design Architecture on Github (Leader: BC5, Participants: All):
The WP2 leader will revise the blueprint of CLINTOS network architecture and the technical specifications, and subsequent to post-revision review by all participants, publish the design blueprint and technical specifications to an appropriate code repository, such as GitHub.

Deliverables

D2.1 CLINTOS Tech Specs & Architecture Documentation [SST, M2]:
A detailed report documenting functional & technical specs of the CLINTOS architecture, covering the formal description of structure, functions & interactions of components, as well as choices, decisions during physical deployment will be made available to all the consortium partners by the end of the 2nd month by partner SST.

D2.2 Smart t-shirt design specs & architecture [OT, M3]
CLINTOS optimized smart t-shirt design and knitting processes will be reported by OT and it will be critically reviewed by all the participants for final revisions and the final design will be made available by month 3.

D2.3 Specs of the Devices, Architecture Documentation [BC5, M3]:
The detailed documentation covering the design variants of the different hardware components of the CLINTOS, their specification and architecture details will be made ready by BC5 by the end of 2nd month of operations. The hardware components of the CLINTOS ecosystem include the wearable SmartHub device and its ancillary subunit designed as a smart T-shirt. The primary report will be circulated amongst the consortium members and the final document will be released by the end of 3rd month.

D2.4 Critical Review Report of CLINTOS Specs & Architecture [SBA, M3]
CLINTOS wearable SmartHub devices and architecture design specs will be critically reviewed by all the participants, and the final report released by 4th month.

D2.5 Online Access to CLINTOS Architecture & Specifications Documents [BC5, M3]:
Once the detailed documentation entailing the CLINTOS infrastructure and its technical specification of hardware and software is critically reviewed and report released, BC5 will provide a web address (URL) of documentation to all the participants, particularly WP6 participants for exploitation and dissemination activities as soon as the IPR committee approves such dissemination.

Work Package 3:

WP No.	**3**			**Lead beneficiary**				BC5			
WP Title	CLINTOS Proof-of-concept (PoC)										
Participant. No.	1	2	3	4	5	6	7	8	9	10	11
Participant	UTB	BC5	EMA	AFL	OT	SST	ISS	ABI	MIA	SBA	HBI
PMs /participant	6	28	4	14	8	8	4	1	4	4	0
Start month	3					End	12				

Objectives: BC5 leads WP3 to build Proof-of-Concept (POC) of the complete CLINTOS RDCT infrastructure deploying wearable device with sensors that monitor victim's vital signs in real time supported by privacy-preserving decentralized network architecture for securing data privacy / anonymity. Create a testbed for testing & validating 3 use-cases. Implement DLT to build secure ID system with improved decentralization, latency, data handling and storage in decentralized Health PODs (Personal Online Data stores). Manufacture 50 units of

CLINTOS wearable SmartHub devices (including the smart T-shirt) for CE Marking and integrating within the CLINTOS framework. Establish DLT Testnet and CLINTOS testbed for testing the complete CLINTOS infrastructure along with companion device app for delivering CLINTOS MVP for QA testing in the next WP4 and subsequently for revised CE marking. Establish the RDCT operating system concept, and generate and deposit CLINTOS framework code in a code repository such as Github.

Description of Work

T3.1 Develop CLINTOS front & backend software: (Leader: BC5, Participants: SBA, UTB, MIA, AFL)
Once the CLINTOS architecture and specifications are finalized, BC5 will Initiate and complete the coding of all the frontend and backend software components / modules of the CLINTOS framework including the decentralized PODs along with server nodes and the client nodes. Integrate and establish full connectivity of the wearable SmartHub device and all the client nodes with the server nodes and the remaining CLINTOS framework components. Develop APIs to connect and interact with third party applications.

T3.2 Manufacture 50 units of CLINTOS Smart t-shirt (Leader: OT, Participants: OT, ISS, ABI, MIA)
The task aims to manufacture 50 units of t-shirt in accordance to the technical specifications & architecture designs produced in WP2. In order to generate the 50 units of t-shirt to circulate in the consortium, OT will produce at least 250 t-shirts to optimize knitting, dyeing and finishing processes; evaluate comfort and performance properties by carrying out all necessary QC tests for the t-shirt. In order to optimize the manufacturing parameters Taguchi experimental design and statistical analysis approaches will be employed.

T3.3 Manufacture 50 units CLINTOS SmartHub devices: (Leader: AFL, Participants: BC5, ABI, ISS, MIA)
Thetask initiates the process to manufacture 50 CLINTOS wearable SmartHub devices (including smart T-shirt) in accordance to the technical specifications & architecture designs produced in WP2, and receive the devices to initiate the CE marking process and make devices available for the next task.

T3.4 CE Marking of CLINTOS SmartHub devices (Leader: AFL, Participants: All)
The task involves retaining a Notified Body for initiating the process of CE marking for CLINTOS SmartHub devices, and providing Notified Body all the technical specifications as well as manufacturing details obtained from the manufacturing site. The task leader will ensure the continuous monitoring throughout the certification process.

T3.5 CLINTOS Resources in GitHub Repository (Leader: BC5, Participants: All):
The complete CLINTOS Resources will be uploaded to a code repository such as Github. The result will be disseminated through consortium's PEDR partners.

Deliverables:

D3.1 Complete CLINTOS Framework [BC5, M9]:
Based on the outcomes of the WP2, BC5 along with the other technical partners will develop the software components of the CLINTOS infrastructure. The deliverable involves the complete frontend and backend software components / modules of the CLINTOS framework integrated with the wearable SmartHub device.

D3.2 Obtain 50 units of tested CLINTOS t-shirt [OT, M12]
OT will provide 50 units tested t-shirt and test reports to the relevant CLINTOS partners.

D3.3 Obtain 50 units of CE Marked CLINTOS SmartHub devices [AFL, M12]
AFL will work in close association with the manufacturer to obtain 50 units of CE marked CLINTOS SmartHub devices (including smart T-shirt for CLINTOS Framework development and revised CE marking.

D3.4 GitHub Location for CLINTOS Resources [BC5, M12]
Once the CLINTOS technical resources are finalized and the technical developments are done, partner BC5 will upload the CLINTOS technical resources and the resources are made available on GitHub repository.

Work Package 4:

WP No.	**4**			**Lead beneficiary**		AFL					
WP Title	Testing of CLINTOS Ecosystem Modules for Alpha release										
Participant. No.	1	2	3	4	5	6	7	8	9	10	11
Participant	UTB	BC5	EMA	AFL	OT	SST	ISS	ABI	MIA	SBA	HBI
PMs /participant	8	8	8	20	5	4	4	2	2	0	0
Start month	12					End	20				

Objectives: WP4 led by AFL, will test the CLINTOS ecosystem as a whole and make it ready for the next WP5 for field-testing (FT) the system. This will entail manufacturing 200 units of CLINTOS SmarHub wearable devices for testing of the CLINTOS product (companion app and always-on mesh-networking) for alpha testing and release to qualify the CLINTOS CT infrastructure for field-testing and piloting for first market replication, and revised CE Marking. An IPR review for securing appropriate IP protection is also undertaken as a part of WP4 activity and filing of patent applications as envisaged in Sec 2.2(a)viii. Acquire 200 CE Smart T-shirts for testing and validating the CLINTOS CT ecosystem for CT-2 use case (vital signs) that will be field tested to replicate market entry in WP5.

Description of work

T4.1 Manufacture 200 units of CLINTOS SmartHub devices: (Leader: AFL, Participants: ABI, ISS, MIA)

CLINTOS SmartHub device is based on enhancement over an existing CE marked smart wearable device - COVID, which is an IoT device with a lighter & simpler front-end human computer interface (HCI) that displays output from an AI-powered complex input matrix that includes body sensors that measure body vital signs to diagnose human morbid conditions. Depending on the outcomes of the WP3, the task involves the processes to develop and manufacture 150 CLINTOS devices incorporating all the changes and fixes discovered during the WP3 development. BC5 will lead the task to obtain the devices within the stipulated time frame of 3 months.

T4.2. Manufacture 200 units of customized CLINTOS t-shirt: (Leader: OT, Participants: OT, ABI, ISS, MIA)

The task aims to manufacture 200 units of t-shirt based on the manufacturing specs determined in WP 3 and feedback received from the consortium partners. T-shirts are manufactured in customized manner based on the requirements of individuals who will take place in field testing.

T4.3 Revised CE Marking of CLINTOS SmartHub wearable devices (Leader: AFL, Participants: All)

The task, led by AFL, involves retaining a Notified Body for initiating the process of CE marking for trial devices both SmartHub wrist device and Smart T-shirt, and providing Notified Body all the technical specifications as well as manufacturing details obtained from the manufacturing site.

T4.4 Drafting & Ethical clearance for CT protocols: (Leader: ABI, Participants: All):

The final prototype will be presented to an ethical commission for clearance in testing in the field. This ethical votum will support T5.1 in the evaluation and final trial set up. As ethical commissions, it is already cleared that several options are at hand that would be willing to arrange a votum: Ethical Commission of the trial location.

T4.5 IPR review and patent filing: (Leader: BC5, Participants: All):

The consortium will appoint appropriate IP firm to undertake "freedom to operate" analysis, and file and prosecute worldwide patents to ensure full IP protection to the novelty of CLINTOS wearable device and network architecture as child patents of the background IP or as foreground IP based on the extent of co-creation. An agreement between the consortium partners will define such IPR.

T4.6 Online Access To CLINTOS Resources in GitHub Repository (Leader: BC5, Participants: All):

The complete CLINTOS Resources will be uploaded to a code repository such as Github by partner BC5. The result will be disseminated through consortium's PEDR partners and will be used to plan the dissemination activities.

Deliverables

D4.1 Acquire 200 units of CLINTOS SmartHub devices [AFL, M16]

Once the technical framework is successfully integrated with the Smarthub devices, Partner BC5 will work in close association with the manufacturer to source 200 units each of CLINTOS SmartHub devices (smart wrist band and smart T-shirt) to initiate the process of revised CE marking with the regulatory authority and make the devices available for field testing.

D4.2. Acquire 200 units of customized CLINTOS t-shirt [OT, M16]

OT will provide 50 units tested t-shirt and test reports to the relevant CLINTOS partners. Based on the feedback

and requirements received from the consortium partners during field testing (WP 5), OT will be able to provide more customized t-shirts.

D4.3 Obtain revised CE Marking of CLINTOS SmartHub wearable devices [AFL, M18]

Partner BC5 in consultation with the technical team will initiate the process for revised CE marking with the notified body and will obtain the CE certification of the CLINTOS SmartHub devices (both the smart wrist band and smart T-shirt) for further use for field trials.

D4.4 Ethical Votum for field trials (CT-1, CT-2, CT-3) [ABI, M18]
The ethical votum will include the application and the votum of the chosen ethical commission. This votum will support D5.1 for the final evaluation plan.

D4.5 IPR Report & Patent Filings [BC5, M20]

A detailed IPR report that delivers "freedom to operate" analysis, followed by filing worldwide patents to ensure full IP protection to the novelty of CLINTOS wearable device and network architecture as child patents of the background IP or as foreground IP.

D4.6 Deposit CLINTOS Resources in GitHub Repository [BC5, M20]
BC5 will provide a web address (URL) of documentation to all the participants, particularly WP6 participants for exploitation and dissemination activities.

Work Package 5:

WP No.	**5**			**Lead beneficiary**			ISS				
WP Title	Validating & Piloting for First Market Replication										
Participant. No.	1	2	3	4	5	6	7	8	9	10	11
Participant	UTB	BC5	EMA	AFL	OT	SST	ISS	ABI	MIA	SBA	HBI
PMs /participant	12	6	18	4	4	4	24	21	21	0	12
Start month	18					End	32				

Objectives: The principal objective of this WP is to undertake usability testing of CLINTOS findings and innovation into at least 3 real-world operations that are diverse and demonstrate the feasibility, scalability, and ease of adoption as well as overall impact of the proposed solution. WP5 comprises of an overall planning and monitoring execution task (namely, T5.1), as well as the use case-specific tasks (T5.2, T5.3 & T5.4), producing reports that consolidate learning conclusions from each of the 3 use-cases following a consistent task structure across all the 3, appropriately adapted for their needs and priorities. Although, this Trials@Home call does not explicitly or implicitly entail conducting full-fledged clinical trials, our focus on RDCT justifies field tests that warrant a concise if not full-fledged clinical trial setting.

This WP is also tasked with auditing the CLINTOS platform code subsequent to the testing and validation, and finally establishes CLINTOS code repository at GitHub for sharing it within the consortium and with the leading privacy/security projects. Accordingly, following are the specific goals for WP5:

- Test and validate usability of CLINTOS cloud solution in 3 diverse real world use-cases to demonstrate the feasibility, scalability, adoption ease and overall impact of the proposed innovation.
- Set up a standard task structure for each of the 3 use-cases testing that includes:

- Get a third party code audit done either using a consortium partner who is neither involved with CLINTOS coding nor testing or an outsider agency and perform final bug fixing if necessary.

- CLINTOS alpha release and code deposit in GitHub repository.

Description of Work
T5.1 Planning, Monitoring, Evaluation of Field Trials (Leader: ISS, Participants: OT, EMA, ABI, MIA, HBI)

This is a management and monitoring task for testing and validation of the 3 use-cases in field trials (CT-1, CT-2 and CT-3). The idea is to provide a standard test-bench to the stakeholders, in order to be able to evaluate the CLINTOS innovation with realistic data (in terms of content, but also in terms of using large data volumes, to test non-functional parameters of the system, such as performance, scalability, responsiveness, usability). The process in testing the use-cases will be agile, so that a constant interaction cycle of progress will be delivering the results incrementally. To this end, the use-case testing will be following the Do–Check–Act cycle. There

will be a constant interplay between the CLINTOS testing progress and its research developments. Ethical clearance will be needed to finalize an evaluation protocol. Because clinical trials (albeit minimal or no risk) involved, ethical issues in involved, it will be necessary to define a clear trial setup in accordance with one or more cooperating hospitals and and their institutional review boards. Regional funding for life science will be requested to support the hospitals in the trials when the study design is finalized.

Main questions to be solved through the evaluation are:

CT-1: Is the technical stability of CLINTOS sufficient as an RDCT OS for clinical evaluation of third party applications in Plug-n-Play operability

Means of realization: Seamless installation and operation of CTMS/CDMS/EHR/HMS, etc. in compliance with regulatory requirements.

CT-2: Is the ability to measure 8 vital signs remotely, delivering additional value to the RDCT sponsor?

Is HRV analysis a good generic marker for general cardiotoxicity testing of new pharmaceutical agents in phase-1 and phase-2 clinical RDCTs?

Is the wearable medication adherance monitoring feature built into the CLINTOS providing a benefit in conducting RDCT?

Means of realization:

Vital signs of study subjects recorded remotely.

HRV analysis pre and post therapy compared with historical data on HRV in various physiological stress or toxicity situations.

Improved compliance rate compared to the historical data from case studies.

CT-3: Validation of RDCT as tool for dermal/cosmetic product trials

The general KPIs will establish the robustness of the RDCT infrastrucutre that CLINTOS builds ensuring privacy, security, interoperability, performance, usability and functional aspects of the various CLINTOS services, but given the diversity of use-cases, case-based KPIs will also be made available.
The first iteration will be submitted to an ethical commission in accordance with T4.7. The results will then support the final evaluation plan for the KPIs.

Monitoring will oversee installations and implementation progress with regards to the CLINTOS platform and infrastructure, performs user surveys and collects data for KPIs. Continuous Evaluation and Assessment provides evaluation reporting and impact assessment for all 3 use-cases, and establishes systematic feedback loops to WP3 & 4 for continuous refinements. In this context, field trials will contribute with assessment and evaluation of the advanced optimistic replication mechanism implemented within the core layer of the CLINTOS platform This Task will also set up a standard operating procedure (SOP) across the 3 use-cases based on the following protocol:

a) **Configuration and Customization**: compliance criteria, user and installation guides, consent forms.
b) **Statistics**: Usage analytics of CLINTOS services, transactions statistics, business workflow non-functional performance indicators.
c) **Feedback**: Use of the Agile approach for bug tracking, privacy and security assessment, usability evaluation, enabling continuous and iterative delivery of PSIaaS services and solutions.
d) **Validation and Reporting**: Validation and analysis

Description of Work:
The three use cases are labeled as CT-1, CT-2 and CT-3 respectively

T5.2 -CT-1: Plug-n-Play operability of 3rd party apps (Leader: MIA, Participants: All)
The task tests & validates CLINTOS as an operating system (OS) for running all third party Trials@Home RDCTs. The task will be carried out by partner MIA in association with ISS, ABI and HBI.

T5.3 –CT-2: Validation of 8 built-in vital signs for benefit of RDCTs (Leader: ISS, Participants: ABI, HBI, BC5, MIA)
The task promotes the detailed plan to successfully integrate and test 8 vital signs to validate CLINTOS as an ideal Operating System (OS) for Trials@Home / RDCTs. HRV is emerging a very important analytical tool for early ethical evaluation of cardiotoxicity and neurotoxicity of pharmaceutical agents. It is also turning out to be a valuable marker in advance diagnosis of routine morbidities. As such HRV has potential to become a key

analytical tool in clinical practice. CLINTOS offers HRV analysis by default to all RDCTs that use CLINTOS as their OS.

T5.4 –CT-3: Validation of RDCT as tool for dermal/cosmetic product trials (Leader ABI: MIA, ISS, BC5)
The aim of this task is to elaborate protocols and perform tests on the suitability of CLINTOS for its use as tool within the cosmetics testing. The task will be executed by ABI with the support of partners MIA, ISS & BC5.
For the purpose of the project the validation of CLINT will be assessed via an integrated approach that combines 3 steps:

- Step 1 the selection of the right panel. The right panel of volunteers is screened and selected according to skin bacterial communities and skin type (e.g. oily skin, dry skin, etc). Screening results to select the right panel for specific efficacy test services are based on the total bacterial count through a direct collection of skin microbiota on volunteers
- Step 2 test the selected products effect on a selected panel. Thanks to the evaluation on skin microbiota before and after product application, we can prove the product effect on selected volunteers with an integrated and multi-tool approach: new microbiological method associated with MALDI-TOF identification and volunteer self-assessment via CLINTOS. The integrated & multi-tool approach exploits the synergies of different techniques and allows for comparison and validation of the results:
    - Quantification associated to rapid MALDI-TOF identification that represent a new microbiological approach to investigate how a product works on skin microbiota.
    - Clinical test & visual remote evidence via CLINTOS and on-site volunteer evaluation: the clinical proof of products effect on the selected panel.
- Step 3 taxonomical metabarcoding study. Study of the composition of skin flora: taxonomical metasequencing. This analysis points of attention are focused on study design with well-defined endpoints, skin flora monitoring and analysis of the data generated by CLINTOS by an expert.

T5.5 Overall Impact Assessment & Feedback: (Leader: ABI, Participants: All)
Feedback obtained after the testing of the CLINTOS infrastructure in the 3 field trials will be analyzed and a primary report will be presented to all the consortium partners by ISS. Assessment of feedback and suggestions received for the identification of potential improvements and the evaluation of the CLINTOS infrastructure with respect to all three real time use cases will be documented in the final impact assessment report.

T5.6 Testing resilience of the overall CLINTOS network (Leader: SST, Participants: All)
During this task, the necessary actions will be taken to validate the resilience of the CLINTOS network. During this task the set of tests (threats and potential attacks) to be performed for this process will be defined. Then, the simulations of the corresponding attacks will be constructed and launched to test the resilience of CLINTOS. Partner SST will carry out an intrusion test on CLINTOS in order to assess the security of the solution. SST will also simulate a series of attacks (Red Teams) in order to evaluate the different integrated protection/detection mechanisms and ensure its resilience against security breaches that could lead to the leakage of personal data.

T5.7 A third party final code audit & deposit in GitHub (Leader: BC5, Participants: All)
This task makes sure that after all the testing and validation of the real world use case, a final third party code audit is performed by a consortium partner BC5 who is neither involved with coding or testing activities. After final bug fixes, a closed beta is announced and code deposited in GitHub repository and shared with consortium partners for facilitating exploiting and dissemination activities.

Deliverables

D5.1 Plan for Use-Case Testing & Validation [ISS, M22]
Once the CE certification for CLINTOS wearables is obtained, the detailed plan for the testing and evaluation of CLINTOS technology and its application within the select use-cases will be presented by partner ISS to all the consortium members. The plan includes use-case scoping, testing protocols and KPIs.

D5.2: Results: CT-1: Plug-n-Play operability of 3rd party apps; [MIA, M28]
The deliverable includes the primary report prepared by partner MIA, entailing the procedure, process and outcome of the third party applications run on the CLINTOS as an OS for Trials@Home setting for RDCTs.

D5.3 Results: CT-2: Validation of 8 built-in vital signs for benefit of RDCTs [ISS, M30]
The deliverable includes the primary report prepared by the partner ISS entailing the detailed procedure and test protocol along with the outcome of the experiments carried out to demonstrate accurate measurement of 8 vital signs, using the continuous monitoring of the wearable CLINTOS SmartHub devices.

D5.4: Results: Validate RDCT as a tool for cosmetic product trials [ABI, M30]

The deliverable includes the primary report prepared by partner ABI, detailing the analysis of the results of the RDCT of the dermal / cosmetic product.

D5.5 Results: Overall Impact Assessment & Feedback [ISS, M32]
Report for the feedback obtained after the testing of the CLINTOS infrastructure and the real time use cases will be prepared by ISS. The primary report will be presented to all the consortium partners. Assessment of feedback and suggestions received for the identification of potential improvements and the evaluation of the CLINTOS infrastructure with respect to all three real time use cases.

D5.6 Report of overall resilience of the CLINTOS network [SST, M32]
Partner MIAwill deliver the overall resilience testing report against security breaches or vulnerabilities in CLINTOS network nodes or client nodes.

D5.7 Final Code Audit Report & GitHub repository address for CLINTOS [BC5, M32]
The CLINTOS prototype release is announced after final audit and the code repository address in GitHub is shared with consortium members for the exploitation and dissemination activities of WP6.

Work Package 6:

WP No.	**6**			**Lead beneficiary**			EMA				
WP Title	PEDR – Plan for Exploitation & Dissemination of Results										
Participant. No.	1	2	3	4	5	6	7	8	9	10	11
Participant	UTB	BC5	EMA	AFL	OT	SST	ISS	ABI	MIA	SBA	HBI
PMs /participant	14	6	20	4	7	4	8	5	4	2	10
Start month	1					End	36				

Objectives: EMA, who will handle the overall dissemination and communication of the project goals, products, reports, results, achievements, and other outputs, will lead WP6. It includes actions taken towards exploiting the project outcomes with stakeholders and related entities across the EU. To build a diverse transnational community by engaging with general public, pharma industry, advocacy groups, NGOs, CROs, public health agencies, hospitals, CTMS/CDOMS vendors, cybersecurity stakeholders for collaborations to engage, educate, explain, & clarify technical nuances of CLINTOS ecosystem to potential beneficiaries, end-users, developers, policy-makers, industry, scientific community and investors with an aim to develop growth strategy for future exploitation after the project concludes. Basically following actions guide the PEDR (Plan for Exploitation & Dissemination, of Research Results) activities:

1. Specify and apply an inclusive stakeholder engagement strategy, to attract extended participation of key players wishing to join forces towards realizing a highly-innovative decentralized CT ecosystem that universally serves as CT Operating System (FROS) to integrate any third party CT applications.
2. Make recommendations particularly regarding the approach and methodology for the adoption of CLINTOS in different types of CT scenarios.
3. Plan and conduct exploitation activities, addressing both individual partner's plans and collaborative arrangements to provide an open solution
4. Provide a communication programme linked to the adoption / exploitation plan

At the outset a project website will be established to publish project's intermediate results, which will also be presented in the form of white papers and presentations in various conferences and industrial/commercial exhibitions, workshops, webinars with the purpose of exploiting results and identifying new partners for collaboration in the EU market. At least four social media channels that include Facebook, Twitter, LinkedIn, & Youtube, will be set up to facilitate dissemination activities. The social media channels will be designed and managed by partner URV with continuous updates from the other members.

Description of work
T6.1 PEDR (Plan for Exploitation & Dissemination, of Research Results (Leader: EMA, Participants: All)
The task involves the formulation of the primary plan for dissemination and exploitation activities. The aim will be to build a diverse transnational community by engaging with general public, scientific community, pharma, CROs, patient advocacy groups, NGOs, etc. The initial plan will be created in M2 and will be updated along with the performed activities in M24. The final plan will be created on M36 once the result of field trials are received and analyzed.

T6.2 Social Media Channels (Leader: EMA, Participants: All)
This task will set up the website and the Social Media channels as mentioned in the dissemination matrix for all

categories of target audience and stakeholders. These will be the main channels for communicating the project findings and promoting the main events. Partners in accordance with the dissemination matrix determined by the project manager will fulfill all social media tasks. All partners will provide input for updating these channels.

T.6.3. Social Impact Report (Leader: OT, Participants: All)
Drawing on the recommendations of social impact that European projects should achieve, approached by the EC research strategy, during the first month of the project, the consortium will design a specific Social Impact Plan (SIP) and prepare a report towards the end of the project. The report will include the outcome of strategies considered to achieve social impact during the implementation of the project.

T6.4 Workshops, Conferences, Webinars TV/Web Shows (Leader: MIA, Participants: All)
To connect, interact & exchange CLINTOS hypothesis, projections, findings with European research community, the partners will get involved in the preparation and publication of articles in scientific journals, peer-reviewed conferences, workshops, including **"Young Women in Healthcare"** event to promote the role of women in healthcare, and attract young talents. Scientific publication will be made in international conferences in order to establish scientific interaction and increase the widespread impact of the project. The conference will be decided according to the plan and conference topics of the relevant year. A stand will be set up in at least one scientific meeting to promote the product. All partners will participate in the dissemination activities and MIA will organize the young women workshop.

T6.5 Business Plan & Sustainability [Leader OT, Participant: All]
This task will explore the means to deliver the CLINTOS outcomes to the market. Together with the team, ways to bring CLINTOS results to market will be explored. Market analysis and SWOT analysis will be supported with the determined road map. The factors affecting the adoption of CLINTOS in the market will be analyzed with multi-criteria decision making methods and potential commercialization expectations will be determined. A market analysis will along with a roadmap to identify the barriers to entry the market will be performed. A first insight of the barriers will be derived from a SWOT analysis, while a roadmap will also be performed among experts providing deeper understanding of the factors that can affect the market adoption of CLINTOS using multi-criteria decision-making methods such as the Fuzzy Analytic Hierarchy Process (Fuzzy – AHP). The potential prospects of commercialization will be identified by the Business plan that will be created. It will also include formulation of a plan to form an alliance in the diverse domains to exploit the results the field trial.

Deliverables

D6.1 PEDR: Plan for Dissemination & Exploitation of Results V1 [EMA, M2]
The deliverable includes the initial plan for dissemination and communication activities of the project. It will define the target audience, the indicators to measure and assignments to each partner. It will also include the initial exploitation plan along with the exploitation part of each partner.

D6.2 Social Media Channels Establishment [EMA, M2]
The deliverable ensures the online presence over at least 4 social media channels that include Facebook, Twitter, LinkedIn, & Youtube and also the project website. The social media channels will be designed and managed by partner MIA with continuous updates from the other members.

D6.3 CLINTOS Social Impact Report [OT, M36]
OT will deliver a report on outcome of the social impact plan designed at the beginning of the project and implemented throughout the project.

D6.4 PEDR: Plan for Dissemination & Exploitation Of Results V2 [EMA, M24]
The inputs from the partners will be gathered and analyzed to present the revised plan (V2) for dissemination and exploitation at M24.

D6.5 Business Plan & Sustainability [OT, M34]
This task will identify the market potential of CLINTOS results and the factors that can affect the market potential. It will also formulate the Business Plan for long term sustainability.

D6.6 PEDR: Plan for Dissemination & Exploitation Of Results V3 [EMA, M36]
Backing on the initial results of the field trials, the detailed plan and activities to disseminate and exploit the results of CLINTOS field trials to attract and engage the general public, scientific community, advocacy groups, NGOs, etc. will be formulated and finalized. The consortium will present the final plan at M36.

D6.7 Conferences, Workshops, Public Webinars, TV / Web Shows [MIA, M36]
Partner MIA will organize 3 conferences, 6 Public Webinars and 2 TV/Web Shows to disseminate the results of the field testing and to create a wider awareness in the diverse community to capitalize on the initial success of

the field trials.

Table 3.1c: List of Deliverables

	Deliverable Name	WP	Lead	Type	Dissemination Level	Delivery Month
D1.1	Project Handbook - Quality Assurance Plan	1	UTB	R	CO	M2
D1.2	CLINTOS Data Management Plan (DMP) Handbook V1	1	SST	R	CO	M6
D1.3	Midterm Project Progress Report	1	UTB	R	CO	M18
D1.4	CLINTOS Data Management Plan (DMP) Handbook V2	1	SST	R	CO	M32
D1.5	CLINTOS Social Impact Plan (SIP) Handbook		UTB	R	CO	M2
D1.5	Final Project Progress Report	1	UTB	R	CO	M36
D1.6	Ethics Impact Assessment Report	1	EMA	R	CO	M36
D2.1	CLINTOS Tech Specs & Architecture Documentation	2	SST	R, Other	CO	M2
D2.2	CLINTOS Device Specs, Architecture Documentation	2	BC5	R, Other	CO	M3
D2.3	Critical Review Report of CLINTOS Specs & Architecture	2	SST	R, Other	CO	M3
D2.4	Online Access to CLINTOS Architecture & Specifications Documents	2	SBA	R, Other	CO	M3
D3.1	Complete CLINTOS Framework	3	BC5	DEM	CO	M9
D3.2	Manufacture 50 units of CE Marked CLINTOS SmartHub devices (Smart T-Shirt included)	3	AFL	DEM	CO	M12
D3.3	GitHub Location for CLINTOS Resources	3	BC5	R, Other	PU	M12
D4.1	Acquire 200 units of CLINTOS SmartHub devices	4	BC5	Other	CO	M16
D4.2	Acquire 200 units Smart T-shirt devices for testing	4	AFL	Other	CO	M18
D4.3	Obtain revised CE Marking of CLINTOS SmartHub wearable device s	4	BC5	Other	CO	M18
D4.4	Ethical Votum for field trials (FT-1, FT-2, FT-3)	4	ISS	R	CO	M18
D4.5	IPR- Patent Filing	4	BC5	DEC	CO	M20
D4.6	CLINTOS GitHub Repository	4	BC5	R, Other	PU	M20
D5.1	Overall Planning for Use-Case Testing & Validation	5	ISS	R	PU	M22
D5.2	Results: CT-1: Plug-n-Play of 3rd party apps	5	MIA	R	PU	M28
D5.3	Results: CT-2: Validation of 8 built-in vital signs for benefit of RDCTs including HRV	5	ISS	R	PU	M30
D5.4	Results: Validate RDCT as a tool for cosmetic product trials	5	ABI	R	PU	M30
D5.5	Results: Overall Impact Assessment & Feedback	5	ISS	R	PU	M32
D5.6	Report of overall resilience of the CLINTOS network	5	MIA	R	PU	M32
D 5.7	Final Code Audit Report & GitHub repository address for CLINTOS	5	BC5	R	PU	M32
D6.1	PEDR: Plan for Dissemination & Exploitation Of Results V1	6	EMA	R	PU	M2
D6.2	Social Medial Channels establishment	6	EMA	R	PU	M2
D6.3	CLINTOS Social Impact Report	6	UTB	R	PU	M36
D6.4	PEDR: Plan for Dissemination & Exploitation Of Results V2	6	EMA	R	PU	M24
D6.5	Business Plan & Sustainability	6	BC5	R	CO	M34
D6.6	PEDR: Plan for Dissemination & Exploitation Of Results V3	6	EMA	R	PU	M36
D6.7	Conferences, Public Webinars, TV / Web Shows Report	6	MIA	R	PU	M36

3.2 Management Structure, Milestones and Procedures

3.2 Overview

The decision making structure is consistent with the size & complexity of the project, and based on sharing of responsibilities. The decision making body is the **Steering Committee** (STC), with a majority vote mechanism, composed by 1 representative for each party, at management level. The STC will approve/decide on strategic matters, on time (schedule), cost and financial aspects, and will approve the reports to the EC. The **Project Coordinator** (PC) will report to the STC and act as advisor to its chair (appointed among members, at the first STC meeting), and will prepare the meetings and agendas.

The PC will be responsible for the overall organization, planning, and control of the project, deliverables, the reporting and the exploitation & dissemination of results. The **Project Management Team** (PMT: WP leaders + PC) will be in charge of the daily management of the project and of technical problem solving, meeting not less than once per month. Web meetings will be used as much as possible to minimize travel costs. Decisions will be taken by consensus, and if not possible, by majority of votes. The consortium will make considerable efforts to ensure gender balance and to support and promote young scientists and women through a range of activities such as "**Young Women in Health**" organized under WP6 (D6.4). One female member of the consortium will lead these programs.

The management of the project has the following goals:

- To ensure that the project is conducted in accordance with EC rules,
- To reach the objectives of the project within the agreed budget and time scales,
- To coordinate the work of, and ensure effective communication between the partners,
- To maximize the potential for exploiting results and active involvement of industry via an External Advisory Board
- To set the quality policy, including quality objectives for the project as well as for Deliverables
- To manage properly Foreground and IPR matters,
- To ensure that decisions are made on the basis of data and factual information,
- To solve any problem or conflicting situation,
- To set the quality policy, including quality objectives for the project,
- To ensure that an infrastructure is set up in order to support the above.

The mandatory internal Consortium Agreement (CA) will be finalized and signed prior to project start. It will describe, among others, the composition, decision-making procedures and responsibilities of the Project Coordinator, General Assembly, and Management Committee; it will also provide clear guidelines to govern the IPR questions and Knowledge Management amongst the consortium.
At the project outset, we will issue 2 documents, which will establish the rules of project management:

Project Handbook - Quality Assurance Plan [D1.1]
The document provides useful information for project partners including procedures and instructions for reporting and using the project management tools. Annual quality reports are included in the periodic project progress reports. It will set the day to day rules of the project: documents and deliverables handling, project planning and manpower, meeting organization, internal reporting and information management, external information management, list of personnel with corresponding responsibilities. Finally, it will detail beyond the terms of the EC grant agreement and the Consortium Agreement, the internal project rules and guidelines concerning the daily management of foreground IP and IPR. It will also define the quality assurances and quality control rules and guidelines to follow, including documentation and information to provide and the different internal milestones in the R&D process, and change control procedures. It will also address Risk Management and will identify detailed risks that can arise during project time scale, provide detailed risk resolving and decision making procedures. Special attention will be turned to handle the relationship with the External Advisory Board.

Data Management Plan (DMP) Handbook V1 & V2 [D1.2 & 1.3]
A DMP for CLINTOS project activities will be initially produced at M6 and updated at M18 and M24. Both documents will be updated throughout the project life. All the deliverables, the work and resources effort for the internal project management is covered and described in WP1.

Social Impact Management Plan (SIP) Handbook

The consortium will design a specific Social Impact Plan (SIP) during the first month of the project. The SIP will include concrete strategies to consider during the project lifespan to achieve social impact. This strategy will be based on fulfilling a set of indicators (short-term, mid-term, and long-term) to measure and monitor the social impact during and after the implementation of the project. In addition, SIP will incorporate the shaping of a set of evaluation instruments in order to collect data on regards of the CLINTOS Social Impact.

3.2.a) Milestones and Technical Decision to be taken

Milestones mean control points in the project that help to chart progress. Milestones may correspond to the completion of a key deliverable, allowing the next phase of the work to begin. They may also be needed at intermediary points so that, if problems have arisen, corrective measures can be taken. A milestone may be a critical decision point in the project where, for example, the consortium must decide which of several technologies to adopt for further development.

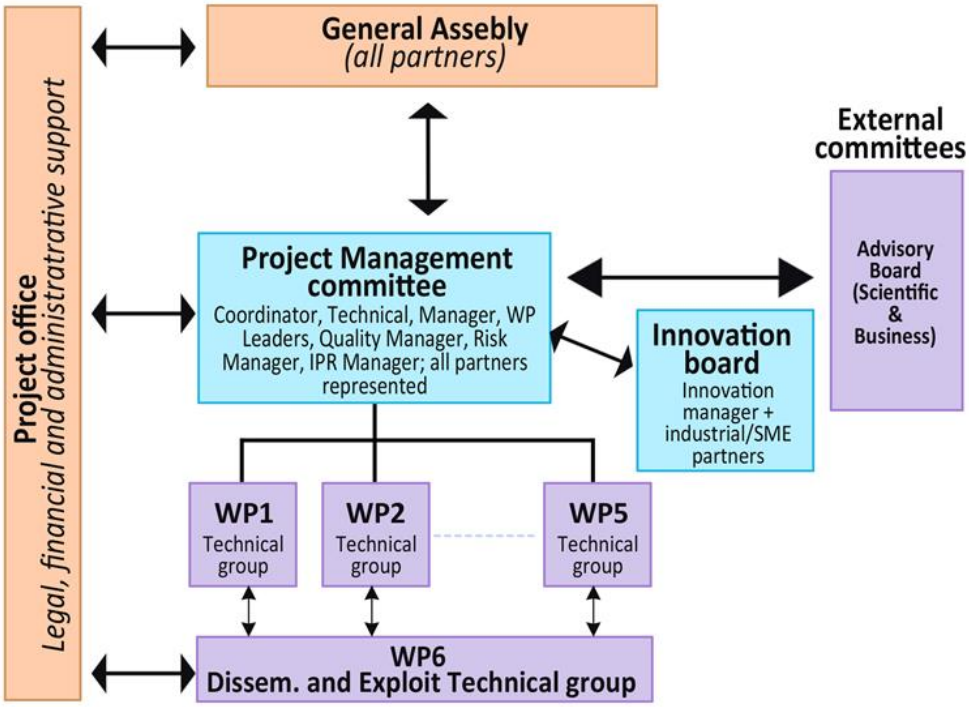
The table below shows all milestones in the table, indicates means of milestone verification and briefly describes major decisions to be made upon achievement of the milestones.

Table 3.2.a. List of Milestones

	Name of Milestone	Related WP /T	Due Date	Means of Verification
MS1	Project Plan, Consortium Agreement, DMP & Website	WP1/ T1.1	M1	STC Approval
MS2	Detailed Technical Specs of CLINTOS Infrastructure	WP2/T2.1	M2	PMT Approval
MS3`	Detailed Architecture of CLINTOS infrastructure including the wearable device design	WP2/T2.2	M3	PMT Approval
MS4	Obtain 50 units each of CLINTOS Wearable SmartHub Devices including Smart T-Shirts	WP3/T3.2	M12	PMT Approval
MS5	Manufacturing 200 units each CLINTOS SmartHub (including Smart T-shirts) devices for use case testing & validation.	WP4/T4.1/T4.2	M18	PMT Approval
MS6	Use case test results	WP5/T5.2/T5.3/T 5.4	M30	PMT Approval
MS7	Overall impact assessment and feedback	WP5/T5.5	M32	PMT Approval
MS8	Plan for Dissemination & Exploitation of Results	WP6/T6.1	M34	PMT Approval

3.2b) Project Structure and Governance Scheme

The light Project Management structure shown in the following figure has been agreed among the partners. It has been adapted to the project size, and already implemented with success in past similar projects.



The operational groups are the following:

- The **General Assembly**, chaired by the coordinator, approves the project budget and the general annual objectives,
- The **Project Management Committee**, chaired by the Project Technical Manager is the effective executive body of the project,
- The **Advisory Board,** chaired by the Project Business Development Manager is the informal strategic body of the project,
- The **WP technical groups** (chaired by the WP Leader) ensure the day-to-day WP technical work,
- The **Project office** supports the several operational groups in all non-technical tasks.

The operational groups are the following:

3.2b)i General Assembly (GA)

Composition: The GA comprises one representative of each partner. Each partner shall nominate a senior representative, with budget responsibility, enabling him to make consistent decisions and to represent contractor's interests. The GA is chaired by the coordinating partner.

Roles and responsibilities: Its role is to ensure the official follow-up of the project and to take the major decisions mainly on:

- Contract and Consortium Agreement amendment.
- Termination of the contract and actions against underperforming partners.
- Budget follow-up and transfers.
- Selecting new contractors to enter contract & CA.
- Deciding on major changes and technical roadmaps in the project.

The GA's role, responsibilities, rules, and decision-making procedures will be extensively detailed in the CA.
Meetings: the GA shall be convened by default once a year. Its ordinary meetings shall be convened together with a project meeting, but a GA extraordinary meeting can be called at any time by the coordinator or any partner under the terms and rules of the CA. To avoid travelling expenses, GA meetings can be organised via teleconference.

3.2b)ii. Project Management Committee (PMC)

Composition: The Project Management Committee is composed of the Coordinator, the Technical Project Leader, the seven (WP1-WP7) work package Leaders. In its tasks, it is supported by the Project Office. The Project Technical Manager chairs the Project Management Committee.

Role and responsibilities: The PMC has the responsibility for the overall project progress (objectives, schedule, milestones, etc.) and results in full conformance with the decisions of the GA.

Role and responsibilities: The Project Management Committee has the day-to-day responsibility and organisation for the overall project progress (objectives, schedule, milestones, etc.), and approves project deliverables. With the assistance of the respective Managers, the PMC also supervises the Quality, the management of foreground and IPR and the Risk Management aspects of the project.

Meetings: Physical meetings of the PMC are organised during the consortium meetings. In between, teleconferences are organised on a regular basis or on request.

3.2b)iii General Advisory Board

Composition: The Advisory board is composed of 10 eminent strategists from the Business and Scientific community. The Advisory Board will be chaired by the member elected by the PMC.

Role and responsibilities: The Advisory Board provides non-binding strategic advice to the PMC

Decision making procedures: Advisory board will only be a strategic body to advise the PMC on several issues and help make the right choice in matters of urgent attention which can impact the project.

Meetings: Physical meetings of the Advisory Board are organised mandatorily once in a year. In between, teleconferences are organised on a regular basis or on request.

3.2b)iv Work package (WP) Technical Groups

Composition: Each WP Technical Group is composed of all the members of the considered WP and chaired by the WP Leader. In practice, the following operational work of the project is performed in the WP Technical Groups, under the responsibility of the WP Leaders (see Table below). In its tasks, it may ask for the help of the Project Office.

Role and responsibilities: WPL responsibility is to plan, manage, coordinate and follow-up the work within the work package; the WPL ensures the work is done in full accordance with the Description of Work (DoW) and proposes proper actions when required. He/She represents the Work Package interests and interfaces with other Work Packages through the PMC meetings. Work packages are further broken down into tasks; Task Leaders are appointed and co-ordinated by the WPL.

Meetings: WP Technical Group's meetings occur at least at the same time and location than the PMC meetings. They are convened just before the PMC meeting to enable reporting and resolution of issues there. In addition, WP meetings can be called and organised by each WP Leader when needed to achieve the technical work. In between, teleconferences are organised on a regular basis or on request.

3.2b)v Ethics Advisory Board

Composition: Ethics Advisory Board is composed of Partners of the consortium with relative expertise and chaired by Dr Sofoklis Kyriazakos, Members: DPO of the Project and other Ethics Experts from first pharma industry, CROs, patient advocacy groups, etc.

Role and responsibilities: Provide advice on the legal and ethical issues that will arise over the course of the project as well as, review the identified ethics sensitive deliverables to mitigate potential risks related to legal or ethical matters

Meetings: Every three months

Table 3.2.(b) Work package leader assignments

WP	X	WP Leader
WP1	UTB	Dr. Lucian Mihai Itu (M)
WP2	SST	Mr. Matthias Pocs (M)
WP3	BC5	Fazal Raheman MD (M)
WP4	AFL	Adlin Ho (F)
WP5	ISS	Dr. Sofoklis Kyriazakos (M)

WP6	EMA	Dr. Vincenzo Costigliola (M)

3.2b)vi. Main Management Roles

3.2b)v.i. Project Coordinator

The project coordinator is UTB, who will act as the focal point for contacts and coordination with the EC, and with other relevant EU and national projects, and for external relationships with relevant bodies and other related activities. The major tasks are:

- Supervision of the overall project progress.
- Consortium Agreement coordination, organization of the General Assembly, Preparation of minutes, and follow-up of its decisions.
- Collection of the audit certificates (when needed) and supervision of distribution of EC's payments to partners.
- Preparation with the support of the Project Management Committee of the reports, cost statements and project documents required by the EC.
- Organisation of EC review meetings.
- Coordination of IPR and knowledge management.
- Representative of the consortium to events.
- Coordination of the dissemination and communication activities.

The Project coordinator staff will perform also the role of Project Office by dealing with administrative, legal, financial and communication issues and will support the several operational groups in all the above responsibilities. The Project Office will get advice from financial and legal specialists whenever required.

3.2b)v.ii. Project Technical Manager

The Project Technical Manager coordinates the activities of all partners in the project according to the technical work plan. The Project Technical Manager is Dr. Aristodemos Pnevmatikakis (ISS) Technical manager will have the following responsibilities:

- Chair of the PMC.
- Liaisons between the PMC and the GA.
- Supervision of the overall technical progress of the project.
- Consolidation of the technical reports and coordination of all technical WPs.
- Transmission of any documents and information connected with the project between the partners.

3.2b)v.iii. Quality Manager [QM]

To keep **CLINTOS** focused on its objectives of high quality technical outputs, market proximity and openness, the Project Steering Committee will appoint Mr. Ali Gökhan Beltekin (**MIA**) as Quality Manager. In the line of the Project Quality Assurance Manual (D1.1), the Quality Manager will be asked periodically to review technical progress such that the project remains innovative, open to collaborations and to market needs, forward looking. That will ensure that **CLINTOS** is producing work of high technical quality.

3.2b)v.iv. Innovation Manager and Innovation Board

Industry players of main market segments that are driving innovation in **CLINTOS** will form the Innovation Board and will review innovation aspect in the technical research and propose enhancements whenever necessary. The board includes marketing and strategic people from the industrial organizations involved in **CLINTOS** and will be responsible for analysis of market factors, early products concepts, threats and opportunities of commercialization, etc. Due to that fact, that innovation aspect highly depends on proper IPR, Innovation Board will also support IPR management. Innovation Board will be chaired by Innovation Manager Dr Marco Minoia (ABI).

3.2b)v.v. Risks Manager

Having in mind that risk may have an impact on the project schedule and project objectives and finally may lead to contractual issues, a Risks Manager will be appointed by the Project Steering Committee at the project start. He/She will be asked periodically to review the project progress and the risks items table to ensure that **CLINTOS** remains online with its main technical objectives. He/She will be in charge of keeping up-to-date the Risk Management Table that will be produced by the WP1. He/She will interact with the PMC and WPs in this task.

The process of risk management is shown in the next two figures: once identified (qualitative analysis), risks will

be weighted by degree of severity according to their probability of occurrence and impact on the project results. The impact on project results (quantitative analysis) will be classified by the PMC according to different information provided by the risk originator, like delay of delivery, decrease of performances, and impact on another deliverable, commercial impact.
Then mitigation and contingency plans will be defined according to risk severity (risk response). Risks will then be monitored on a regular basis, with a combined top-down and bottom-up approach:

- At the project start, and during monthly project management committee (PMC) meeting, high level risks will be defined and assessed
- Risks at the task and WP level will be defined and followed-up weekly or bi-weekly at each WP meeting

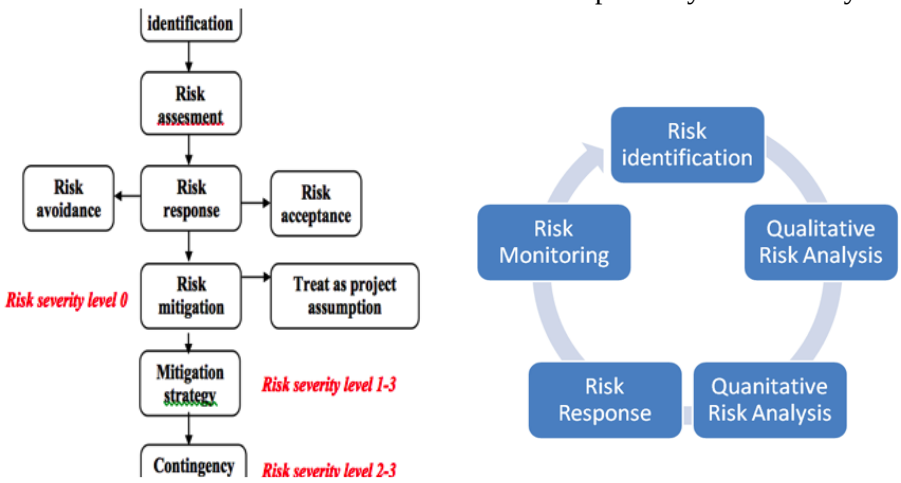


Figure1. Risk management in CLINTOS and risk management process

3.2b)v. vi Data Protection Officer

CLINTOS consortium will appoint a Data Protection Officer (DPO) to ensure that the the processes, personal data of staff, customers, providers or any other individuals (data subjects) is in compliance with the applicable data protection rules. The appointment of the DPO will be done in accordance with the applicable Data Protection Regulation[78] (Regulation (EU) 2018/1725). Consortium will pay particular attention to his/her expert knowledge of data protection while assigning this role.

3.2b) vi. Conflict Resolution

A clear decision making procedure will allow a simple conflict resolution process.

- When a conflict occurs in a WP technical group, consensus seeks to solve the problem. If the problem cannot be solved it is escalated to the Project Management Committee: the WP leader prepares a description of the problem and its possible solutions.
- If consensus cannot be reached within the Project Management Committee, the Project Technical Manager escalates it to the Steering Committee, using the same process as described above.
- If the problem cannot be solved by consensus, the Steering Committee escalates it to the General Assembly and a vote occurs, requiring a simple majority.
- In practice the conflict resolution process can be very fast, as:
- Extraordinary GA meetings can be organized using audio-conference (with the terms and delay defined in the Consortium Agreement),
- Email voting is allowed (again according to the rules defined in the Consortium Agreement).

[78] https://edps.europa.eu/sites/edp/files/publication/reg_45-2001_en.pdf

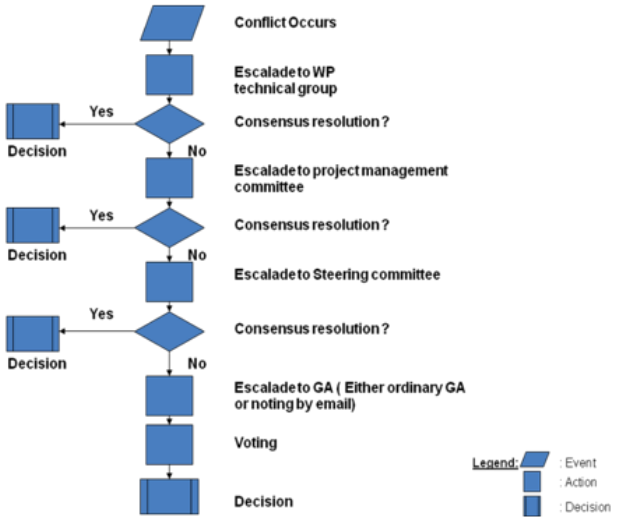


Figure 2. Conflict resolution in CLINTOS Consortium

In case where the simplified conflict resolution process described above fails to satisfy the CLINTOS members, then the World Intellectual Property Organization (WIPO[79]) and/or the International Chamber of Commerce (ICC[80]) methods for the settlement of disputes will be pursued. All members are committed to settle their disputes amicably. Any dispute, controversy or claim arising during the project's period will be subject to Alternative Dispute Resolution (ADR) mechanisms, like mediation and arbitration. CLINTOS members are committed to exploit ADR methods aiming to achieve a fair, reasonable and non-discriminatory (FRAND) resolution.

3.2 b)vii. Operations and Communication Tools

3.2 b)vii.i. Planning

Drafting coherent plans for the project work is an essential prerequisite to enable the work to progress. The current document only presents a high-level overview of the project, setting out the ground rules on which the project will proceed in terms of objectives, technical approach and time scales.

At the project start a consolidated planning will be produced and maintained by the Project Office. A detailed work plan will be produced for each subtask level to avoid redundancy in tasks, to ensure all tasks are covered, and to allow an efficient follow-up of progress. The work plan can be revisited only with the approval of the PMC.

3.2 b)vii.ii. Meetings and Travel Management

Meetings are organized at a frequency defined above: see sections 3.2b) i-3.2b)iv. In order to minimise travel costs and guarantee maximum efficiency, the partners agree to meet 2-3 days every four months in joint consortium meetings. During these days, all meetings of the various bodies will take place (at a minimum, WP Technical Groups meetings and a PMC meeting will take place). Every three meetings, a GA meeting are organized. Ad-hoc meetings for integration, test, or solving special issues can be organized.

At the project start, the PMC defines a provisional planning for meetings and teleconferences. The calendar (time and place for one year) of the various meetings will be defined during the kick-off meeting, and from then, one year in advance. In between physical meetings, regular Teleconferences are scheduled.

3.2 b)vii.iii. Deliverables

Complete deliverables handling will be defined in D1.1 (Project Management Handbook), while the review and approval procedures will be described in D1.3 (DMP Handbook).

Deliverables consist in reports, white papers, documents, laboratory models, demonstrations, field trials, etc. WP Leader first approves them, and then appoints reviewers, then Project Technical Manager and then Project Coordinator. Reviewers are named by the PMC, and are usually internal to the project. On special occasions, external reviewers can be consulted after appropriate confidentiality measures have been taken.

3.2 b)vii.iv. Quality Control Principles

In the line of the Quality Assurance Plan (D1.1), the T1.1 leader will be asked periodically to review technical progress such that the project remains innovative, driven by requirements of end-users, open to collaborations and to market needs, forward looking. That will ensure that the **CLINTOS** project is producing work of high

[79] http://www.wipo.int/amc/en
[80] https://iccwbo.org/dispute-resolution-services/

technical quality.
Handling of the quality of deliverables is described below; however, quality shall not only be addressed for the deliverables but also for the project process itself. Thus management process and developments of the project will be submitted to periodical reviewing with respect to:

1. Staying focused on project objectives of focusing on end-user requirements, high quality technical outputs, market proximity and openness
2. Adequacy of the project management plan and how the work performed complies with it including IPR management and results dissemination,
3. How well the project processes are synchronized and inter-linked
4. Identification and evaluation of activities and results that would adversely affect the achievement of the project objectives,
5. Process improvement in the project by identifying deviations and changes
6. Quality assurance is the joint responsibility of all partners and will be applied at all levels of the project's activities.
7. Management will continuously monitor and control (i.e. taking corrective actions) expenses, resources and schedules versus plans (i.e. technical and financial annexes to the EC Grant Agreement). Root causes for deviations, be it shortages or excesses, in costs, resources and schedules shall be identified, recorded and used as input for continual improvement. Possible impacts of schedule changes on the budget and resources of the project and on the quality of the results should be determined.

3.2 b)vii.v. Documentation

Document management rules and guidelines (template, classification, numbering and distribution level), the review/approval procedures will be detailed in D1.1 and D1.2 (Project Management QA & DMP Manual). All project documentation will be stored electronically in a secured web-based collaborative platform. The usual tools (e-mail, web collaborative tools and audiovisual teleconference systems) will be used for the exchange of documents/information.

3.2 b)vii.vi. Reporting Process

Internal (within Consortium): Every partner commits to write a quarterly report to the PMC with copy to the WP Leaders. It will describe the technical and management project work done, listing effective time spent on the project. It will mention difficulties, milestones and deliverables (or contributions to deliverables in case of joint deliverables) that have been reached, patents, publications, travel and visits.

External (to EC): The Project Coordinator will coordinate and consolidate quarterly, annual and final activity, and management and financial reports which need to be submitted to the EC. Every partner will provide audit certificates when needed (according to H2020 rules), prepared by an external auditor selected by the partner, and certifying that the costs incurred during the period meet the conditions required by the grant agreement.

3.2 b)vii.vii. The Project's Website and Collaborative Platform

The consortium will use a website such as http://www.theCLINTOS.eu (domain name to be confirmed) for external communication. This site enables the consortium to manage the large dissemination of the project results, as well as the events and information related to its scope of interests.

The consortium will use for its internal communication an interactive web collaborative platform. This website will be secured and will enable the consortium to manage the limited diffusion of private information, to convene meetings and audiovisual teleconferences, to follow resources and allow easy exchanges between partners.

3.2 b)viii. Addressing effective innovation management

In order to keep the innovation potential and capacity at a maximum level, the project shall establish a simple, yet effective procedure for the analysis of developments in each of the envisioned architecture systems, subsystems and components.

Thus, the Consortium has decided to establish the procedure of periodical reviews of all critical blocks foreseen by the architecture envisioned by the **CLINTOS** project. This analysis shall combine technical and marketing points of view and will answer the following questions:

- are the targeted KPIs still relevant?
- does the architecture concept (still) have the potential to ensure the envisioned KPIs?
- do sub-systems and components (still) have the potential to ensure the envisioned KPIs?
- have competitive alternatives (architectural, sub-systems, components) been identified?
- do market factors promote the commercialization of the developed sub-systems or components?
- do regulations/standards promote/threaten further development?

Such assessment of viability will be performed for at least the following most critical systems, sub-systems and components: CLINTOS wearable SmartHub UI, CLINTOS wearable SmartHub UX, BLE5 mesh-networking, companion app UI & UX, CLINTOS wearable SmartHub optical, thermal & G sensors, MAC layer protocols, resource management algorithms, privacy and anonymizing algorithms.
With this knowledge, the Consortium will be able to make informed decisions that address both technical and business challenges and reduce innovation risks of the project. The assessment will be done every 6 months and be reported by the minutes of the Innovation Board meetings.

The described assessment will be made in the specially introduced Innovation Board, chaired by the Innovation Manager. The Innovation Manager of the **CLINTOS** is Dr Marco Minoia (ABI) who will chair the Board consisting of representatives from all partners.

3.2c) Critical Risks

Although risks are quite diverse and in some occasions unpredictable, a common process for tackling them does exist, which starts with the **identification and classification of the risk**, continuous with the **resolution approach** and **implementation**, and is completed with **monitoring and evaluating its effectiveness**. In general, risks can be broadly classified into two categories, one related to the smooth execution of the project work-plan by the collaborating partners and a second regarding specific technical/research obstacles/limitations appearing during the project. For the former category specific project management actions will cope with those issues, while for the latter category technical resolutions will be provided. Table 3.2.3 below presents the major risks and respective management/contingency plans

3.2c. Critical Risks for Implementation

The risks identified & scored for the project will be assessed by PMT, reviewed by STC, and monitored at set milestones. In case a threat is realized, mitigation actions already identified will be proposed under PMT responsibility and implemented to minimize impact. Major technological risk stays with user compliance rather than the performance of the CLINTOS solution. However, thanks to the sample size multi-center trial sites for two of the three use cases, this risk is mitigated by excluding the non-compliance, and for the same reason the good performance of the whole project will not be affected, if absolute trial targets are not fully reached.

Table 3.2.c: Critical Implementation Risks & Contingencies | P: Probability, I: Impact

Description of risk	P	I	WPs	Proposed risk-mitigation measures
Although the benefits of CLINTOS extend across all healthcare sectors and individual citizens, its global adaptation largely depends on government policies regulating RDCTs.	H	M	WP5	The wearable SmartHub that CLINTOS deploys has broad applicability beyond RDCT settings, such as useful first responder tool and Health Passport for every citizen. An effective PEDR implementation along with involvement of CT sponsors and CROs. Hence this high risk will be mitigated to moderate risk.
CLINTOS is a new approach to running clinical trials based on monitored body sensors. Citizens may have privacy concerns.	H	M	WP6	The challenge is to properly communicate to end-users how CLINTOS saves lives in emergency situations maintaining privacy / anonymity of the users. It complies with GDPR & privacy preserving PEPP-PT / DP-3T standards.
Risk that the project does not deliver a solution matching the consortium goals. Produce solutions that introduce new user experiences that end-users are not used to, and not willing to change.	M	L	WP2	CLINTOS deploys decentralized user-centric design (T2.1, T2.2 & T2.3), to build a versatile wearable gadget for the convenience of CT subjects that doubles as a high-end wristwatch, which people are already used to. The hardware deployed is mature & its usage requires no change in user practices. Hence low risk.
Budget (time/cost) issues may hinder development due to complexity and possible changes as the requirements for optimum solutions evolve.	L	L	WP1	Project baseline has been discussed, agreed & defined, using outputs from existing projects. Budget and resources carefully allocated resources, which will be monitored through the project. Agile development strategy will keep project on track (T1.1, T1.2 & T1.3)
Project execution risks, such as, critical deliverables are delayed or sub-standard quality. Possible delays in work plan.	L	L	WP1	Strong dependency analysis. Quality procedures, templates and guidelines are key elements for mitigating this risk. (T1.1, T1.2 & T1.3) More significantly, consortium coordinator & key partners are very experienced.

Partner problems such as, underperforming partner; a key partner leaves the project; partner disagreements, etc.	L	H	WP1	Key partners are experienced. Consortium Agreement fully covers conflict resolution. Escalated problems will be referred to the project coordination team & general assembly. Probability is low although impact may be high.
Technical specs & requirements of CLINTOS device may be ambiguous to some consortium partners.	L	L	WP2	Project begins with clear specs & architecture (T2.1, & T2.2) with a dedicated WP. The tech specs will be approved by all partners (T2.3), which project's iterative process timely validates, leaving no room for ambiguity.

3.3 Consortium as a Whole: Extraordinary Team In Extraordinary Circumstances

The CLINTOS consortium was originally lead by **CERTH** along with the support of **FHJ** and **MLC**, all three of them are partners in the Trials@Home center for excellence. A late discovery (4 working days before the submission deadline) that the countries of these 3 participants either did not have an agreement with ECSEL (Greece) for co-funding this call or had very restrictive agreement that imposed conditions (Netherlands & Austria) that made their participation as partners virtually impossible. Hence, these 3 Trials@Home partners along with a couple of universities had no option but to pull out of the consortium as partners. However, the CLINTOS consortium has decided to retain their expertise as third party **Special Trials@Home Advisory Board** largely to ensure that this project will *be "timed and tuned to facilitate a close complementary activity between Trials@Home.*[82] Moreover, these T@H partners had played a key role in development of the CLINTOS proposal throughout the process of its' evolution, and hence considered as active contributors to the CLINTOS consortium as a whole. The following table lists the members of this special advisory board:

Special Trials@Home Advisory Board

No	Advisory Organization name		Country
1	**CERTH: Ethniko Kentro Erevena Kai Technologikis Anapty***	Research Org	Greece
2	**MLC: Stichting MLC Foundation (MLCF)***	Research Org	Netherlands
3	**FHJ: FH: JOANNEUM Gesellschaft mbH***	University	Austria

The legal participants of CLINTOS consortium along with the Trials@Home advisory board have a collective experience of over 412 EU-funded projects. It is a well-balanced mix of experience and skills in diverse disciplines ranging from Trials@Home, cybersecurity, EMS, epidemiology, ICT data sciences, computer hardware / software, IoT, AI, data science, social equities, ethics, humanities, manufacturing, so on and so forth. Their contribution to CLINTOS is detailed herein and in section 4.

3.3.(a) Overview of the CLINTOS team coherence

The CLINTOS consortium has an optimum mix of representative industrial players and key academic institutions with leading roles in the value chain towards the use and exploitation of CLINTOS wearable SmartHub device, not only as a remote vitals monitoring tool for CTs, but as a seamless, privacy-preserving human mobility regulator for preventing future pandemics / epidemics in the post Covid-19 era when global and local human mobility will be adversely affected, and states will be compelled to adapt some kind of digital health passports to authenticate their citizens cross-border or cross-jurisdiction transfers.

The members of the Consortium complemented by its special Trials@Home advisory board are all organizations which are very active and experienced in current activities on national, European and international levels in the sectors of ICT, eHealth, Trials@Home, social equity, IoT, software / hardware technology design, manufacturing for future growth.

As such, they are excellently placed to act as leaders in bringing new wearable public health technologies for moving CTs from brick and mortar based activity to remotely conducted decentralized clinical trials. Thus setting up a new standard for future clinical trials, economizing the cost of clinical trials on one hand, and speeding up the approval times on the other, thereby setting a new standard for a new normal that the Covid-19 pandemic has introduced.

Together, these CLINTOS stakeholders can take the leadership beyond the CT activities by being the first to have practical and usable solution that provides complete protection against future epidemics/pandemics, makes healthcare easily accessible to citizens via telemedicine, makes cross-border human mobility safe and morbidity free, breaks the data silos that exist in our current EHR (electronic health record) systems, and most importantly

[81] ECSEL Joint Undertaking, Work Plan 2020, Version 16, page 16
[82] ECSEL Joint Undertaking, Work Plan 2020, Version 16, page 16

does all this in a clever, efficient, seamless and non-intrusive way.

In the design of the CLINTOS project, specific thought has been given to aligning the goals of the project with the interests, ambitions and capabilities of the participating organizations. Because of this alignment, the commitment of the individuals and their organizations to their roles in the CLINTOS project is very high. Part of the project strategy is to involve the industrial players in key roles to ensure that the research strategy is appropriate and can benefit the European industry. Moreover, most of the partners have or are already working successfully together in other EC projects, which are expected to speed up the bootstrapping of all CLINTOS activities.

This development is important as the SmartHub wearable device of the CLINTOS infrastructure is a versatile device that massively impacts multiple industries beyond CT, which has the potential to create opportunities to involve a lot of SMEs. This approach to accelerate the development of the emerging concepts in public safety will open an ecosystem market to thousands of SMEs providing value added services/applications and/or cutting edge technology to a stable ecosystem evolution strategy. This Trials@Home wearable device is already being developed as Health Passport, as SmartHub for first responders and in different regimes.

The roles assigned to the consortium partners and advisors in the project reflect their main areas of expertise and experience and are described in full in Section 4. They are summarized in the table below for reference:

3.3.(b) Complementary partner roles in the CLINTOS project

No.	Participant	Role in the Project
1	**UTB**	Coordinator & overall manager of the project, UTB participated in / coordinated numerous European and National research projects with focus on biomedical engineering and has strong know-how in modeling and simulation (both mathematical modeling and data-driven modeling, i.e. machine learning), and high-performance computing (GPU/cloud/cluster). Will contribute its security, AI & cryptographic expertise in designing, implementation & evaluation of CLINTOS ecosystem's resilience.
2	**BC5**	As the original inventor of the EU-funded (Fed4Fire+) wearable SmartHub, BC5 will use its experience in decentralized privacy, security and interoperability (PSI), IoT, epidemiology and healthcare in leading WP3 for building the CLINTOS prototype.
3	**EMA**	As EU's premier network of medicos, EMA will head several tasks in WP6 including creating the PEDR and managing social media, including social & policy impact of research & social equity as part of WP6 activities. As expert will oversea overall quality of proposal, and will implement tasks in WP6 dissemination and exploitation, organizing workshops, seminars, conferences & TV/Web shows.
4	**AFL**	Lead WP4 for manufacturing CLINTOS devices through its affiliate company in China. Will also provide DLT expertise for POC.
5	**OT**	The participation of one of Europe's leading textile brand Ozanteks in the consortium to produce a smart T-shirt itself is a testimony to the potential of the innovations. OT will design, produce and test the smart T-shirt determining and analyzing yarn properties (antibacterial, thermal, thermo-regulative, conductive, etc.). OT will also contribute to relevant dissemination activities and carry out the indirect market analysis for the smart textile product.
6	**SST**	SST will lead the analysis and coordination of legal aspects and regulation concerning data protection and privacy by design. Moreover, SST will contribute to the requirements definition, technical platform development and the pilot preparation. SST's main task will be to carry out legal research on personal data protection and privacy. SST will lead WP2 for drafting and designing the technical requirements, specifications and the architecture of the CLINTOS ecosystem. As experts on security, privacy, big data and compliance, will contribute to research, design and evaluation of the overall resilience of CLINTOS.
7	**ISS**	As a CLINTOS end user as well as third party CT services vendor, ISS will play key role in the field-testing of CLINTOS. It's main task being the integration of ISS eCLinical platform Healthentia in all three CTs. This will facilitate data collection for modeling of patients and attempting biomarker discovery that predicts achievement or not of any defined significant clinical outcome. This will also establish CLINTOS as a

		versatile operating system for RDCTs. As WP5 lead, will conduct use-cases field trials along with ABI & MIA, and also provide end user perspective as a end user, contributing as technical advisor for the end product design, and also as tester of product simulations.
8	**ABI**	ABI brings the CRO and early clinical testing experience to CLINTOS consortium, and as such will play a key role in testing and validation of the CLINTOS ecosystem. It will leverage all its resources in the field of cosmetics testing and molecular biology as well his experience in the development of protocols for medical devices trials and usability validation. Specifically, it will undertake the following actions: (i) study of the device and in its relative classification for the purpose of validating it as a predictive tool in assessing the effectiveness of the response to therapy; (ii) test the use of the device versus classical design cosmetic tests protocols; (iii) validate the device for its use within cosmetic testing and define a protocol. Will also be responsible for ethical & IRB approvals for field trials.
9	**MIA**	MIA's diverse experience in health related technologies including a hospital management system, qualifies them as potential end user as well as a vendor. MIA will contribute to the WP3: CLINTOS Proof of concept (POC) T3.1, development of CLINTON'S front backend software, and WP5: Validating & Piloting for first market replication T5.1 planning, monitoring, evaluation of field trials by contributing to designing & executing field trials for uses cases. As an end-user MIA will conduct field trials along with ISS & ABI. It will also lead the T5.2 for testing and validation of the plug-n-play interoperability of CLINTOS with third party applications, which includes MIA own in-house hospital information management system.
10	**SBA**	**FeatureCloud**, **CONCORDIA**, **SOCTT**, **MH-MD** & **CYBERROAD** projects that SBA participated in are linked via the privacy, security, decentralization and AI expertise provides a basis for SBA's contribution to the CLINTOS project.
11	**HBI**	Dr Peter Hauschild's research and expertise on HRV (heart rate variability analysis and wearable device will feed into the CLINTOS SmartHub wearable device.
	Special Trials@Home Advisory Board	In the extraordinary circumstances of this proposal, special contribution comes from a special T@H advisory board in terms of best practices and integration from the TECH WP of the Trials@Home project to scale pilots and conduct RDCTs. This board is constituted by two research organizations CERTH (Ethniko Kentro Erevena Kai Technologikis Anaptyxis, Greece) and MLC (MLC Foundation, Netherlands), and a university, FHJ (FH Joanneum Gesellschaft mbH, Ausria)

3.4 Resources to be Committed

3.4. Resources and Budget

The total project effort is 511 person-months for a total duration of 36 months. The effort distribution is proportional to the WP workload and to the involvement of each partner in the project, but the differences in total effort per partner cannot be taken as an indicator of higher or lower involvement in the project objectives. The effort per WP distribution is also consistent with the project objectives and the characteristics of the work to be carried out. The higher effort of BC5 results from its responsibilities in technology designing and technology development section which forms the backbone of the CLINTOS infrastructure. Work packages WP5 concentrate the highest effort, since it implements the field-testing of the CLINTOS wearable SmartHub devices.

3.4a: Summary of Staff Effort

The project duration is 36 months and the total budget requested to achieve its objectives is **€2.72 Million**. The MOOSNHOT budget does not contain further (additional) funding from neither national nor other programs. The personnel share of the total budget is **71.19%**, which is usual for a design intensive project. This cost includes the manpower for the manufacturing of the CLINTOS SMART HUB for the pilot manufacturing. The summary of staff effort of CLINTOS is summarized in Table 3.4a.

Table 3.4a: Summary of Staff Effort

Participant	WP1	WP2	WP3	WP4	WP5	WP6	Total PMs /Participant
UTB	30	6	6	8	12	14	76
BC5	8	14	28	8	6	6	70
EMA	6	4	4	8	18	20	60
AFL	6	8	14	20	4	4	56
OT	6	12	8	5	4	7	42
SST	6	16	8	4	4	4	42
ISS	6	4	4	4	24	8	50
ABI	2	1	1	2	21	5	32
MIA	5	2	4	2	21	4	38
SBA	4	8	4	0	0	2	18
HB	2	3	0	0	12	10	27
TOTAL	81	78	81	61	126	84	511

3.4b:'Other direct cost' items (travel, equipment, other goods and services, large research infrastructure)

Other direct costs include acquisition of secretariat consumables, office equipment, device manufacturing cost, and costs due to dissemination, training, travelling (project progress, conferences, technical or dissemination meetings). Other direct costs also include the audits subcontracted to specialized companies to be conducted as per the rules of the Commission (audit certificates mandatory for EC contributions larger than 325K Euro). Most of the meetings will be made by videoconference.

The equipment costs are 2.80% of the total; **travel** expenses are kept below 3%. The "other direct cost" items do not exceed 15% of personnel costs for any of the CLINTOS participants except for OT for which justification is given below:

Participant No/Short Name 5 / OT	**Cost (€)**	**Justification**
Travel	14000	Participation in project meetings
Equipment	53000	M290 - MMT® MOISTURE MANAGEMENT TESTERfor precisely measure the fluid management properties of fabrics
Other goods and services	37000	academic consultancy, promotional activity organizing tools
Total	104000	

Remote Decentralized Clinical Trials Operating System For Trials@Home (CLINTOS)

Part B, Sections 4-6

SECTION 4: MEMBERS OF THE CONSORTIUM

4.1. Participants (Applicants)

4.1.1 UTB: Universitatea Transilvania Din Brasov

Partner profile

Transilvania University of Braşov is a Romanian public academic institution with over 800 full-time scientists and professors and around 20,000 students (including over 500 students in PhD programs). The University has 16 faculties, eight focused on engineering areas and eight focused on various other academic profiles. The Research Departments are defined in the strategy as autonomous structures of the University, with their own staff, Ph.D. students, research master programs and high-level infrastructure. The Department of Automation and Information Technology is affiliated to the Faculty of Electrical Engineering and Computer Sciences. It has participated in / coordinated numerous European and National research projects with focus on biomedical engineering and has strong know-how in modelling and simulation (both mathematical modelling and data-driven modelling, i.e. machine learning), and high-performance computing (GPU/cloud/cluster).

Role in the project

UTB will coordinate the project and will ensure that the project activities are going as per the project plan. It will lead the WP1: Project Management and Coordination and will contribute to the other tasks along with the other partners.

Key personnel

Lucian Mihai Itu (male) is the Research Group head of the Artificial Intelligence team at Siemens SRL. He received the Dipl.-Eng. degree in Systems Engineering from the Transilvania University of Brasov in 2009 and the PhD degree in Systems Engineering in 2013 after having collaborated with Siemens Corporate Research, Princeton, USA during doctoral studies. He has participated in numerous European, National and Industry funded R&D projects. His research interests are: artificial intelligence with focus on machine learning, modeling of the human physiology, and high performance computing. He has published over 50 papers in various international journals and conferences. He is joint author of over 30 international patent applications.

Constantin Suciu (male), received the Dipl.-Eng. degree in Electrical Engineering in 1994, the M.Sc. degree in Electrical and Computer Engineering in 1995, both from the Transilvania University of Braşov and the PhD degree in Electronics and Computer Engineering in 2000 from the Nottingham Trent University, UK. He has coordinated numerous European, National and Industry funded R&D projects. His main research interests are: human physiology, artificial intelligence, and distributed control and processing. He is author or co-author of more than 60 scientific publications in various international journals and conferences.

Relevant Publications

1. CF Ciușdel, S Coman, C Boldișor, T Kessler, A Muradyan, A Kovachev, H Lehrach, C Wierling, LM Itu, Effect of Linearization in a WNT Signaling Model, Computational and Mathematical Methods in Medicine, Volume 2019, Article ID 8461820, 2019.
2. A Vizitiu, CI Niţă, A Puiu, C Suciu, LM Itu, Applying Deep Neural Networks over Homomorphic Encrypted Medical Data, Computational and Mathematical Methods in Medicine, Volume 2020, Article ID 3910250, 2020.
3. Itu, L. M., et al., A Machine Learning Approach for Computation of Fractional Flow Reserve from Coronary Computed Tomography, Journal of Applied Physiology, Vol. 121, 2016, pp. 42-52.
4. Itu, L. M., et al., Non-invasive assessment of patient-specific aortic haemodynamics from four-dimensional flow MRI data, Interface Focus, Vol. 8, 2018, pp. 20170006.
5. Itu, L. M., Suciu, C., et al., Journal of Computational Physics, A Parameter Estimation Framework for Patient-specific Hemodynamic Computations, Vol. 281, 2015, pp. 316-333.

Relevant Previous Projects

1. FLAG-ERA, ITFoC: The project develops a radical new approach to a true personalisation of drug therapy in medicine and prevention, and its demonstration in a subarea of oncology (breast cancer), based on a deep molecular characterisation of individual tumours and patients and the establishment and use of digital medicine approaches to model effects and side effects of therapy options (2017-2020). https://itfoc.eu/
2. HORIZON2020, MHMD: the project developed an open biomedical information network for sharing data between hospitals, individuals, research centres and businesses, as well as algorithms for privacy-preserving data publishing and secure computation (secure multiparty computation, homomorphic encryption and distributed learning), synthetic data generation and validation, and physiological modelling for clinical decision support (2016-2019). http://www.myhealthmydata.eu/
3. FP7, MD-Paedigree: a clinically driven VPH project validating patient-specific computer-based predictive models of various paediatric diseases (2013-2017). http://www.md-paedigree.eu/
4. UEFISCDI (National project), FUNCTIONAL-ACS: The project develops deep learning based methods for computing in real-time functional coronary diagnostic indices for non-culprit lesions of acute coronary syndrome patients from routine angiographic medical images (2018-2020). http://aut.unitbv.ro/FUNCTIONALACS/
5. UEFISCDI (National project), HEM-ML: The project develops machine learning-based methods for determining in real-time hemodynamic quantities from medical images and routine patient-specific measurement. http://aut.unitbv.ro/HEMML/

Infrastructures and facilities

GPU-based computational cluster: a High Performance Computing server equipped with CPU Intel Xeon E5-2630 v3 2.4GHz, 256 GB RAM DDR3, 2x NVIDIA K80, and eight workstations equipped with NVIDIA GTX Titan Black / Titan X / 780.

4.1.2. BC5: Blockchain 5.0 OÜ

Partner profile:

BC5 is an Estonia based SME specialised in new technology and product development in diverse fields such as health and wellness, ICT, softwares,, IoT, cybersecurity and decentralised technologies. With a team of experienced and passionate industry experts, BC5 designs and develops cutting edge technologies that can potentially revolutionise multiple industries. Our products range from designing and developing hardware and software of the Health & Wellness products and also for the next generation Internet (NGI) that are cybersecure, privacy-preserving and seamlessly interoperable enabling Web 3.0. BC5 deploys its expertise as consulting services to clients as well as builds in-house research products, of which most recent projects include at least three market ready IoT devices (Redoxer, Xeno & COVID). We provide services in the health and wellness, ICT, Software that go beyond the state of the art. We are specialized in developing products and services using technologies based on decentralized network architecture. Our network decentralizing approaches include DLT, blockchain and our own proprietary non-ledger approach. The company has recently built a Consortium of Europe's top Universities and research organizations to develop and commercialize one of its proprietary cloud decentralization technologies. See https://liquidus.info/consortium/. The company has wide experience in developing Health and Wellness wearable devices. In fact the founder of Blockchain 5.0 is an MD with specialization in epidemiology and over a decade of experience in the US biotech industry as research epidemiologist.

Main tasks

BC5 will use its vast experience in building diverse innovation solutions to lead CLINTOS' WP3 effort to code and build a proof of concept according to the specifications and technical architecture delivered in WP2. It will also be a lead partner in commercialising the CLINTOS solution.

Key Personnel assigned to the project:

Dr Fazal Raheman (M): Founder of Blockchain 5.0 OÜ and a serial inventor with over 3 decades (including a decade in the US biotech industry) of product development experience in diverse fields ranging from healthcare, cybersecurity, cloud computing, blockchain, IoT, mobility, etc. He is the CEO of BC5 and is a serial inventor and an entrepreneur. He is a medical doctor and an Epidemiologist with extensive experience in conducting research in epidemiology of infectious diseases such as HIV, Tuberculosis, and ICT projects. He holds several patents in areas that range from healthcare to Internet technologies. He started his career in academia as Epidemiologist and then moved to the healthcare industry as Research Epidemiologist involved in designing and conducting clinical studies in communicable and non-communicable diseases for a biotech company in Cambridge, USA. He has over 31 patent applications at various stages of patent process in the field of healthcare & ICT combined.

Within the field of infectious diseases and immunology, he holds patents on Tuberculosis, HIV, Neutropenia, Thrombocytopenia and ITP (Idiopathic Cytopenic Purpura). For a complete list of patents attributed to him please check here: https://www.bc5.eu/DrFazal-Patents/

Dr Ravi Chavan (M): He is a MD. D Card, Cardiologist & Diabetologist. An alumni of Asian Heart Institute & Research Center, Mumbai (India), he is a Head Cardiologist with Reserve Bank of India, Sunridges Hospital & Suburban Diagnostics in Mumbai (India). He is the Founding Director of Aacaar HealthCare Pvt Ltd & Vivify Lifecare Pvt Ltd that works in corporate and community wellness domain. He is the Medical Director of Sanskritech Smart Solutions Pvt Limited (Swayam AHM Project) and Founder of NGO (Trust) - Aaacar - Shaping Lives.

Professional Affiliations & Fellowships

1. Medical Council of India
2. Maharashtra Medical Council (India)
3. Indian Association of Clinical Cardiologist
4. European Society of Cardiology
5. American Society of Preventive Cardiology
6. American College of Preventive Cardiology
7. Evidence Based Diabetes and Advance Cardio Diabetes Management (Public Health Foundation of India)
8. World Health Federation
9. SHAPE - Society of Prevention and Eradication of Heart Attacks
10. International Olympic Committee (Sports Medicine)
11. Royal College of Physicians (UK): PG in Advance Cardiology
12. Certified expert in Cyber Security in Healthcare
13. Awarded with a certificate of achievement in Community Health by Harvard(X)

Tejas Bhagat (M): An engineering professional with impeccable academic record as a Gold Medalist of class of 2013, Tejas holds bachelor's degree in Energy Engineering and is closely associated with new innovations and technologies in the diverse domains ranging from healthcare, wellness, ICT, softwares to blockchain. He accumulated extensive experience in technology research analysis, project management and business development, first as BC5's product licensee and subsequently as a Team Lead for project Algoshare and head of India operations, Redoxer. He has been associated with many technical ventures in the field of Wellness, Blockchain, ICT, and Decentralised Technologies. As Chief Data Analyst & Technology Implementer at Blockchain 5.0 OÜ, he is one of the core team members for designing and development of BC5 product portfolio that includes LIQUIDUS, Xeno & and the most recent one COVID. He is in-charge of the Xeno and COVID mesh-networking project, which recently won H2020 grants for demonstrating Xeno and COVID's BLE5-based always-on connectivity in areas that lack GPRS or WiFi connectivity. He is also a key member of the ZEROV development team, he brings his privacy-preserving decentralized networking experience acquired in the LIQUIDUS project, and the always-on IoT mesh-networking experience gained in Xeno & COVID project. He has gathered wide

experience in designing and development of Healthcare Wearable Devices by serving as a Head of Indian operations for project Redoxer, which aims to commercialise the World's First Patented General Wellness OTC Wearable Device. He is also a founding member of Vivify Lifecare Pvt Ltd, India which provides wellness solutions to corporate employees using the most advanced technological tools for lifestyle disease prevention, early detection and integrative treatment solution.

David Bell (M): David Bell is one of the core team members of BC5.0, is a Management Analyst at U.S. Department of Veterans Affairs. He holds the PG degree in Business Administration and Management with special emphasis in Organizational Innovation from University of Phoenix. He has extensive experience in different decentralised technologies and has been a backbone of the BC5's decentralised technology projects. He is the Co-Founder and CEO of Algoshare INC, Drovonics and the Co-Founder of SDG One project. David Bell is a powerful business driver whose entrepreneurial instincts have carried multiple companies. He looks after the international relations of Blockchain 5.0 and serves as the head of the overseas business. His Linkedin profile: https://www.linkedin.com/in/david-bell-38969894/

***Kamruzzaman Ansari (M)*:** He has Masters in Computer Application, and has over 13 years of experience in ICT Industry & Over 3+ years of Management experience in planning, controlling, executing, and closing various ICT projects. He is currently heading IoT Cloud Services Business Development at Blockchain 5.0 OÜ. Since 2010 he has been project manager at leading French Software Development Company Prior to this, he had worked with Glob Tech Solutions as a Senior Software Engineer (Dec2009 – July2010), Teamware Solutions as a JDE Consultant (July2009 – Nov2009), Logiglide Software Factory as a JDE Consultant (Dec2008 – June2009) & Systime Computers as an Associate Consultant (Feb2007 – Nov2008). He has successfully managed $14M deployment of CMS at all phases, and achieved 70% process time savings through implementing process automations and IT upgrades. He has expertise in integrating AWS Cloud Services integrated with on premise Oracle Applications. His technical proficiency in EnterpriseOne (JD Edwards), AWS (EC2, S3, SQS etc), Oracle SOA 12C, Oracle Cloud PaaS, SaaS and EDI 850, 810, 855, 856, 820. He has vast experience in implementations, customizations, production support, upgrade, development and testing of JD Edwards EnterpriseOne. He is extensively experienced in Web applications and Interoperability, and also experienced in Sales & Distribution, Procurement, Manufacturing & Inventory Management.

Danielle Bell (F): Experienced growth marketing manager with a background in sales. She is a marketing specialist with 5+ years of experience in managing all aspects of organic SEO and PPC campaigns. She was responsible for the increase in online presence and website traffic building campaigns. In her previous roles she boosted the number of monthly unique visitors by 300% and increased CTR by 22% in marketing emails. Skilled in oral and written communication as well as negotiation techniques, she has proficiency in building customer loyalty by leveraging interpersonal skills and offering top customer service. Danielle is handling social media marketing at Blockchain 5.0 OÜ.

***Akash Dayma (M)*:** Akash is software engineer and programmer with 6+ years of experience as a coder well versed in several programming languages. As a senior developer at Blockchain 5.0, he has extensive experience in decentralized networking (DLT, Blockchain & Non-DLT). He has worked with all major public/private blockchains including Bitcoin, Ethereum, EOS, Hyperledger, TRON, IPFS and other decentralized security protocols. He has built smart contracts on several blockchains. He has proficiency in several programming languages such as C, C++, Angular NodeJs, React-Native, Typescript, JavaScript

etc. He has passion to learn and acquire new skills. His understanding of technology and ability to skillfully navigate the product development process has proven to be of great value. He has a proven track record of having developed a few commercial solutions for clients and a couple of BC5's flagship products such as LIQUIDUS, AlgoShare, COVID-PASS and XENO & was instrumental in first experiments to demonstrate technical feasibility of the Supra OS application for implementing zero vulnerability in Windows PC. Akash will be one of the key developers on the CLINTOS project.

Musheer Ahmed (M): A software engineer by qualification (BE Information Technology) with 10+ years of full stack software development experience using a wide range of coding languages & web tools. From his previous jobs as a freelancer he brings extensive experience in building client-server PHP projects. He is also experienced in 3D printing and handles IoT device hardware modeling and 3D printing prototypes for BC5 projects. As a team player he coordinates with a distributed global team to build Web 3.0 technologies and HCI (human computer interfaces) for diverse computing devices and will be playing a key part in the software development of project CLINTOS.

Nazish Ahmad (F): Accomplished and highly-organized Project Manager with a masters in commerce and over 10 years of professional experience managing complex projects in the IT industry. Her tasks included product roll-out strategy, track progress against goals, and manage execution of projects. As an administration and operations manager, managed a globally distributed team of 20, fulfilling projects cumulative worth of over $300,000. Worked as a dedicated customer service representative with over 5 years of professional experience. Has expertise in identifying sales opportunities, providing exceptional service to customers. She attained >85% positive customer ratings and maintained customer retention rate of 25% above the average and on-boarded and mentored 10+ new employees.

Tanvee Phulzele (F): A business administration graduate and an aspiring entrepreneur with excellent administration, interpersonal and marketing skills. While pursuing her masters in business management, she assists Danielle Bell in social media marketing for BC5.

Relevant projects:

The founder of Blockchain 5.0 OÜ brings 3 decades of experience in areas that bear relevance to the execution of the project. These areas can broadly divided into 4 categories:

1. **Healthcare & Wellness:** Blockchain 5.0 founder is a medical doctor, specializing in public health and epidemiology. His career started with tuberculosis research, which resulted in an American company commercializing his technology in the early 90s. He has extensively worked on immunotherapy of HIV using an immunostimulant of bacterial origin. The bacterial origin immunostimulant was also developed for treatment of autoimmune disorders such as Neutropenia, Thrombocytopenia. This work resulted in 6 patents[1]. In the field of wellness Blockchain 5.0 founder has the credit of pioneering wearable devices for health and wellness. His first wellness device was based on a technique invented by him ORIP (Optimal Remote Ischemic Preconditioning), which was patent in 2014.[2] This followed by an improvised version of the ORIP device[3] and a wellness device - XENO for women's safety. The initial work of the XENO devices has resulted in COVID, which has recently won EU's Fed4fire grant for its BLE5.0

meshnetworking capabilities. Project CLINTOS the result of all our previous experience in Wellness, Healthcare & Wearable Devices Technologies.

2. **Cybersecurity- Privacy & Anonymity:** Company has recently submitted a proposal MOONSHOT which is the novel first responder (FR) infrastructure based on a wearable device technology that made an ideal use case for the application of our proprietary cybersecurity solution ZEROV. ZEROV is actually a culmination of almost two decades of efforts to circumvent OS vulnerabilities in a 2007 patent[4],which disclosed a **R**eal **O**nline **C**ard Key (ROCK) device that circumvented the computer OS by running a thin OS on a CD Rome to execute an online transaction. This primitive idea eventually evolved into ZEROV. Besides the radical approach to circumvent computer vulnerabilities, BC5 inherits founder's incremental innovations in security[5], privacy,[6] access control[7] and anonymity.[8]
3. **Web Technologies:** Our work on web technologies include software for new[9] generation ISPs[10], cursor-responsive windows that generated revenues.[11] This expertise is used in enabling next generation Web 3.0 enabling technology in the ZEROV infrastructure. The wide experience acquired in web technologies will form an integral part of CLINTOS solution..
4. **IoT Device:** BC5 has developed at least 3 IoT[12] devices[13] that are market ready. The expertise is relevant to hardware and IoT components of CLINTOS project.
5. **Decentralization & LIQUIDUS** (**Li**nkable **Qu**arantined **I**nternet **D**ata of **U**nique **S**ubjects) Decentralization of networks is the core expertise of BC5. We have several products using decentralized networks.[14] Our proprietary expertise is in using non-DLT approach to decentralization[15] in use cases where DLT / Blockchain is inefficient. LIQUIDUS is a radical new way to reclaim the user's privacy, security and interoperability that's been under siege from technology for eons. Liquidus is based on the vision of Sir Tim Berners-Lee, the inventor of the World Wide Web. In addition to maximizing the privacy of personal data, Liquidus affords protection against security breaches to the companies and introduces the much ignored interoperability to the traditional data silos. BC5 has partnered with 12 other European entities (includes universities, SMEs and non-profits) to form a consortium that will use LIQUIDUS technology to build a novel Privacy, Security, Interoperability-as-a-Service (PSIaaS) cloud computing solution, which is being pursued as a proposal for a recent HORIZON 2020 cloud computing call. LIQUIDUS forms the backbone of CLINTOS infrastructure.

[1] Raheman, S.F., "Use of Reference Sera in Immunoassays for Detecting Antibodies Against Mycobacteria" U.S. Patent Pending, Serial No. 07/654,340.

Daniel, Thomas M., and Raheman, Fazal S., "Methods and Articles of Manufacture for Initiating a Delayed Hypersensitivity Reaction to Mycobacterial Antigens" Serial No. 07/982,785. Filed November 30, 1992.

Raheman, F.S., "Methods & Articles of Detecting Antibodies Against Mycobacteria" U.S. Patent Pending, Serial No. 07/654,340.

Istrate, N., Muni, G., Brauner, E., Raheman, F.S., "Methods for Treatment of Human Immunodeficiency Virus Infection with Pseudomonas Phosphoaminilipid Extract" US 5853738. Issued on December 29, 1998.

Raheman, F.S., Muni, G., Brauner, E., Istrate, N., "Methods for Treatment of Neutropenia", US5851534. Issued December 22, 1998.

Raheman, F.S., et.al., “Methods for Treatment of Thrombocytopenia”, US6183756. Issued February 6, 2001.

[2]Methods and apparatus for optimal remote ischemic preconditioning (ORIP) for preventing ischemia-reperfusion injuries to organs **https://patents.google.com/patent/US8911469B2/en**

[3] Raheman, Fazal, Raheman Ali. Wearable Decentralized Apparatus For Remote Ischemic Preconditioning. PCT/IB2019/055436.

[4]Fazal Raheman (2007) Method and system for using an optical disk drive as a biometric card reader for secure online user authentication. US Patent 228424B2, filed August 12, 2002 and granted June 5,2007.

[5] Raheman, Fazal, Multifunction keyless and cardless method and system of securely operating and managing housing facilities with electronic door locks. US Application No. US11/507,557 (2006).

[6] Raheman, Fazal, A Novel Method and System of Network Integrity via Digital Authorization (NIDA) for Enhanced Internet Security. Non Provisional Application No. 11/892,186 (2007).

[7] Raheman, Fazal, A method of self-service access control for frequent guests of a housing facility. Filed April 2007. US20090066476A1

[8] A novel card-less, name-less, number-less and paper-less method and system of highly secure completely anonymous customer-merchant transactions. 11/892187(2007).

[9] Raheman, Fazal. A novel method and system of fortifying networks for achieving a very high level of data security and privacy on the World Wide Web. Filed in June, 2001 (abandoned)

[10] Raheman, Fazal, Method and system of reselling in retail, preferred internet access services to the end user via a communications network. Published 20020023003, February 21, 2002.

[11] Raheman, Fazal, Method and system of creating floating windows for displaying sponsor information or messages in the substrate areas of the graphic user interface of a software application. US Patent No. 7,039,872. Issued May 2, 2006

[12] Raheman, Fazal, Raheman Ali Decentralized, Secure, Vandal-Proof & Ubiquitous Rideshare Implementation via Dockless Operations (RIDO). Filed 2018.

[13] Raheman, Fazal, Raheman Ali. Wearable Decentralized Apparatus For Remote Ischemic Preconditioning. PCT/IB2019/055436.

[14] Raheman Fazal, Raheman Ali. Decentralized Algo-sharing Infrastructure For Zero-Loss Algorithmic Trading. PCT/IB2019/050949

[15] Raheman Fazal. A novel compliance by design 4-layered cloud computing architecture. In preparation (2020)

4.1.3. EMA: European Medical Association

Partner profile:

The European Medical Association (EMA) was created in 1990 by doctors initially from the 12 member States, as an international foundation pursuing a scientific aim. It is a forum bringing together medical Health Professionals, mainly MDs, throughout the EU via the distribution of information and services. It is committed to improve the quality of professional education and care by updating knowledge and skills of its membership. EMA seeks to influence positive and innovative developments in European health care by reflecting its members 'views.EMA is a unique, independent non-profit organization offering every EU medical doctor the opportunity to add a European dimension to professional activities and to add on European healthcare standards.

EMA's objectives include too:

● Collect and distribute information on:

1. Doctor associations and specialist medical centers within the Member States

2. Legal aspects in healthcare and medical ethics in the Member States

3. Therapeutic protocols, European Medical Journals, training centers and scientific meetings

4. Continued medical education and VET in medical sciences;

● Support

1. Collaborative projects between Medical Doctors who uphold the objectives of EMA.

2. Medical Doctors, who decide to practice in another EU Member State.

3. Medical Information Campaigns for the public.

4. Encourage and promote projects like summarized edition of a European formulary of all drugs used in Europe, including trade and generic names, standardized information for medical documents, standardized laboratory tests and medical devices.

5. SOPs in medical care and continued medical education

Main tasks

EMA, with their prior or ongoing projects dealing with health security and crisis management, and their Europe wide network of public health professionals will boost the dissemination of CLINTOS amongst stakeholders / first adopters. As the EU's premier network of Medical Doctors, EMA will head several tasks, including creating the PEDR and managing social media. EMA's task involves primarily the formulation of the primary plan for dissemination and exploitation activities, collecting inputs from all the interested Partners.

EMA will participate, with other Partners leading these activities:

a. to the implementation of the website and of the Social Media channels

b. to the productions of policy brief and recommendations related to the social impact that European projects should achieve, and to their dissemination;

c. to the planning and organization of Workshops, Conferences, Webinars TV/Web Shows;

d.to the contribution to development of the business plan is a task that should engage mainly the enterprises involved in this project, with their explicit definition of interests and contacts.

Among EMA's Operational Objectives, regarding dissemination and exploitation - within this project are included:the Creation of content platforms by social media: Facebook, LinkedIn, Twitter and YouTube Channels, also using the already existent EMA's links, or new tailored accounts or pages for this and related specific projects; Sending, through qualified mailing lists (doctors' orders or specialized companies), Newsletters to all health workers in the countries involved in the project (doctors and nurses), i.e. short information by mailchimp (or similar tools) and survey questionnaire for detecting interest of stakeholders, MDs and other general audiences.

Press releases

Note: the task of creation, implementation and maintenance of the web page of the project is reserved to the leading partner of the Project, and not to EMA, which will contribute to the Clintos webpage along to the dissemination strategy planned in social media and meetings/events.

Expected Results

- Reaching a relevant number of followers, views and "I Like" on social media publications (Posts, tweets, videos etc)
- Collect Survey questionnaires answers, with related report. Graphs and analysis;
- Communication models (3 posters, 300 memes, 5 videos-interviews, 2 publications in peer-reviewed

- Journals)
- Construction of mailing lists of at about 40,000 European health workers and from 10.000 Health Workers from non-European countries.

Key Personnels assigned to the project:

Vincenzo Costigliola, MD (M) **-** President of E.M.A. (European Medical Association) https://www.linkedin.com/in/costigliolavincenzo/?originalSubdomain=be. Member of Editorial Advisory Board of "Psychiatry In Primary Care Journal". Good experience in clinical trials. Extensive experience in European health care. Main contractor and participant in many EU projects. Selected as expert-evaluator in the 5th Framework programme. Extensive experience in informatics' health programmes. Teaching experiences. Invited speaker in numerous nationals and internationals conferences. Sound publishing experiences https://pubmed.ncbi.nlm.nih.gov/?term=costigliola+vincenzo&sort=date.

Management. Mortality and Morbidity (M&M) lead for Intensive Care in Kinston Hospital ICU.

Ms Jacqueline RUDOLPH-GERMAIN (F) **-**EMA Assistant administrative since 30 years. Laboratory Technician in Faculty of Medicine at the Free University of Brussels. Employee (Société Belge de Banque). - Chambre Syndicale des Médecins - Layer Office.

Relevant ongoing projects:

· iProcureSecurity Project deals with major EMS challenges across EU: https://project.iprocuresecurity.eu/

· GDPR4H project tackles privacy in health data: https://gdpr4h-project.eu/

· The BioS Project is an Erasmus Plus action aimed to increase Knowledge and Digital Skills on Bioinformatics and Computational Biology, including Computational Statistics, among Health Professional by the development and delivery of an e-learning course (edXplatform) https://www.bios-project.eu/site/it/index.html

Guglielmo Trovato, MD (M): Former Professor and Researcher in Internal Medicine (1984-2007) at the School of Medicine at the University of Catania, Italy; in the same University, Lecturer at the Faculty of Psychology (Health Psychology), and at several Postgraduate Specialization Schools (Internal Medicine, Cardiology, Rheumatology, Health Care Management, e-learning and ICT in Health Sciences). Research Project Coordinator at the University Hospital (2012-2015).

Cardiovascular scientist and clinician: Research advancements in the field of clinical ultrasound (Lung, Liver and Kidney) and echocardiography, NAFLD relationship with nutrition, obesity, renal and heart disease; innovative contribution in the field of human adipogenic adenoviruses ADV36 and ADV37.

Expert Evaluator to the European Research Commission, Marie Curie (1992-until now), REA and in other Calls.

Member of the Board of EMA (European Medical Association, Brussels) https://emanet.org/ and EMA Director for Media, e-learning and e-medicine at EMA. Full Member of the American Society of Biochemistry & Molecular Biology (ASBMB) & of SIMI, and of the Italian Internal & Emergency Medicine Society. Projects within EMA: Emerging Technology, E-Health; Environment, Quality of Life and Smart Cities Sustainability and Development; Research Planning, Implementation, Dissemination and Assessment; EMA's task force for assuring integrity in research and in peer-review, related with guidelines and recommendations; development of debunking strategies.

See also:

http://archivio.medicina.unict.it/Public/Uploads/links/CV%20%20GM%20TROVATO.pdf

https://www.linkedin.com/in/guglielmo-m-trovato-md-european-medical-association-29369244/

https://www.researchgate.net/profile/Guglielmo_Trovato

https://www.ncbi.nlm.nih.gov/pubmed/?term=trovato+g+catania

Dr. Matteo RUSSO (M) is a young scholar and scientist; BSE Bachelor of Science and Engineering degree in Computer Science from Princeton University, with Certificates in Applied and Computational Mathematics, Statistics and Machine Learning and Technology and Policy, graduating with High-Honors. He has strong interests in Theoretical Computer Science and the applications of Mathematical Analysis and Information Theory to Theoretical Machine and Deep Learning. Projects: a.Credible, Truthful, Optimal and Bounded-Round Mechanisms through Commitment Schemes; b. Exploiting Mean-Based Bidders in Symmetric Settings; c. Robust OOD Detection in Secure Open-World Learning. Machine Learning Intern at NASA GSFC (Jun 2019 – Aug 2019), working on Tweet Stream Anomaly Detection for GPM Data, that is implementing an end-to-end Twitter and Satellite data collection procedure, while investigating and implementing GAN techniques to create an homogeneous map in regions that lack tweets and, eventually, developing probabilistic anomaly detectors to compare robustly satellite data with Twitter stream data. Undergraduate Research Assistant at the Imperial College London (Jun 2018 – Aug 2018), working on the Adversarial Machine Learning (this area concerns itself with both attack techniques against machine learning algorithms, whether it is to evade them at test time or poison them during training and with techniques that enable to improve the robustness of the algorithms to such attacks). Design and implementation of efficient poisoning and evasion attack strategies against deep learning algorithms, and, in particular, in the use of Generative Adversarial Networks to craft and defend from stealthy poisoning attacks; the development of a library of attacks implemented in TensorFlow, which can allow the efficient evaluation of these attacks using GPUs. Teaching Assistant at Princeton University Computer Science (Jan 2018 – Jan 2019) for COS 226 (Algorithms and Data Structures), COS 217 (Introduction to Programming Systems), COS 126 (General Computer Science).

Dr. Daniele ARCES (M): MBBS, MD, AFICM, Associate Fellow of Royal College of Anaesthetist. Specialist in Anaesthesia, Intensive Care and Pain management (School of Medicine, University of Turin Italy). Member of European Society Intensive Care Medicine (ESICM). Member of the Italian College of Physicians. Member of Ordre des Médecins Bruxelles - Brabant Wallon (Belgium). Permanent Staff doctor in Intensive Care and Anaesthesia within the Intensive Care Dept, Hôpitaux Iris Sud. Employment

in United Kingdom post Certificate of Completion of Training (specialization in Intensive Care, Anesthesia and Pain

Relevant publications:

Golubnitschaja O, Topolcan O, Kucera R, **Costigliola V**; EPMA. 10th Anniversary of the European Association for Predictive, Preventive and Personalised (3P) Medicine - EPMA World Congress Supplement 2020. EPMA J. 2020 Aug 19;11(Suppl 1):1-133.

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Golubnitschaja O, Kinkorova J, **Costigliola V.** Predictive, Preventive and Personalised Medicine as the hardcore of 'Horizon 2020': EPMA position paper.EPMA J. 2014 Apr 7;5(1):6.

Golubnitschaja O, Watson ID, Topic E, Sandberg S, Ferrari M, **Costigliola V**. Position paper of the EPMA and EFLM: a global vision of the consolidated promotion of an integrative medical approach to advance health care. EPMA J. 2013 May 10;4(1):12.

Costigliola V. Healthcare overview: global process of personalization in medicine. EPMA J. 2010 Dec;1(4):525-8.

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Buckley AJ, Thomas EL, Lessan N, Trovato FM, **Trovato GM**, Taylor-Robinson SD. Non-alcoholic fatty liver disease: Relationship with cardiovascular risk markersand clinical endpoints. Diabetes Res Clin Pract. 2018 Oct;144:144-152.

Sperandeo M, **Trovato GM**. Lung ultrasound early detection and monitoring in COVID-19 pneumonia: fact and fiction. QJM. 2020 Aug 1;113(8):601-602.

Trovato GM. Arterial Blood Pressure and Lifestyle Variability: In Quest of a Comprehensive Approach. Am J Hypertens. 2017 Jul 1;30(7):655-657.

Trovato GM, Tamura K. The lesson of ankle-brachial index for long-term clinical outcomes: Time is not a line, but a series of now-points. Atherosclerosis. 2016 Jul;250:186-8.

Trovato GM, Sperandeo M. Objectively Measuring the Ghost in the Machine:B-Lines as Uncertain Measures on Which to Base Clinical Assessment. JACC Cardiovasc Imaging. 2015 Dec;8(12):1470.

Trovato GM, Catalano D, Sperandeo M. Top or Flop: The Need to Improve Knowledge and Skills Achieved by Ultrasound Medical Curricula. Acad Med. 2015 Jul;90(7):839-40.

Trovato GM, Catalano D, Sperandeo M, Graziano P. Artifacts, Noise and Interference: Much Ado about Ultrasound. Respiration. 2015;90(1):85.

Trovato GM. Simplicity is the ultimate sophistication. PR electrocardiographic intervals for smart forecasting of decline in renal function. Atherosclerosis. 2015 Jun;240(2):550-1.

Trovato GM. Sustainable medical research by effective and comprehensive medical skills: overcoming the frontiers by predictive, preventive and personalized medicine. EPMA J. 2014 Aug 27;5(1):14.

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Trovato GM. Behavior, nutrition and lifestyle in a comprehensive health and disease paradigm: skills and knowledge for a predictive, preventive and personalized medicine. EPMA J. 2012 Mar 22;3(1):8.

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4.1.4. AFL: Autonio Foundation Limited

Partner profile:

Autonio Foundation is a UK-based non-profit organization established in December 2018 with the vision To build a prosperous community around AI, Blockchain & algorithmic trading.

Autonio Foundation was founded on the belief that professional quality financial tools should be democratized and accessible.

Autonio Foundation as a tech R&D firm is experienced in developing decentralized financial trading tools and infrastructure. The organization previously worked on developing decentralized applications based on Ethereum, EOS, BitShares, and IPFS based biometric authentication solutions.

The team has years of product designing, prototyping, 3d printing and manufacturing experience having previously developed a number of wearable IoT devices powered by a decentralized network. It's relevant to note that the team has worked on manufacturing medical devices in the past as well as software solutions for decentralized applications. The manufacturing activities of the company are basically handled by its affiliate company, Trimark Health Ltd, Xian, China.

The company has a wide product development and manufacturing range and has successfully monitored the product development activities. The details of some of them are given below:

1. RIDO - Bikeshare 4.0 - Dockless But Not Stationless:

RIDO aims to bring some order to the chaotic helter-skelter of dockless bikeshare. RIDO is a green tech for sustainable cities that combines the appeal of dockless bikeshare, but eliminates the chaos of stationless helter-skelter by using blockchain & AI to automate the entire process into a low cost, safe, secure, convenient & ubiquitous infrastructure.

RIDO is a system, apparatus and infrastructure for a network of smart, geo-fenced, dock-less, autonomous, virtual ride sharing stations (VRS) in real world geo-territorial spaces comprising at least three nodes, viz. a smartphone user node, a GPS, GPRS, radiofrequency equipped vehicle node, and a geo-fenced VRS node for vehicle pick-up and drop-off, each of the nodes authenticated to the system by their corresponding cryptographic identities for facilitating the process of locating one or more vehicles parked in one or more pick-up VRS nodes by means of a GPS-enabled application on the smartphone user node, wirelessly unlocking the vehicle, commuting from a pick-up VRS to a drop-off VRS, manually locking the vehicle at the drop-off VRS, and consummating the smart rental contract with payment of the rental fee by the user node to the system administrator node.

Main task

AFL will lead WP4 in general and tasks specific to manufacturing of wearable devices through its affiliate company, Trimark Health Ltd, Xian, China. Moreover, AFL's expertise in blockchain / DLT will be deployed in WP3 for building CLINTOS' DLT testnet.

Key Personnel assigned to the project:

***Adlin Ho (F)*:** Adlin Ho is a young scholar motivated by excelling in everything she is involved with. Her passion and hard work throughout the years has resulted in an impeccable academic and professional record. With keen interest in medicine, public health and entrepreneurship she has come out on top in each field. As an entrepreneur she co-founded Trimark Technologies, a technology consulting & project management firm based in Xi'an. The business has generated over $500,000 since its inception in 2018. She also co-founded Trimark Health, a subsidiary of Trimark Technologies, building software and hardware solutions to tackle lifestyle diseases.

Her management and communication skills have contributed significantly in the growth of all her ventures. Apart from growing success and fame, Adlin Ho also won the most prestigious award considered as a national title "Outstanding International Student and Achiever of The Year-2019". As a clinical medicine student, her academic record is impeccable being the first student to win a provincial award for excellence four times in a row. Having a proven track record from an early age along with an undying passion for excellence, Adlin is on track to be one of the young upcoming female leaders of the world.

***Ali Raheman (M*)**: Inherited a passion for science, medicine, invention and acquired a taste for entrepreneurship and product designing. He began working on my craft at 15 years of age exploring different vocations and skills like content writing, designing, video editing, 3D modeling & animation, android app development. Every summer since then was spent working on a project tackling a problem that mattered most at the time. This led to the creation of a dozen projects which enriched him with priceless experience of success, failure and management skills. Having bootstrapped his businesses, he worked in practically every role and department within an organization gaining invaluable experience and understanding. He discovered his strengths in product designing, backend/front end development, management, R&D & sales.

- Being a medical professional himself, he has affiliations with many innovations and technologies in Healthcare and Wellness.
- The focus of his projects were in different fields such as Healthcare, blockchain, AI, AR/VR, Autonomous mobility, Decentralized finance and more.
- Was granted his first patent at age 17 on virtual teleportation.
- Co-founded Trimark Technologies, a technology consulting & project management firm based in Xi'an. The business has generated over $400,000 since its inception in 2018.
- Trimark Health, a subsidiary of Trimark Technologies, building software and hardware solutions to tackle lifestyle diseases and has wider manufacturing experience specifically in Iot devices.

- Co-founded Autonio Foundation, a non-profit software company based in the UK, democratizing access to AI-powered trading tools and infrastructure.

Ikram Ansari (M): He completed his degree of Bachelor of Engineering (B.E.) (Electrical), from Northwestern Polytechnical University in 2017 and is currently pursuing Masters in Chang'an University. He is a young ambitious individual who has been involved with startups at early stages leading them to success alongside his team. Over the course of the last 5 years, Ikram and his team launched many decentralized applications and services for startups and 3rd party clients. During this course the projects he was involved with saw exponential growth and success. Having managed projects worth over a million dollars his expertise in development and operations management resulted in great success for the organizations he has been involved with.

- Co-founded Trimark Technologies, a technology consulting & project management firm based in Xi'an. The business has generated over $500,000 since its inception in 2018.

- Co-founded Trimark Health, a subsidiary of Trimark Technologies, building software and hardware solution to tackle lifestyle diseases
- Was part of the team that led Autonio Foundation to $50 Million+ market cap in 2017-18

Rahul Pipaliya (M): Rahul Pipaliya is the chief developer at Autonio Foundation and Trimark Technologies and is responsible for development and architecting all decentralized applications and frameworks. Since 2016 Rahul has worked with his team at Autonio Foundation and Trimark Technologies to launch several successful products with thousands of users of these products. He is experienced in Cryptography, decentralized network frameworks and distributed ledger technology.

Rahul completed his bachelor of engineering in computer science in 2017 and is currently pursuing his masters in cybersecurity. His skills and areas of expertise include - web designing, backend development, Node.js, react.js, react native, angularJs, API development, cryptocurrency, blockchain and more.

Relevant projects:

Decentralized Trading Infrastructure:

Autonio Foundation has developed a decentralized Ethereum blockchain based exchange as part of its NIOX Suite. The decentralized exchange is based on 0x protocols smart contracts enabling truly transparent, peer-to-peer exchange of financial assets.

UBI Technology - Universal Biometric Identification Network based on Interplanatary file system

The founding team developed UBI technology; a biometrical authentication system and protocol enabling users to biometrically secure their financial assets. This protocol utilized IPFS and EOS blockchain to enable biometric authentication on a decentralized network. The system was utilized as the core technology in https://ubuckpay.com/

- collapsed structures and advanced wearables for risk assessment and first responders safety in SAR operations

4.1.5. OT: Ozanteks Tekstil

Partner profile

OZANTEKS started to produce coverlets, tablecloths and bedspreads and has now been continuing its operations and developing with the production of towels, bathrobes, bed linen, bed linings, cushions, quilt and sleep sets, bedspreads, coverlet and underwear.OZANTEKS is one of the pioneering industry leaders

in Turkey with more than 2000 employees, It has been developing under the management of Ozan KATRANCI, General Manager by creating the difference with its quality standards. The first export country was England in 1981 and the export was realized with the turnover of 2 million $. By this way, foundations of OZANTEKS was laid in 1995 and since then, one of the biggest 500 enterprises of Turkey has been in the market.

Role in the project:

OT will have active role in clinical trials and will lead the task to manufacture tested t-shirt and test reports to the relevant CLINTOS partners

The main role of Ozanteks will be in WP2, WP3 and WP4. OT will lead designing, development and manufacturing of smart t-shirts which will be home for sensors and other data providing equipment to be made available by the other partners in the consortium. OT will determine technical and user based requirements of t-shirt; convert them into design specifications using the Quality Function Deployment (QFD) approach and multi-criteria decision tools such as Analytic Network Process; carry an extensive theoretical and industrial research to determine and analyze yarn properties (antibacterial, thermo-regulative, conductive, breathable, quick dry, soft-touch etc.); and design alternative t-shirt concepts and knitting processes considering the specs determined. Designers will try different types of knits on different parts of the shirt to provide comfort features. OT will manufacture a required number of t-shirts to optimize knitting, dyeing and finishing processes; evaluate comfort and performance properties by carrying out all necessary QC tests for the t-shirt. In order to optimize the manufacturing parameters Taguchi experimental design and statistical analysis approaches will also be employed. OT will also contribute WP1, WP 5 and WP 6.

Key personnels involved in the project

Mustafa Çörekcioğlu,(M) Industrial Engineer. After completing his bachelor's degree at Sakarya University, he completed his master's degree at Pamukkale University. After specializing in business development in the field of software for about 10 years, he has been working as a quality planning and production manager in the textile industry since 2012. He is also the manager of the R&D center in the textile industry since 2016.

Aslı Özmen Selçuk,(F) Industrial Engineer. After completing her undergraduate degree at Anadolu University in 2015, he is currently continuing her master's degree at Pamukkale University. She has been working as a researcher at the R&D center since 2016. She is an expert in multi-criteria decision making methods in the application of lean manufacturing techniques to the textile industry.

Fatma Filiz Yıldırım,(F) Textile Engineer. She completed his undergraduate and graduate studies at Pamukkale University. Shee is studying for a doctorate at Pamukkale University. After working in the software industry for 5 years, she has been working as a researcher in the textile industry since 2017. Her master thesis was on the dyeability of elastic polyesters. She is an expert in textile finishing, finishing processes, textile weaving technology.

Perinur Koptur Tasan, (F)Chemical Engineer. After completing his undergraduate education at Gazi University in 2015, he is currently continuing his master's degree at Pamukkale University. He has been working as a researcher in the textile industry since 2018. He is an expert in textile finishing and microcapsule applications in textiles.

Sultan Aras Elibüyük, (F)Textile Engineer. She completed his undergraduate and graduate studies at Süleyman Demirel University. After working as a lecturer at Süleyman Demirel University for two years, she started working as a researcher in Ozanteks in 2018. She made her master thesis on tissue decellularization and reconstructing textures with technical textiles. Bioengineering is an expert in technical textiles.

Ahmet Çelik, (M) Textile Engineer. He completed his undergraduate education at Uşak University. He worked as a production engineer in the textile industry for 8 years. He has been working as a researcher at Ozanteks R&D Center since 2019. He is an expert in textile weaving and knitting technology.

Şaban Yumru,(M) Chemist. He completed his undergraduate education at Pamukkale University. He has been working as a chemist in the dyeing process in the textile industry since 2001. He has been working as a researcher at Ozanteks R&D Center since 2017. He is an expert in textile finishing, application of textile tests.

Relevant Publications

1.Çörekçioğlu M., Kundakçi O. E., Akkaya H., Ercan E., Özmen Selçuk A., Prof. Dr. Güngör A. "Reliability Determination of Critical Weaving Machine in a Textile Plant", 9th International Maintenance Technologies Congress and Exhibition Proceedings, 2018,
2.Çörekçioğlu M., Erdoğan A., Özmen Selçuk A., Prof. Dr. Güngör A "Effective Management of Incidental Maintenance Activities in a Textile Business with Software Applications", 9th International Maintenance Technologies Congress and Exhibition Proceedings, 2017, p. 63-69.
3.Fatma Filiz Yıldırım, Şaban Yumru, Perinur Koptur, Sultan Aras, Ezgi Çetin Kılıç, Mustafa Çörekcioğlu, "Low temperature dyeing of polyester seamless fabrics with different molecular size dyestuffs",2. International Congress of Innovative Textile-IconTex, 2019.
4.Esra Gelgeç, F.Filiz Yıldırım, Şaban Yumru, Mustafa Çörekcioğlu, Improving The Flame Retardant Properties Of Cotton Fabrics With Boron Compounds, 1st International University Industry Cooperation, R&D and Innovation congress, 18-19 December, 2017

Relevant Projects

1.17su01 - Desıgn T.C. Mınıstry Of Trade Developıng Busıness Product Desıgn Processes Wıth An Innovatıve Approach 01.03.2017 31.05.2020
2.17u02 / 3171008 - Developıng Innovatıve Swımwear In Swımwear Tubıtak Seamless Machınes 01.04.2017 30.04.2020
3.17sy01 / 3170871 Mapgi Tübitak Mapgi: Key Performance Indicators Mobile Monitoring Soft
4.18u03 - Fdm T.C. Mınıstry Of Industry And Technology Developıng Thermal Regulatıon Products Usıng Phase-Changıng Materıals 01.10.2018 30.09.2019ware 01.07.2017 31.08.2020

4.1.6. SST: Stelar Security Technology Law Research UG (haftungsbeschränkt)

Partner profile

Stelar Security Technology Law Research UG (haftungsbeschränkt) is an organisation established in Hamburg (Germany) that aims to promote education and research through the implementation of research projects and scientific courses and the award of research contracts. In particular, the organisation is specialised in the "privacy by design" approach to new security technologies and other ICT. STELAR was founded as a spin-off of an integrated project funded by the German Federal Ministry of Education and Science within its Framework Programme Research for Civil Security. STELAR's main researcher developed proposals for methodologies on privacy by design for the EC first on the occasion of the draft GDPR that aimed to set up a technical committee on data protection by design (Article 23(4) COM(2012)11 final). The efforts of legal scholars to incorporate the law into technology and the lack of development of privacy by design in the EC's policymaking led the researcher to create his own organisation.

STELAR has extensive expertise in research on legislation, GDPR, data protection, privacy and fundamental rights management in European innovation projects and research projects on ICT and digital transformation (leadership in H2020 OPERANDO (DS-01-2014), SHiELD (DS-03-2016), DeepHealth (ICT-11-2018), PANACEA (SU-DTS-02-2018), PHArA-ON (DT-TDS-01-2019), FP7 eWALL (ICT-2013.5.1)) as well as the experience of its main researcher with the European consumer organisation for technical standardisation (ANEC) and the European Standardization Organizations CEN, CENELEC and ETSI and the International Standardization Organization ISO concerning security, data protection, privacy and eHealth standardisation.

Main tasks

In this project SST will lead the analysis and coordination of legal aspects and regulation concerning data protection and privacy by design. Moreover, SST will contribute to the requirements definition, technical platform development and the pilot preparation. SST's main task will be to carry out legal research on personal data protection and privacy.

Key personnel involved in the project

Matthias Pocs, LL.M. (Male) is a researcher specialised in the legal approach of privacy and data protection by design. He is a work-package leader in H2020 projects OPERANDO (DS-01-2014 'Privacy'), SHiELD (DS-03-2016 on secure health data) and PHArA-ON (DT-TDS-01-2019 on AHA), and tasks leader in H2020 projects DeepHealth (ICT-11-2018 on supercomputing) and PANACEA (SU-DTS-02-2018 on security/privacy in hospitals) and FP7 project eWALL (ICT-2013.5.1 on active ageing).

Apart from that, he participates in standards bodies as a chair of CEN/TC 251/WG I (www.ehealth-standards.eu), as a member of ETSI/TC CYBER and as a partner of both CEN-CENELEC/JTC 8 and ISO/TC 215/WG 4, liaison officer of CEN/TC 391 and member of the DIN mirror group for CEN-CENELEC/JTC 13 concerning data protection, privacy, eHealth, societal security and cybersecurity. He is project leader of ISO/AWI 22697 on privacy management in health data and the CEN/TC 251 standing

document on GDPR and action proposer of the EU 2018 Rolling Plan on ICT Standardisation concerning data protection by design in eHealth products and services.

He represents ANEC The European Consumer Voice in Standardisation, where he contributed to the European Commission Decision concerning a privacy management system for security industry (M/530). As data protection expert, he also represents the German DIN Consumer Council. He is an expert of the ENISA study group on privacy standards gap analysis and IT system supporting the cybersecurity certification framework as well as Frontex, JRC and FP7-SEC FastPass project.

Before that, he worked at a German legal research centre with a track record in data protection legislation, a European institution (European Data Protection Supervisor), the Cyberspace Law and Policy Centre in Sydney. He wrote numerous peer-reviewed publications, after legal studies in Hamburg (Business law), Scotland (European business law), and Oslo/Hanover (LL.M. ICT law including data protection law).

Ricardo Morte Ferrer, LL.M. (Male) is a Lawyer, Data Protection, IT-Security Consultant (Lead Auditor ISO 27001) and PhD Candidate at the University of Granada. He holds a Master in Law (UdL) and a Master in Information and Knowledge Society (UOC). He is a member of the board at LI²FE (Laboratorio de Investigación e Intervención Filosófica y Ética), of the German Working Group for the Standard Data Protection Modell (SDM) and of the Working Group Digitalization and Health at the German Academy for Ethics in the Medicine (AEM) where he is the head of the subgroup Data Protection, Data Security and New Technologies.

Dimitrios Tsolovos, M.Sc. (Male) is a researcher specialised in data privacy. He has worked on at Inria in France conducting research on privacy-preserving crowd-sensing systems. During his research he has proposed novel privacy properties for managing user data and enforcing user consent, while enabling rich computations. He has also proposed solutions for achieving these privacy properties using Trusted Execution Environments. Prior to that, Dimitrios did his Master's studies at the University of Patras. In parallel with his Master's studies he worked on the H2020 project Privacy Flag.

George Kolostoumpis, Ph.D. (Male) holds a B.Sc. as Software Engineer from the University of Manchester and a Master Degree (M.Sc.) in Business Systems Analysis and Design from the City University of London. He has completed his Ph.D. at City University of London in the area of medical informatics. He is experienced combining his knowledge with privacy concerns, legal principles and ethics.

Relevant publications, products, services or other achievements relevant to the call

1. Matthias Pocs "Will the European Commission be able to standardise legal technology design without a legal method?" Computer Law & Security Review 28 (2012) 641-650, overview of publications at www.matthiaspocs.de

2. Head of delegation to CEN-CENELEC/JTC 8 (Matthias Pocs), ANEC The European consumer voice in standardisation, draft opinion for European Commission Standardisation Request M/530 to the European Standardization Organizations to develop a European Standard (EN) on privacy and data protection by design for the security industry (http:// ec.europa.eu/growth/tools-databases/mandates/index.cfm?fuseaction=refSearch.search#), ANEC-ICT-2014-G-020final.

3. CEN-CLC/CWA 17147:2017 (security certification including privacy evaluation), Guidelines for the evaluation of installed security systems, based on the STEFi dimensions, developed under active participation of ANEC Representative Matthias Pocs.

4. Project leader of ISO/AWI 22697 Working draft of International Standard on privacy management in personal health information (Matthias Pocs), ISO/TC 215/WG 4 Safety, security, privacy, April 2017 Hangzhou (China) and subsequent meetings.

5. Matthias Pocs, policy recommendation for EU 2018 Rolling Plan on ICT Standardisation, eHealth section, addition of action on European Commission Standardisation Request concerning 'Data protection by design' in eHealth products and services.

Relevant Projects

PHArA-ON. H2020 research project "PHArA-ON - Pilots for Healthy and Active Ageing" (857188), DT-TDS-01-2019, 2019–2023, ca. 22 M€, STELAR leads work package on legal, ethical, data protection and cybersecurity

DeepHealth. H2020 innovation project "DeepHealth - Deep-Learning and HPC to Boost Biomedical Applications for Health" (825111), ICT-11-2018-2019, ca. 13 M€, STELAR leads legal, privacy, data protection and ethical tasks

PANACEA. H2020 research and innovation project "PANACEA - Protection and privAcy of hospital and health iNfrastructures with smArt Cyber sEcurity and cyber threat toolkit for dAta and people" (826293), SU-TDS-02-2018, ca. 5 M€, STELAR leads legal, privacy, data protection and ethical tasks

SHiELD. H2020 research and innovation project "SHiELD - European Security in Health Data Exchange" (727301), DS-03-2016, 2017-2019, ca. 4 M€, http://www.project-shield.eu/, STELAR leads legal work package

OPERANDO. H2020 innovation project "OPERANDO - Online Privacy Enforcement, Rights Assurance and Optimization" (653253), DS-01-2014 'Privacy', 2015–2018, ca. 4.5 M€, http://www.operando.eu, STELAR leads legal work package

4.1.7. ISS: Innovation Sprint SPRL

Partner profile:

Innovation Sprint Sprl offers edge technology solutions to the eHealth and Life Sciences business sectors, focusing on Big Data analytics & Artificial Intelligence on Real World Data (RWD). Innovation Sprint has a multidisciplinary team with expertise in IT solutions, Data Science, eHealth and Clinical Research, with more than 20y of experience in Healthcare domain and a strong research background with more than 500+ peer-reviewed papers, 35.000+ research citations. The company's main product, Healthentia, is an eClinical platform that supports Pharma to achieve cost savings, while obtaining valuable insights during clinical studies to improve design of drugs of higher efficacy. Healthentia captures clinical outcomes from

mobile-, medical- and IoT-devices, using a patient-centric app and offers AI-driven smart services, such as deep behavioural phenotyping, in-silico trials and virtual coaching.

Healthentia is an eClinical platform from Innovation Sprint Sprl that responds to two of the biggest challenges in clinical research: patient retention and data integrity by improving patient experience and communication between stakeholders in the eClinical Market and empowering patient makers to innovate. The product increases data integrity by enabling fusion of clinical and IoT data and patient retention by enhancing patient motivation with tools and rich insights to monitor, communicate and improve their health, with a gamified return for their contribution. Healthentia is a (CE-marked) Class I Medical Device observing ISO 9001:2015 Certification, ISO/IEC 27001:2013 Certification and featuring GDPR compliance based on BS10012 standard.

Main tasks

ISS's main task is the integration of our eCLinical platform Healthentia in all three CTs. This will facilitate data collection for modelling of patients and attempting biomarker discovery that predicts achievement or not of any defined significant clinical outcome.

Key personnels involved in the project

Dr. Aristodemos Pnevmatikakis (Male) is the R&D Director of Innovation Sprint. He has 25 years of experience in signal processing and machine learning. His prime research interest is in intelligent systems that observe, understand and assist. To this extent he analyses signals from diverse sensors. He is co-author of the books Audio-Visual Person Tracking: A Practical Approach and Delta-Sigma Modulators, Modeling, Design and Applications (Imperial College Press, London, UK, 2011 and 2003). His research has resulted to a series of scientific publications and has been featured on regional and international media and events, while the resulting systems have been successfully evaluated at international evaluation campaigns. He has been involved in numerous research (EU & national) and industrial projects. He received his BSc in Physics from University of Patras, Greece in 1993 and his MSc and PhD from Imperial College, University of London in 1995 and 1999 respectively. Since February 2019 he is with Innovation Sprint and since January 2020 he is a part time instructor at American College of Greece. He has been heading the Multimodal Signal Analytics group of Athens Information Technology (2003-2020), an instructor at Athens Tech College (2016-2019), technical advisor to MoodMe (2016-2018), Chief Technical Officer at Dynasense PC (2014-2015), with the Development Programs Dept. of Intracom Telecom (2001-2003) and with the Analogue and RF Design Group of Integrated Systems Development (1999-2001).

Dr. Sofoklis Kyriazakos (Male) graduated Athens College in 1993 and obtained his Master's degree in Electrical Engineering and Telecommunications in RWTH Aachen, Germany in 1999. Then he moved to the National Technical University of Athens, where he obtained his Ph.D. in ICT systems in 2003 and an MBA degree in Techno-economic systems. Sofoklis holds the position of Associate Professor in the University of Aarhus in Denmark, where his activities are focused around Innovation Management and Entrepreneurship in the eHealth domain. He has managed, both as technical manager and coordinator, a large number of multi-million ICT projects, both at R&D and industrial level. Sofoklis has published

more than 100 publications in international conferences, journals, books and standardization bodies and has more than 400 citations. In 2006 Sofoklis founded Converge SA, an ICT startup with specialization in software integration. In 2016, after having steered successfully the company from the position of Managing Director, he resigned to co-found Innovation Sprint Sprl, a company in the eClinical sector, where he is currently the CEO. Sofoklis has served as member of Board of Directors in several companies in 3 countries and has also been a member of the BoD of Athens Information Technology, a Center of Excellence for Research and Education.

Dr. Alfredo Cesario (Male) is the Chief Scientific Officer of Innovation Sprint (BIO). He has worked in the European Commission in Brussels and he has been a senior consultant to the Directorate General for Research of the Italian Ministry of Health for international activities. Alfredo is also an active researcher and active clinical researcher (H-index=30; > 215 publications; global I.F. > 630); member of the Board of the European Forum for Good Clinical Practice (www.efgcp.eu); expert in international research matters (advisor to the Director General for Research of the Italian Ministry of Health (delegate into the General Assembly of the JPI More Years Better Lives, WP leader "Dissemination", CSA "J-AGE" in support to the JPI MYBL; WP leader "Stakeholders' Dialogue Platform", CSA "PerMed"; member of the FP7 Health Configuration Program Committee; Seconded National Expert in the Directorate General for Research of the European Commission (2005-09) with duties as desk officer for Directive 20/2001 and liaison officer with DG ENTR – DG SANCO and the EMA. Role: contribution to communication to the EC and discussions on systems medicine and valorisation approaches in the different WPs; liaison with other WPs; assists in Dialogue Platform coordination. Communication and Outreach Officer of EASyM.

Prof. Dr. Ir. Hermie J. Hermens (Male) did his masters in biomedical engineering at the University of Twente and became head of the research group of the Roessingh Re-habilitation Centre. In 1990 he was co-founder of Roessingh Research and Development, now the largest research institute in the Netherlands in the area of rehabilitation technology and Telemedicine. He did his PhD in surface Electromyography and became in 2001 Professor in Biomedical Engineering, specialized in human motor control and in 2010 professor in Tele-medicine. Currently, he supervises 15 Ph.D. students; over 20 PhD students finished under his (co)supervision. He is (co)-author of over 300 peer reviewed scientific journal publications and his work was cited over 13000 times (H-index 51). Additional professional functions include: Editor in chief of the Journal of Back and Musculoskeletal Rehabilitation, Past-President and fellow of the int. Society of Electromyography and Kinesiology. The research focus of Hermens is the creation of innovative health care services by combining biomedical engineering with ICT. He coordinated 3 European projects (Seniam, Crest and Impulse (award successful project)) and participated in over 25 other European projects as key partner. He is strongly involved in many E-Health and Personalised Health related projects, especially at European level (recent: eWall, Perssilaa, In-Life, Deci, Mobiguide, IMI-Sprint).

Dr. John Soldatos, PhD, (Male) (born in Athens, Greece in 1973) is partner and Chief Scientific Officer in Innovation Sprint for IT solutions. He is also working for INTRASOFT in the scope of the incorporation of his IoT group in INTRASOFT International. Dr. Soldatos has had an active role (WP-leader, technical manager, project manager) in more than 25 EC co-funded research projects in the scope of the ACTS, ESPRIT, FP5-IST, FP6-ICT, FP7, ICT-PSP and Horizon 2020 programmes. Dr. Soldatos has also considerable experience (senior developer, IT systems architect, team leader, technical project manager) in several enterprise IT projects, where he worked for leading enterprises (INTRACOM S.A,

IBM Hellas S.A, PEGASUS S.A, OTE S.A, TEMAGON S.A). Dr. Soldatos is the co-founder of the AspireRFID Open Source project (http://wiki.aspire.ow2.org/) and of the award-winner OpenIoT project (openiot.eu) (voted/named one of the top ten open source projects of 2013 by Back Duck). He has currently a leading role in the H2020 SecureIoT project as WP leader and member of the Technical Management Board of the project. He has been involved in several large-scale industry projects (both public and private sector) as a principal IT consultant. As a result of his research activities he has co-authored more than 180 papers published in international journals and conference proceedings, while he has also co-edited two books and two journal special issues. His current research interests are in Industrial Internet of Things, Cloud Computing and Artificial Intelligence. He has been co-editor and co-author of five books dealing with Internet of Things Analytics and Internet of Things security.

Relevant Publications

1. S. Kyriazakos, A. Cesario, et al., E-health and Personalised Radiation Oncology: Cloud technologies and advanced sensing, Elsevier, Clinical and Translational Radiation Oncology, Vol. 123, 21.11.2017.
2. S. Kyriazakos, A. Pnevmatikakis et al. eWALL: An Open-Source Cloud-based eHealth Platform for creating Home Caring Environments for Older Adults living with Chronic Diseases or Frailty, Springer, Wireless Personal Communications, 08.2017, p. 1-41.
3. Cesario A, et al., A Systems Medicine Clinical Platform for the Understanding and Management of Chronic Diseases. Curr Pharm Des. 2014, 20: 5945-5956.
4. A. Pnevmatikakis, "Recognising Daily Functioning Activities in Smart Homes," Wireless Personal Communications, vol. 96, no. 3, pp 3639–3654, Springer, Oct. 2017.
5. A. Pnevmatikakis, F. Talantzis, J. Soldatos and L. Polymenakos, 'Robust Multimodal Audio-Visual Processing for Advanced Context Awareness in Smart Spaces', Personal and Ubiquitous Computing, Vol. 13, No. 1, pp. 3-14(12), Jan. 2009.

Relevant Projects

1. COUCH (Council of Coaches, EC/H2020/PM-15, http://council-of-coaches.eu/). Provide an autonomous virtual council of coaches assisting people to achieve their health goals.
2. vCare (Virtual Coaching activities for rehabilitation in elderly, EC/H2020/PM-15, http://www.vcare-project.eu/). Provide smart, highly adaptable personalised coaching, in accordance with the clinical pathway of patients.
3. CO-ADAPT (Human and Work Adaptation Support to ageing citizen, H2020-SC1-DTH-03-2018, https://coadapt-project.eu/). Build a platform supporting the ageing workforce.
4. GOAL (Games Of Active Life, H2020-ICT-2016-1, http://www.goal-h2020.eu/). Provide a platform for games & apps, aiming to motivate a socially and physically active lifestyle.
5. eWALL (E-Wall for Active Long Living, FP7-610658, www.ewallproject.eu). Processing diverse sensors' signals for user context extraction in an e-care home environment, representation of the resulting metadata and reasoning for care recipient's state.

4.1.8. ABI: Abich SRL

Partner profile:

Abich S.r.l. is a SME providing research, analysis and consultancy for the industry, mainly manufacturers of large consumer products (cosmetics, medical devices, textiles and others), drugs and chemicals. Research activities are focused on the development of new biotechnology–based methods to assess the safety and effectiveness of industrial and consumer goods such as chemicals, raw materials, botanicals, cosmetics, medical devices, detergents and textiles. ABICH has developed and implemented many alternative in vitro assays to test the biological properties and safety of products and ingredients for human use since 2002. For this reason, the company received a special innovation prize from the Italian Chamber of Commerce in 2004. ABICH is member of the Eu-Netval laboratory network, based in Ispra at JRC, for the Validation of Alternative Methods. 3 sites are operative in Italy (Verbania and Milan) with 2000 m2 of laboratory surface, one 500 m2 laboratory in Canada (Montreal).

Strong partnership with the Molecular and Cellular Immunology Laboratory of the San Raffaele Hospital in Milan gave also birth to a spin-off service testing company (ALLTOX), setting up innovative testing methods and research projects concerning allergies related to consumer products. ABICH laboratories are equipped with a state-of-the-art molecular biology and cell culture facility, a fully equipped analytical chemistry division, two microbiological laboratory, two clinical and cosmetic testing facilities, a laboratory dedicated to product formulation & development, a regulatory division and a training facility in Milan. ABICH owns a ISO 9001 quality system certified by TUV and operates according to GLP standard certified by the Italian Health Ministry for in vitro toxicity testing. Montreal site is FDA registered for Sunscreen testing (SPF) and GMP approved by Health Canada for OTC testing. The Italian facilities is undergoing the GMP certification process within may 2018 for chemical and microbiological quality control of drugs. Nowadays, the company employs 30 people among technicians and scientific researchers (80% graduated and 80% female) in Italy and 13 employees in Montreal.

Main tasks

Within the project, Abich will leverage all its resources in the field of cosmetics testing and molecular biology as well his experience in the development of protocols for medical devices trials and usability validation. Specifically, Abich will undertake the following actions: (i) study of the device and in its relative classification for the purpose of validating it as a predictive tool in assessing the effectiveness of the response to therapy; (ii) test the use of the device versus classical design cosmetic tests protocols; (iii) validate the device for its use within cosmetic testing and define a protocol.

Key personnels involved in the project

Marco Minoia (M), Coordinator Innovation and Business Development, has 12+years of experience in molecular biology. He holds a M.Sc. in Biotechnology at the University of Milan, and a Ph.D. in molecular biology at the University of Lausanne. He has Postdoc experiences at the Georgia Institute of Technology (USA), Copenhagen University and Tampere university. In 2014 he obtained a M.Sc. in bio-business and administration at the Copenhagen Business School. Since then, he has worked in the biotech

and pharma industry. He was the co-founder of CHARON biotech, the business development manager and deputy CEO of Enantis s.r.o.. He is now coordinator of the R&D, innovation and business development at Abich. He has deep experience in negotiations scenario planning, market forecast, project management, competitor analysis, SWOT and PEST analysis, business plan development, fundraising, IPR analysis, market opportunity assessment and commercial strategy

Renato Colognato (M), Scientific Coordinator, is the cofounder, scientific director and medical laboratory director of different start-upsin the biomedical and digital health space, active in the fields of experimental in vitro/in vivo nano-toxicological, genetical screening and reproductive medicine. He has 15+ years of experience in predictive medicine (longevity and pathologies susceptibility genes), next generation sequencing, nanomedicine (targeted drug/gene delivery) and regenerative medicine (stem cell therapy).

Roberta Cattaneo, (F). Coordinator of the Cosmetic testing unit in Milan since 2004. She holds a degree in Chemistry and Biology with a specialization in laboratory techniques from I.T.S.O.S. State Technical Institute in Milan. She has 30+ years of experience in the field of cosmetics and medical devices, with a specific focus on clinical trials and usability assessment of medical and wellness devices. Her technical expertise span from Rapid Automated Bacterial Impedance Technique, Microbiological control on cosmetics medical devices and raw materials, to Basic Microbiological techniques, Molecular biology, Chemical and Physical QC of formulations and raw materials.

Relevant Publications

1. E. Ripamonti, E. Allifranchini, S. Todeschi and E. Bocchietto. Endocrine Disruption by Mixtures in Topical Consumer Products. Cosmetics 2018, 5, 61; doi:10.3390/cosmetics5040061.
2. M. Detering, E. Steels, S.R. Koyyalamudi, E.Allifranchini, E. Bocchietto, L. Vitetta. Ageratum conyzoides L. inhibits 5-alphareductase gene expression in human prostate cells and reduces symptoms of benign prostatic hypertrophy in otherwise healthy men in a double blind randomized placebo controlled clinical study, Biofactors, 2017, doi 0.1002/biof.1389.
3. E. Bocchietto, A. Guglielmetti, F. Silvagno, G. Taraboletti, G.P. Pescarmona, A. Mantovani and F. Bussolino. Proliferative and migratory responses of murine capillary endothelial cells to granulocyte - colony stimulating factor. 1993. J. Cell Physiol. 155:89-95.
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Relevant Projects

1. Sensitive MeAsuRemenT, detection, and identification of engineered NANOparticles in complex matrice (SMARTNANO), 7TH Framework Programme (grant number: 280779), started the1st of June 2012, ended the 31st May 2016.
2. An advanced biological remedy against jellyfish stings (SOS Jelly), Horizon 2020, Call: H2020-SMEInst- 2016-2017, SME-1 (grant number 728647), started the 25th of May 2016, ended the 21st of November 2016.
3. EPATOCARE (grant number 313-50) concerning identification of non-invasive early biomarker for hepatic fibrosis by means of extracellular vesicles analysis (Piedmont Region POR FESR 2017-2020 Innovation in SME) – starting from October 20th, 2017 to October 20th, 2019. ABICH is Project coordinator.
4. EV-ER (grant number:320-39) engineered nanovesicles as biological drugs (Piedmont Region POR FESR 2017-2020 Health and Wellness Platform) 5 partners; Starting from January 23rd 2018 to July 23rd, 2020.
5. DeFLECT (grant number: 320-41) creation of a biobank of organoids from human lung and of new polymeric lab-on-chip devices to monitor and detect lung tumors (Piedmont Region POR FESR 2017-2020 Health and Wellness Platform) 20 partners; Starting from June 2018 to December 2020

4.1.9. MIA: Mia Teknoloji

MIA Technology has operated in Turkey since 2006, R & D and innovation company. With our increasing experience, we use our unique innovation and R&D activities in order to meet the needs of our customers. We follow certified technology in order to create satisfactory products and services for both government and private based business partners and projects.

As a privately owned company, we as MIA Teknoloji provide the following services:

- Integrated Health Information Management
- Biometrical Identity, Recognition & Control Systems
- Smart And Safe Facility, Building And Campus Solutions
- Public Safety
- Critical Zone & Soft Target Protection
- E-ID Projects
- Payment, Card Solutions & Fintech
- Data Analytics & Big Data Management
- Cyber Security

Our R&D activities: THz Biometrical Access, Analytic CRM, Assure Id, Public Safety Image Processing Projects, Neuro Linguistic Programming NLP, Development of Face Biometrics Based Psychoanalysis Support System, Development of Health Care Tracking Application System with Motion Sensors, Smart Biomedical Cabinet, Biometrically Verified Video Conference System, Depth Analysis for Aircraft and Obstacle Detection with Image Processing.

MIA Technology has ISO 9001, 14001, 18001, 20000 1, 27001, Facility Security Clearance (NATO & NATIONAL), S ISO IEC 15504/SPICE Lvl 2 SOFTWARE DEV., Quality Assurance Department, HIMSS6 EMRAM (Health Information), Approved Supplier of General Directorate of Military Factories, EAL 4+ Assessment Phase quality standards.

COVID-19 Smart Safety Measures :

MIA-ID-100: Multi Biometric Identification System Card Reader

MIA-ID-100B: Multi Biometric Identification System // Card Reader – Finger Print

MIA-ID-100BT: Contactless Fever Measurement Multi Biometric Identification System

MIA-YTAv6: It can measure the body temperature of 6-8 people in 1 second and detect whether they are wearing a mask. Our smart body temperature sensing and analysis system, which gives an alarm when it detects a person who does not wear a mask and/or whose body temperature is above the specified degree, is also capable of generating reports at the end of the day.

CLEANMASK-TECH: Controlled Mask Dispensing & Hand Sterilization Point: Our product, which enables the guests and staff coming to the institution to take their masks and disinfect their hands without contact, also has the feature of working integrated with the personnel tracking and access control system.

MIA BioID H: Fever Measurement, Mask Dispensing and Controlled Access System:

MIA Density Detection: It can count the persons entering and leaving the institution instantaneously and can create an audible alarm to prevent people from entering above the specified number. It can also report human density on an hourly and daily basis.

MIA-Fever Detection Door Detector: It is a suitable solution for all institutions that need high security measures. In addition to detecting the metal on the person with the metal detector, it measures the body temperature of the person without contact with its thermal camera and displays it on the screen. It also generates an alarm when it detects high fever.

MIA-Smart Helmet: It ensures that security personnel can measure the targeted person's fever in the crowded area and detect people with suspected health conditions day / night without contact. In addition, thanks to its license plate and face recognition capability, it has the ability to measure fever and report by matching the plate with the person in the vehicle.

MIA Sterilization Robot: Thanks to its autonomous working ability, it travels in closed areas in accordance with the determined route, avoiding obstacles. After detecting that there are no people inside, it sterilizes the targeted area with UVC rays and Mist.

MIA-Hygiene Door: Our product, which covers a small area with its aesthetic design, is positioned at various points within the institution and allows us to sterilize our clothes in just one second at the points we pass through during the day

MIA-Hygiene Tunnel: It allows us to sterilize our clothes, which we cannot disinfect during the day, through the hygiene tunnel in a few seconds before entering the institution.

MIA-NO-TOUCH+: With NO-TOUCH, you can easily and quickly perform high-precision fever measurements with one button.

Bio Urban: Biourban is an award winning solution all over the world. It captures and destroys carbon dioxide, carbon monoxide and nitric oxide and supplies oxygen instead. BioUrban 1.0 is equivalent to 18 trees. It transforms the indoor space into a spacious open space.

Key Personnel assigned to the project:

Mr. Ali Gökhan Beltekin – Project Manager : Mr.Ali Gökhan Beltekin graduated from Atılım University Computer Engineering Department. Mr.Beltekin was employed at software specialist position in IT sector and he is a co-founder and the CEO of MİA Technology company which provides solutions to a large area of expertise such as Integrated Health Information Management, Biometrical Identity, Recognition & Control Systems, Smart And Safe Facility, Building And Campus Solutions, Public Safety, Critical Zone & Soft Target Protection, E-ID Projects, Payment, Card Solutions & Fintech, Data Analytics & Big Data Management, Cyber Security. He is involved in both academic field research and a variety of scientific R&D projects in Integrated Health Information Management, Facial Recognition Technology , Advanced Analytics and Big Data technologies. Within this framework, he has been conducting studies regarding the development of R&D products.

Mr. Osman Çebin - Software Development Engineer: Mr. Osman Çebin graduated from Gazi University Computer Engineering Department. He has experience in C# , Visual Basic.Net, ASP.NET, Language Integrated Query (LINQ), Entity Framework, Silverlight WCF WCF, Microsoft Silverlight, MS SQL Server, Oracle 10g, MS Access XML, JavaScript, C++, C, Java, HTML, PL/SQL, ASP Adobe Flash, CorelDraw, InDesign, Paint Shop Pro, Painter, Photo Paint, Photoshop, DNS, HTTP, IP, NAT (Network Address Translation) SNMP, TCP/IP, DOS, Linux, Windows Server 2008, Apache HTTP Server, IIS 5.0, IIS 6.0, SMTP (Simple Mail Transfer Protocol) Cisco Routers, LAN (Local Area Network), WAN (Wide Area Network), AutoCAD, DSL (andxDSL Variations), Ethernet Switches, Fiber Optics Firewall, GSM, Remote Access, VoIP, Wireless, FPGA, Wireless applications, Microprocessors, Assembler x86.

Projects: Hospital Information Management System-Director

Mr. Bedrettin Sümer - Software Development Engineer: Mr. Bedrettin Sümer graduated from Eskişehir Osmangazi University Computer Engineering Department. He has experience in .NET Development (with C#, VB.Net programming languages) • ASP.NET Web Forms, ASP.NET MVC , .NET CORE • Restful and SOAP Web Services (Web Services, WCF, ASP.Net MVC Web API services and JSON, XML data types.) • HTML5, JavaScript, Typescript, JQuery, Angular 8, Bootstrap, DevExpress, DevExtreme • Object Oriented Programming, Design Patterns, N-tier architecture • MVVM, MVC Architectural Patterns • Object Relational Mapping Technologies based on .NET (Entity Framework, Linq to SQL) • T-SQL, Microsoft SQL Server, ORACLE DB • Team Foundation Server, GitHub, SVN for source control.

Projects: Healthcare Management System, Hospital appointment system, Pizzy Web, Demand Tracking System, Unlicensed Energy Generation Monitoring.

Mr. Oğuzhan Doğan - Software Test Engineer: Mr. Oğuzhan Doğan graduated from Karadeniz Technical University (KTU) Computer and Teaching Technologies Teaching Department. Mr. Doğan continuing his Computer Engineering master program TOBB University Of Economics and Tech.. He has experience in ASP.NET Web Forms,ASP.NET MVC,.Net Core Web Service,WCF,Web Api AngularJS, Angular, MS SQL Server, PostgreSQL, Entity Framework,Entity Framework Core,Ado.Net JavaScript,jQuery C#, Objective C, Xamarin, Android WebSocket.

Relevant projects:

1-EUROSTARS

E10325 - ASSURE-ID / The development of an Accurate System for the SecUre, Rapid, BiomEtric, verification of IDentity

- Time to completion 30 months
- Total cost for all parts 905,236 €
- Participant:
- Onfido Limited UNITED KINGDOM R&D SME

MIA Technology TURKEY R&D SME

Identity fraud accounts for approximately 50% of all fraud in Europe, affecting 8.2m EU citizens, and costing €20bn. An estimated 20m fake documents are in circulation, including 4m fake IDs, which cost EU business €500bn or 0.4% of GDP p.a. Companies also face a growing need to comply with legislative checks (e.g. right to work, etc) but existing solutions are simply not accurate enough, too slow and too expensive for our target market. There is a large, growing, unmet need for our solution. The ASSURE-ID project will develop the world's fastest, most accurate, reliable and cost effective identity verification system to improve EU security. Our

research will develop sophisticated biometric facial recognition technology, novel image processing algorithms and machine learning techniques. Our platform will increase security and levels of trust, providing industry with enhanced confidence and compliance, especially in the recruitment of lower-skilled, high turnover, high-risk roles.

2-TUBITAK 1501 - Industrial R&D Projects Grant Programme

- Time to completion 23 months
- Total cost: 1.598.558,75 TL
- 3160152-Analytic CRM

In Shopping malls and stores

- Age
- Gender
- Ethnicity
- Frequent Visit Analysis
- Shelf Stand Visit Density
- Emotions
- Ad Suggestion

We provide services with technologies that increase the efficiency and generate semantic data for the shopping sector by producing solutions in the field.

Main Tasks:

MIA will participate in the following tasks;
In the WP3: CLINTOS Proof of concept (POC) T3.1, development of CLINTON'S front backend software, and WP5:Validating & Piloting for first market replication T5.1 planning, monitoring, evaluation of field trials. It will also lead the T5.2 for testing and validation of the plug-n-play interoperability of CLINTOS with third party applications, which includes MIA own in-house hospital information management system.

4.1.10. SBA: SBA Research

Partner profile:

SBA Research is a research centre for Information Security funded partly by the national initiative for COMET Competence Centres for Excellent Technologies. As part of a network of more than 70 companies, 15 Austrian and international universities and research institutions, and many additional international research partners, SBA jointly works on research challenges ranging from organizational to technical security to strengthen Europe’s Cybersecurity capabilities. SBA can look back at multiple important projects on a national and international level, gaining expertise e.g., in IoT and CPS security,

safe components and applications for connected and autonomous vehicles, combinatorial testing, and various cyber crisis support activities focused on risk analysis, which will be the basis for the analysis of the threat landscape relevant for this project. In addition, SBA is a member of the H2020 consortium to interconnect Europe's Cybersecurity capabilities (Concordia).

Main tasks

As a research centre focusing on IT security and privacy, SBA will contribute to the research, design and evaluation of the overall privacy and security aspects.

Key Personnel assigned to the project:

Univ.-Prof. Dr. Edgar Weippl (M) is the scientific director at SBA Research and a professor for Security & Privacy at University of Vienna. His research expertise includes information security and privacy, with a focus on basic and applied research on distributed ledger technologies and the security of production systems, as well as aspects of privacy-preservation. Edgar Weippl will contribute his expertise on security and privacy related aspects.

Ao.univ.Prof. Dr. Andreas Rauber (M) is a Key Researcher at SBA Research, and the head of Information and Software Engineering Group of the Institute of Information Systems Engineering at the Vienna University of Technology. His research expertise covers the broad scope of digital libraries and information spaces, information retrieval and organization, information visualization, as well as data analysis, neural computation and machine learning, as well as data privacy, and secure data analysis.

Rudolf Mayer (M) is a Senior Researcher at SBA Research leading the Machine Learning and Data Management Group, and a Lecturer in Machine Learning at Vienna University of Technology. His research expertise includes data mining and machine learning, as well as information security. He specifically works with privacy-preserving methods for data analysis and machine learning, and security aspects of data analysis and machine learning algorithms.

Relevant projects:

- MyHealth – MyData (EU H2020). MHMD aims at fundamentally changing the way sensitive data is shared and is poised to be the first open biomedical information network centred on the connection between organisations and individuals, encouraging hospitals to start making anonymized data available for open research.
- DEXHELPP (Decision Support for Health Policy and Planning: Methods, Models and Technologies based on Existing Health Care Data) (National project funded by the Austrian Research Promotion Agency, 2015- 2018). The aim of DEXHELPP is the development of new methods, models and technologies to support analysis, planning and control of health care systems. A special focus is put on preserving privacy of individuals, as well as providing secure

analysis environments, including fine-grained and fully controllable information sharing mechanisms

- PIPE (Pseudonymization of Information for Privacy in e-Health) (National project funded by the Austrian Research Promotion Agency)
- Injecting Security Features into Constrained Embedded Firmware (ISaFe) (National project funded by the Austria Research Promotion Agency (FFG)) aims at addressing security issues in embedded systems and will provide automated approaches to implant security features into connected embedded system to counter the lack of security features in the backbone of the IoT.
- FeatureCloud (EU H2020): FeatureCloud's transformative security-by-design concept will minimize the cyber-crime potential and enable first secure cross-border collaborative data mining endeavours. FeatureCloud has two key characteristics: (1) no sensitive data is communicated through any communication channels, and (2) data is not stored in one central point of attack. A key task for SBA Research is in the analysis of novel attack patterns, e.g. in the form of adversarial machine learning, which is facilitated by the distributed nature of the system.
- Automated Device Independent Honeypot Generation of IoT and Industrial IoT Devices) (National project funded by the Austria Research Promotion Agency (FFG)): The project develops a generic honeypot framework that automatically generates tailored honeypots for the (Industrial) Internet of Things. Combining real world device information with virtualization technology, the honeypots are attracting attacks for a wide variety of hardware and software architectures and beyond convince an adversary that she actually breached a real device instead of decoy.

4.1.11. HBI: HeartBalance Innovations GmbH

Partner profile:

HeartBalance Innovations GmbH is a company that has been in existence since 2001. They develop solutions in the area of heart rate variability(HRV) analysis based on scientific research of its founder, Dr. Peter Hauschild, jointly with the Sigmund Freud University in Vienna. Their
working thesis is that a variety of maladies may be detected far in advance - actually before they become full-blown maladies - by changing patterns of the HRV profile. This has potential for both physical and psychological issues. Therefore, collecting data from various health-related sources with the help of the WellFort platform, and comparing this to HRV profiles of participating customers has a huge potential for HeartBalance in terms of verifying and refining their base assumptions. The company is managed by the owner MMag. Dr. Peter Hauschild, who currently owns 99 % of the company shares, while 1% is in the hands of an investor.

HeartBalance currently sets a new focus, shifting from the established customer base (doctors, occupational physicians, therapists, psychologists, coaches, sports trainers) to the consumer market (sports,wellness, health care,...). Thus, a hardware device that collects psychophysiological health data (heart rate variability) and presents them to the individual user or whole families at an affordable price, is currently developed. The integration of the device within a platform such as WellFort would be a significant benefit for both the company and its customers. A major USP of HeartBalance is its solid foundation on scientific research, conducted by Dr. Peter Hauschild and Sigmund Freud University. As this scientific angle will continue to be a major differentiator to potential competitors, the perspective of being able to integrate data with other sources will be a crucial competitive edge, both from a scientific and a marketing perspective.Being able to validate the product via studies that are made possible by the WellFort platform, and by providing individuals with personalised results in relation to these studies will, as well as allowing further integration of the heart rate monitors with other complementary products, will make the product interesting to new customer segments.

Main tasks

As an innovator and researcher in HRV (heart rate variability) HBI will contribute development of HRV as 1 of the 8 vital signs that CLINTOS SmartHub device monitors. HBI will also participate in the development of technical specifications and architecture of the CLINTOS platform.

Key Personnel assigned to the project:

Peter Hauschild is the founder of the partner Heartbalance and as such will contribute in the use case definition, as well as evaluation, exploitation and dissemination activities. In addition, he will contribute his expertise on data analysis. He has gained extensive experience in previous research projects with Heart Balance.

Academical education:
• Studies of Psychology, Sociology and Philosophy at the University Vienna
• Studies of Business Administration at Vienna University of Economics and Business
• Studies of Visual Arts - artwork at the University of Applied Arts Vienna
• Ph.D. Studies of Psychology and Sociology at the University Vienna
• Coaching studies at MOC – Coaching International, Vienna
• Studies in Theoretical Physics with Prof. Dr. Dröscher, Vienna
• Ph.D. Studies at Sigmund Freud Private University, Vienna

Business experience:
• 25 years experience in Business Administration, CEO
• 15 years experience in Business Consultancy, corporate reorganisation, financial restructuring, marketing and controlling
• Management-Coach and management-consultant

• Founder and CEO of HeartBalance Innovations GmbH, technical and commercial development of heart rate variability technologies since 2000
• Formation of the Academy of Chrono-Psychology and Chrono-Medicine
• Invitation to found the Institut for Chrono-Psychology and Chrono-Medicine at Sigmund Freud Private University, Vienna
• University Lector for Chrono-Psychology and Chrono-Medicine readings at Sigmund Freud Private University, Vienna

4.2. Third parties involved in the project (including use of third party resources)

Does the participant plan to subcontract certain tasks (please note that core tasks of the project should not be subcontracted)	Yes, third parties involved
If yes, please describe and justify the tasks to be subcontracted Please see Section 4.3 below for details Special Trials@Home Advisory Board as third party engagement	
Does the participant envisage that part of its work is performed by linked third parties[1]	Yes third parties involved
If yes, please describe the third party, the link of the participant to the third party, and describe and justify the foreseen tasks to be performed by the third party. Please see Section 4.3 below	
Does the participant envisage the use of contributions in kind provided by third parties (Articles 11 and 12 of the General Model Grant Agreement)	No
Does the participant envisage that part of the work is performed by International Partners[2] (Article 14a of the General Model Grant	No third parties involved

Agreement)?	
If yes, please describe the International Partner(s) and their contributions	

[1] A third party that is an affiliated entity or has a legal link to a participant implying a collaboration not limited to the action. (Article 14 of the Model Grant Agreement).

[2] 'International Partner' is any legal entity established in a non-associated third country which is not eligible for funding under Article 10 of the Rules for Participation Regulation No 1290/2013.

Special Trials@Home Advisory Board as Third party involvement

The CLINTOS consortium was originally lead by **CERTH** along with the support of **FHJ** and **MLC**, all three of them are partners in the Trials@Home center for excellence. A late discovery (4 working days before the submission deadline) that the countries of these 3 participants either did not have an agreement with ECSEL (Greece) for co-funding this call or had very restrictive agreement that imposed conditions (Netherlands & Austria) that made their participation as partners virtually impossible. Hence, these 3 Trials@Home partners along with a couple of universities had no option but to pull out of the consortium as partners. However, the CLINTOS consortium has decided to retain their expertise as third party **Special Trials@Home Advisory Board** largely to ensure that this project will *be "timed and tuned to facilitate a close complementary activity between Trials@Home.* Moreover, these T@H partners had played a key role in development of the CLINTOS proposal throughout the process of its' evolution, and hence considered as active contributors to the CLINTOS consortium as a whole. The following table lists the members of this special advisory board:

Special Trials@Home Advisory Board*

No	Advisory Organization name		Country
1	**CERTH: Ethniko Kentro Erevena Kai Technologikis Anapty***	Research Org	Greece
2	**MLC: Stichting MLC Foundation (MLCF)***	Research Org	Netherlands
	FHJ: FH: JOANNEUM Gesellschaft mbH*	University	Austria

*These third party contributors to the CLINTOS consortium are members of the **Trials@Home center of excellence** funded under IMI Joint Undertaking (JU), and were original partners in the CLINTOS consortium but were compelled to pull out at the last moment on discovery of funding limitations imposed by their countries' funding agreement with ECSEL. Their engagement with CLINTOS as advisory board will ensure that this project will be "timed and tuned to facilitate a close complementary activity between Trials@Home[1].

CERTH: Ethniko Kentro Erevena Kai Technologikis Anaptyxis

The Centre for Research and Technology-Hellas (CERTH), founded in 2000, is the only research centre in Northern Greece and one of the largest in the country. CERTH has important scientific and technological achievements in many areas including: Energy, Environment, Industry, Mechatronics, Information & Communication, Transportation & Sustainable Mobility, Health, Agro-biotechnology, Smart farming, Safety & Security, as well as several cross-disciplinary scientific areas. Today CERTH consists of the following five institutes: (a) Chemical Process & Energy Resources Institute (CPERI), (b) Information Technologies Institute (ITI), (c) Hellenic Institute of Transport (HIT), (d) Institute of Applied Biosciences (INAB), (e) Institute for Research and Technology Thessaly (IRETETH). In this proposal CERTH participates through ITI.

CERTH is essentially a self-supported Research Centre generating an average annual turnover of ~€22 Million coming from: (a) >30% from bilateral industrial research contracts, (b) >60% from competitive research projects, (c) <10% as government institutional funding. More than 800 people work at CERTH with the majority being scientists. CERTH has received numerous awards and distinctions such as the European Descartes Prize, the European Research Council (ERC) Advanced Grant, Microsoft International Contest Prize, the Trading Agents Competition Award and many more and is listed among the Top-20 of the EU's Research Centres with the highest participation in FP7 and H2020 competitive research grants. CERTH has participated successfully in more than 1,000 competitive research projects (with a total budget exceeding €423 M and involving more than 1,100 international partner organizations) financed by the European Union (EU), leading industries from USA, Japan and Europe and the Greek Government via the General Secretariat of Research and Technology (GSRT).

Information Technologies Institute (ITI)

The Information Technologies Institute (ITI) of CERTH was founded in 1998 as a non-profit organisation under the auspices of the GSRT, with its head office located in Thessaloniki, Greece. Since 2000 it has been a founding member of the GSRT-supervised CERTH. It is one of the leading Institutions of Greece in the fields of Informatics, Telematics and Telecommunications. It has participated in more than 100 EC H2020 projects, 50 FP7 projects and 100 national projects and subcontracts in different research areas.

[1] ECSEL Joint Undertaking, Work Plan 2020, Version 16, page 16

Only in the last five years, CERTH-ITI researchers have authored more than 200 journal papers, 600 conference papers and 50 book chapters. ITI's areas of research relevant to CLINTOS include social media analysis, Semantic Web, knowledge structures, ontology construction, reasoning and personalization, semantic multimedia analysis, indexing and retrieval, but also big data analysis and visualization for data-driven policy making.

The participating team, namely the **Multimedia Knowledge and Social Media Analytics laboratory (MKLab)**, has significant experience and scientific expertise on the technical aspects of CLINTOS, namely semantic integration of heterogeneous resources, knowledge representation and reasoning, ontology engineering, semantic multimedia analysis, indexing and retrieval, multimedia representation, event detection, distributed architecture design and big data collection, analysis and visualisation but also eHealth applications, clinical trials, large-scale piloting at patient homes or at the CERTH-ITI Smart Home, in use cases such as elders, dementia and MS. In addition, MKLab has significant experience in the development of data services and marketplaces for IoT data and apps. Finally, MKLab also specializes in big data analytics for different domains (smart cities, security, e-health, etc.), efficiently collecting, analysing and visualizing heterogeneous data from various environmental, social and economic data sources (e.g. sensor data including IoT data, social media, economic data from statistical agencies, satellite data, health data etc.). Over the last fifteen years, the MKLab research team has authored over 190 publications in scientific journals, 71 books and book chapters, and over 620 presentations in international conferences. MKLab is currently the coordinator of the H2020 projects: 2020-RIA-MindSpaces, H2020-RIA-CUTLER, H2020-RIA-V4Design, H2020-BeAware, H2020-RIA-MOVING, H2020-Roborder, H2020-IA-aqua3S. In addition, it has or had leading roles in more than 50 H2020 and FP7 projects (e.g. IMI2 RADAR-AD and Trials@Home, H2020 ACTIVAGE and GATEKEEPER), the full record of which can be found at http://mklab.iti.gr/projects.

Main tasks

In this proposal, CERTH contributes its expertise in IoT biomedical and lifestyle data collection, interoperability and analysis as well as best practices and integration from the TECH WP of the Trials@Home project. Specifically, CERTH contributes expertise in intelligent systems to unanimously store, using ontologies, and analyse, using machine learning and knowledge-based techniques over lifestyle and biomedical data. CERTH brings expertise from applications of the aforementioned techniques in existing large-scale pilots and clinical trials.

Key Personnel assigned to the project:

Dr. Ioannis (Yiannis) Kompatsiaris (M): is a Researcher Director at CERTH-ITI, the Head of Multimedia Knowledge and Social Media Analytics Laboratory and Deputy Director of the Institute. His research interests include multimedia, big data and social media analytics, semantics, human computer interfaces (AR and BCI), eHealth, security and culture applications. He is the co-author of 129 papers in refereed journals, 46 book chapters, 8 patents and more than 420 papers in international conferences. Since 2001, Dr. Kompatsiaris has participated in 59 National and European research programs including direct collaboration with industry, in 15 of which he has been the Project Coordinator and in 41 the Principal Investigator. He is co-editor of the books "Semantic Multimedia and Ontologies: Theory and Applications" and "TV Content Analysis: Techniques and Applications", the guest editor of eight special

issues, including “Social Media as Sensors” in IEEE Transactions on Multimedia and he has served as a program committee member and regular reviewer for a number of international journals and conferences. He has been the co-organizer of various conferences and workshops, such as the MMM 2019, IEEE IVMSP 2018, ACM CIVR 2009, WIAMIS 2007 and SSMS 2012 and he was a program co-chair for ACM MM 2016. He is a Senior Member of IEEE and member of ACM.

FHJ: FH Joanneum Gesellschaft

FH JOANNEUM Gesellschaft mbH is located in Steiermark, Austria and is part of the Colleges & Universities Industry. FH JOANNEUM Gesellschaft mbH has employees across all of its locations. There are 359 companies in the FH JOANNEUM Gesellschaft mbH corporate family. FH Joanneum is the second largest university of applied sciences in Austria. It has about 4,600 students and about 651 employees. FHJ, who is a Trials@Home partner, was one of the original CLINTOS consortium participants of CLINTOS, and will be contributing as a member of third party Special Trials@Hom Advisory Board along with CERTH and MLC.

MLC: Stichting MLC Foundation

Stichting MLC Foundation gives legal advice and does legal and ethical research on matters related to health care, medical research, biobanking and biotech start-ups.

With a thorough knowledge of Dutch Medical Law and European and national Privacy legislation, Stichting MLC Foundation advises on research contracts, transfer agreements for tissue and data, also between member states of the EU, privacy issues and related intellectual Property affairs as well as on the proper governance of data collections and data sharing in general.

Stichting MLC Foundation’s clients range from government agencies and university hospitals to registries and home- and social care institutions. In addition, Stichting MLC Foundation has participated in the MLC is a member of Trials@Home center of excellence along with CETH and FHJ.

SECTION 5: ETHICS

5.1 Introduction to CLINTOS Ethics

The CLINTOS project aims to build a versatile, future-ready, user-centric, cloud based universally compliant Operating System for Trials@Home and at the same time, develop technologies that will be saving lives and preserving society’s safety and security. Human participants will be involved and personal data of citizens will be collected and processed from various interconnected sources, in order to build a futureready, user-centric, universal backbone infrastructure for interconnecting all the different components for providing a seamless and secure path for the exchange of information between different components.

The CLINTOS project seeks to support the expected impacts of the call by developing, testing and validating CLINTOS,an integrated OS platform, which is a novel set of tools, technologies and methods

towards the facilitation of Remote Decentralised Clinical Trials. These include development of novel monitoring infrastructure and improvement of existing ones. Intelligent assessment tools that will face individual needs of the involved stakeholders will be available to them during all stages of the project.

CLINTOS functions as a universally compliant CT Operating System (CLINTOS) of future RDCTs, seamlessly connecting with the entire care continuum as plug-n-play federated cloud ecosystem generating new financial opportunities for partner SMEs in the multi-billion CT industry.. The major societal impact of CLINTOS will be to build, test & validate CLINTOS for at least 3 use-cases. All project activities will comply with European legislations and societal values, increase societal safety and allow the cross-domain and cross-country response team collaborations. All legal, societal, ethical and security considerations will be ensured by the consortium.

The project involves ethics issues that need to be assessed, mitigated and monitored throughout by complying with high standards of ethical research.

As part of the application process, the consortium has completed the ethics self-assessment, where the following aspects are highlighted:

• No research with human embryos/fetuses will be conducted

• No research with human cells/tissues will be conducted

• Research involves human participants

• Research does not involve physical interventions.

• Research does not involve invasive techniques

• Research collects biological samples

• Research involves collection or processing of personal data, especially health data

• Research does not involve animals

• No third countries are involved

• Mitigation of any possible dual use or misuse

While data protection and human rights laws exist to protect individuals, there are no ‘ethics laws’ as such. It is the responsibility of each person to carry out their tasks in a way that incorporates respect and protection of the human values that underlie the existing legislation. Although universally understood, ethical principles are also context specific in most cases, and therefore the ones most relevant to the CLINTOS project will be presented in the Ethical Risk Assessment, which will set out individual responsibilities and required compliance actions. The Ethical Risk Assessment (ERA) process will be used to identify, quantify and mitigate any ethical risks that may surface in the course of the development or deployment of emerging techniques and methodologies (ethical governance of the technology and/or value sensitive design approach).

During the lifetime of the project all ethical, societal and legal aspects will be taken into account to ensure the project’s compliance with EU values. The ethical and legal regulations in Europe will be reviewed to identify the possible ways that the proposed and deployed tools and processes may be affected by these regulations.

The Consortium commits itself to address the ethical dimension of the project and respect all principles representing the shared values of the EU.

Within this context, the Consortium shall respect the key ethical principles and the applicable national European and international legislation, such as:

• The Charter of Fundamental Rights of the European Union

• The European Convention on Human Rights and its additional Protocols

• The Universal Declaration of Human Rights, United Nations

• Ethics in Social Science and Humanities, European Commission, October 2018 • The H2020 Rules for Participation with special focus on articles 13 ("Proposals"), 14 ("Ethics Review"), 18 ("Grant Agreement"), 23 ("Implementation of Action") as well as Articles 34 ("Ethics") and 39 ("Processing of Personal Data").

• The European Code of Conduct for Research Integrity, ALLEA (All European Academies) and ESF (European Science Foundation), 2017.

• Codified and widely accepted principles of research ethics and ethical treatment of research participants including the Nuremberg Code, the Helsinki Declaration, and the Belmont Report. The Consortium will, in this spirit: :

- respect human dignity and integrity
- ensure honesty and transparency towards research subjects
- respect individual autonomy and obtaining free and informed consent
- ensure privacy and confidentiality
- promote justice and inclusiveness
- minimise harm and maximise benefit
- demonstrate social responsibility
- commits itself to deliver high quality scientific outputs

5.1.1 Ethical monitoring of CLINTOS

The CLINTOS Consortium having consciousness on the significance of the legal and ethical aspects, envisages all related challenges which may be raised during the project and commits itself to uphold ethical standards. To this end, specific tasks have been developed, to tackle all potential related issues; at the same time, the Ethics Advisory Board (EAB) has been set up; the ethics monitoring throughout the project is going to be conducted by the:

• **Ethics Advisory Board (EAB):** The EAB will give advice on the legal and ethical issues that will arise over the course of the project as well as, review the identified ethics sensitive deliverables to mitigate potential risks related to legal or ethical matters.

• **Data Protection Officer (DPO):** To ensure compliance with personal data protection rules, the Consortium will appoint an Internal DPO, for ensuring the adoption of personal data policies in accordance with the General Data Protection Regulation (GDPR) and the applicable national legislations.

5.1.2 Human embryos & foetuses

CLINTOS **does not** involve research on human embryos & foetuses.

5.1.3 Human beings

CLINTOS will involve human subjects but does not involve as research participants neither: a) persons unable to give informed consent, including children and minors or

b) patients or healthy volunteers for medical studies or

c) physical interventions on the study participants.

Individuals that may be considered as vulnerable individuals will be involved. More specifically, patients' personal data will also be collected and processed. Patients shall not be in critical situations, they will not be in danger and there will be no risk for their lives; on the contrary any act has the purpose to minimize the possibility to subsist any risk. In addition the number of the patients involved in the Project will be very low, which permits the Consortium to be very cautious with such data. Furthermore, all participants will be in position to give their informed consent and they will participate voluntarily.

The consortium of CLINTOS is conscious of the ethical, legal and societal issues that the project could potentially raise during the lifetime of the project. Any humans, citizens, patients or first responders, that may be involved during the pilot cases, will participate **on a voluntary basis.** Respect for people and for human dignity and fair distribution of the benefits and burden of research are ensured. In alignment with the "Science with and for Society'[2] approach", it is important to work together with the people that will benefit from the research to ensure the project takes into account their needs, expectations and rights. The project recognises that while the overall aim is to protect individuals and society in general, the extensive scale of the proposed solution may raise concerns in the public domain in the same way as surveillance techniques for the purposes of keeping people safe. Therefore, extra care will be taken to disseminate information at all stages of the research in a sensitive and effective manner. The project is also aware that even with anonymised data, where this is possible, there may be residual or consequential ethics issues to address. In particular, if categories of individuals are referred to, or general characteristics. No anonymised data will be made publicly available unless such risks have been eliminated or mitigated.

The participants will be informed about the benefits and risks -if any- stemming from their participation and have enough time to decide on their participation freely and **voluntarily**. They will be, among others, informed that, in case they wish to withdraw from their participation in the trials, they will be free to do so, without any repercussions, at any time. To ensure that consent during all CLINTOS activities will be informed, we will prepare participant Information Sheets written in lay terms to ensure that it is 'user friendly' and that it will meet the information needs of the potential participants who will be informed that they can ask questions regarding their participation.

[2]European Commission 'Science with and for Society', web page: https://ec.europa.eu/programmes/horizon2020/en/h2020-section/science-and-society

In brief, researchers will abide by key ethical research practices, including but not limited to:

- Informed consent for participation and for data collection
- Ethical recruitment of research participants
- Verification of participants' absence of any form of obligation
- Right to withdraw at any time without providing any explanation or justification and without any consequences
- Avoiding harm to research staff and participants in the course of research
- Best practice standards relating to the processing of personal data • Data security including storing data securely on a password-protected computer or an encrypted hard-drive kept in secure premises, only used for the purpose for which it was collected and deletion immediately after that purpose is fulfilled
- Protection and safety of research participants
- Protection and safety of researchers. Description of any reasonable foreseeable risk, discomfort or disadvantagesDescription of how incidental findings will be handled
- Data minimisation
- Accuracy of data and ensuring it is up to date
- Confidentiality of information
- Respect for gender, culture, ethnicity, religion and sexual orientation
- Providing participants with a complaints mechanism
- A description of the purpose of the research, who is organising and funding the research, and explanation about what will happen to the results of the research

Human participation (patients & other), gender issues, personal data protection will be treated according to EU, national and international legislation with respect to human rights and data protection. For this purpose, a special task and deliverables under WP1, has been designed/ elaborated. The project's Ethics Advisory Board (hereinafter EAB) will be responsible for overseeing the compliance of the individuals conducting project activities in respect to ethics, legal, privacy and data protection norms. The EAB will:

- Oversee the legal and ethical compliance in the project,
- Assess the ethical requirements in all project outputs and activities,
- Provide support, training, guidance and advice to all consortium members
- Create appropriate and relevant documentation and record-keeping methods,
- Liaise with the project coordinator and EAB;
- Facilitate collaboration with other actors (e.g. public representatives, external organisations etc.)

The above factors will be incorporated in the comprehensive risk management approach, in respect of data protection and ethics that will form part of WP1. This will ensure the legal, ethical, societal, privacy and security framework of the CLINTOS project. Potential risks to the above aspects will be identified and minimised and the impact of CLINTOS on the rights and freedoms of individuals, groups and society as a whole but the governance regimes as well will be critically assessed. The objective of Task 1.4 is to perform an in-depth analysis of identified critical issues as a basis for further development of methods and to conduct ongoing communication with communities and individuals about the representation and use of their data. During this task, Partners, where foreseen under national legislation, will seek ethical approval from the Ethics Committees when foreseen under their national legislation. The report on challenges and limitations, as well as the ethics requirements and legal framework will be presented in two deliverables, namely D1.2 and D1.3.

5.1.4 Human cells or tissues

CLINTOS does not involve research with human cells or tissues.

5.1.5 Protection of personal data

5.1.5.1 Compliance with GDPR

CLINTOS will be adhering to the standards of the following legislation, when applicable:

- **Regulation (EU) 2016/679** of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (Text with EEA relevance).
- **Directive (EU) 2016/680** of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data by competent authorities for the purposes of the prevention, investigation, detection or prosecution of criminal offences or the execution of criminal penalties, and on the free movement of such data, and repealing Council Framework Decision 2008/977/JHA.

All activities will be conducted using fully rational adults, which means that they will be able to understand their role in the project. Participants will be given information in the form of an information sheet on who will benefit from their participation in the research and what risk or burden they might undertake by participating. CLINTOS will collect personal data, including medical data from participants since the process of those data is crucial to the development of the CLINTOS ecosystem. All participation will be voluntary and informed; patients participating in the studies will not be in critical situations nor in any danger. Researchers will not put pressure on research participants to participate in the project and will not allow the responsible institution to apply pressure. There will be no offer of monetary incentive. During the first 6 months of the project, a data protection policy aligned with relevant EU national and local policies will be designed and agreed amongst the consortium partners. Finally, all data protection documentation will be centrally held by the project and will therefore be available for audit. Personal data will be protected and stored only where necessary, in secure systems. For WP1, EAB will produce specific guidance related to conducting the demonstration/experimentation programme (including, for example, ethical guidelines on ensuring that research participants are provided with accurate information about the purpose of the programme, that the programme is an example rather than a real-life situation, participation procedures, etc.). EAB will also provide in-depth guidance on recruiting participants.

To ensure that consent during all CLINTOS activities will be informed, CLINTOS will prepare participant Information Sheets written in lay terms to ensure that it is ‘user friendly’ and that it will meet the information needs of the potential participants who will be informed that they can ask questions regarding their participation. To ensure that consent is voluntary, ‘opt in’ and ‘opt out’ option to their participation will be provided to the potential participants. In addition, the team will ensure that participation is entirely voluntary throughout the trials/workshops by informing the research participants that they can withdraw without penalty at any time. EAB will ensure that information provided is transparent and easily understandable. Data collected from these research participants will be processed in accordance with the GDPR and any relevant national variations. Data collected from research participants will be processed and stored in accordance with The Charter of Fundamental Rights of the EU, the European Convention on Human Rights and the EU GDPR. Where medium or high risks relating to

ethics considerations are identified, members of the consortium will seek the approval of local ethics committees, where this has not been already obtained.

As informed consent is the cornerstone of research ethics, it shall be given by a clear affirmative act establishing a freely given, specific, informed and unambiguous indication of the subject's agreement to the processing of their personal data. Therefore, we will ensure that:

- Informed consent procedures will be implemented for the processing of personal data of the data subjects and
- Templates of the Informed Consent forms and Information Sheets on the processing of the data subjects' personal data will be provided.

The data subjects who will be participating in the pilot cases will be fully informed about their personal data handling during the data lifecycle, including: where and how their personal data will be stored, who will have access rights to it, how long it will be stored, how it will be anonymised and processed and when it will be securely deleted. They will be also informed about their data protection rights and specifically the right to request information , the right to access, the right to rectification, the right to erasure, the right to the restriction of the processing operations, the right to data portability, the right to lodge a complaint with a supervisory authority and the right to withdraw their consent at any time.

Consortium will comply with the personal data protection framework and among others, with the principles of **lawfulness, fairness, transparency, purpose limitation, data minimisation, accuracy, storage limitation, integrity and confidentiality (security) and accountability**, as explained in detail below. Additionally, a **Privacy by Design** approach will be followed through the technology design, in coordination with the Consortium, as certain legal requirements to be guiding the technology design and the implementation of the pilots will be provided under **D1.2**.

The Consortium is going to issue internal guidelines to respect all related ethical issues, including the protection of personal data, under **Task 1.3** and **Task 1.5**. The methodology to be applied personal data handling during the project activities including trials and workshops will be subject to approval by the ELOs. Additionally, the Data Management Plan to be developed under **Task 1.3** will include the procedures for data handling and ethics aspects on personal data handling.

5.1.5.2 National Data Protection –Ethical Agencies Notification and Approval

Although the GDPR eliminated the automatic requirement to notify national data protection supervisory authorities of data processing activities, at the outset of the project all consortium partner organisations will be required to confirm whether this is required in their country and evidence that it has been done, if so. Otherwise, each partner organisation will be required to name a data protection representative or the formal Data Protection Officer, where the organisation has one. The organizational data protection compliance policy will also be confirmed and provided where necessary.

Copies of ethical approval at least Hospitals (as well as other partners of the Consortium when ethical approval is foreseen) will be included in deliverable D1.4 Renewal of notifications, when necessary, will be carried out. Any additional risks identified through the assessments carried out in respect of all work will be notified to ethics committees as necessary and in advance of any activity being commenced. The renewal requirements will also be leveraged to react to change in the project and the adoption of survey, research, development and test tasks. Regarding the request asking for approval from the competent local/national Ethics Committees/authority it shall include the following:

● Clear and detailed information on the source and type of the monitoring data to be collected;

● Detailed information on the procedures that will be used for the recruitment of volunteers, and

● Copies of examples of Informed Consent Forms and Information Sheets that must be in language and terms understandable to the participants.

Prior to any field-tests proper ethical and individual rights study and analysis will be carried out in order to ensure that the appropriate safeguards for participants in the tests have been considered and addressed properly (even if the individuals are not aware about their personal rights to protect their personal data from improper use). All data processing must be lawful, transparent and fair. This requires all data processing within the project to have a legal foundation, which must be identified prior to the processing taking place. For most of the planned activities, this will be fully informed consent, though the legal basis will be reviewed prior to each activity, as part of the data protection by design process.

5.1.5.3 Procedures for Voluntary Participants

In line with the principles set out in the GDPR, data processing within the project will be kept to a minimum. In many cases it will not be necessary to process any personal data, as the objective can be achieved without it, for example the testing of technical features. The screening document that will form part of the data protection by design approach incorporates the data protection principles and encourages partners to consider first whether any processing of personal data is necessary.

Where the processing is necessary, a legal foundation must be established. This will be informed consent. It is essential that those participating in the research receive sufficient information about what is expected, what activities are involved and what will happen to their information, including personal data. It is also important that people understand who is carrying out the research and who to contact for questions, further information or to withdraw their consent. The method of communication between researcher and participant should be through means that are easy and accessible to the participant and effort should be made to accommodate preferences or alternative arrangements.

It is important to allow the participant to withhold consent for certain activities or parts of activities, while remaining involved in others. To facilitate this, consent forms should be very specific and list actions separately. No detriment must be suffered by the participant for withholding consent and they must be able to withdraw all or part of it at any time. If data is to be later aggregated or anonymised the date at which this happens will be clearly explained.

5.1.5.4 Data transfer

It is not anticipated that personal data will be shared with third parties during the lifetime of the project, however the necessity of this will be reviewed as required. In any case, full compliance with the requirements set out in the GDPR in this respect will be achieved. It is acknowledged that data sharing or transfer goal is to process, and the CLINTOS' goal is to reduce this to a minimum and only where it is necessary to satisfy a specific purpose. More specifically, the use of third-party servers and services will be deemed data sharing and attention will be given to acquire assurance of appropriate compliance procedures and security measures where it is required. When any consortium member uses a data processor, they will be asked to declare it by signing a formal contract. Regarding personal data transfer from/to the United Kingdom, as a partner from the UK is involved (Autonio Foundation Ltd), it is worth

mentioning that due to BREXIT, the United Kingdom will be considered as a "third country" from 01/01/2021 onwards. Thus, the GDPR will no longer apply directly for the UK. However, this is not the case yet, hence, the UK cannot be considered as a third country at this stage. The CLINTOS DPO will pay attention to the developments in relation to the position of the UK in the near future and respond accordingly with appropriate arrangements for sharing data outside of Europe.

5.1.5.5 Security Measures for Storage and Data Handling

The European Commission[3] sets out examples of things to be considered in a research and development context; these measures will be implemented where necessary by the project:

- Pseudonymisation or anonymisation of personal data;
- Data minimization;
- Applied cryptography (e.g. encryption or hashing);
- Using data protection focused service providers and platforms.

Well-designed and tested information technologies will be deployed for secure storage, delivery and access to data, as well as managing the rights of the users in order to safeguard the information and protect the personal data during its lifecycle. The implementation of these tools will follow the legal and ethical framework for data privacy that will be drafted by CLINTOS in **D.3**, which will be in full compliance with the EU legislative and regulatory framework for data protection based on the uniform approach of the EC Directive 95/46/EC3, and the national legislative and regulatory framework for data protection of each project member country. CLINTOS will also comply with ISO/IEC 27000 family of standards, which provide best practice recommendations on information security management, risks and controls within the context of an overall information security management system.

5.1.6 Third Countries

The Consortium does not include partners from third countries. Regarding personal data transfer from/to the United Kingdom, as a partner from the UK is involved (Autonio Foundation Ltd), it is worth mentioning that due to BREXIT, the United Kingdom will be considered as a "third country" from 01/01/2021 onwards. Thus,

the GDPR will no longer apply directly for the UK. However, this is not the case yet, hence, the UK cannot be considered as a third country at this stage.

No local resources are foreseen to be used.

No personal data (contact details) will be imported from third countries to the EU or exported from the EU to third countries. Moreover, the Consortium will demonstrate compliance with the applicable personal data protection legislation and a declaration confirming compliance with Chapter V of the GDPR will be provided for by the responsible partner.

In any case, it is declared that **no imports (from third countries to the EU) or exports (from the EU to third countries)** are going to take place.

[3]European Commission (2018) 'Ethics and Data Protection' [Online publication, 14 November] Available at: https://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/hi/ethics/h2020_hi_ethics-data-protection_en.pdf

No low and/or lower-middle income countries are involved in the research.

Lastly, all safeguards for the safety and physical integrity of participants will be implemented.

5.1.7 Environment & Health and Safety

Demonstrations that appropriate health and safety procedures conforming to relevant local/national guidelines/legislation are followed for participants involved in this project during the Validating & Piloting project phase will be submitted by the respective partners to ensure the safety and physical integrity of all human participants.

Does your research involve the use of elements that may cause harm to the environment, to animals or plants? No

Does your research deal with endangered fauna and/or flora and/or protected areas? No

Does your research involve the use of elements that may cause harm to humans, including research staff? No

5.1.8 Dual use

The Project aims to develop technologies (such as software) which are of generic nature (i.e. that can have both civil and military applications). However, the Project does not involve exporting of goods/technologies outside the EU, thus regulation 428/2009 is not applicable. All activities will be deployed in EU territory. Therefore, in principle, there is **no** dual use concern. Taking into account, though, that the Guidance note of the European Commission considers that even publications of research findings dealing with dual use items (e.g. in a scientific article in a journal from outside the EU) may be classified as an intangible technology transfer (ITT), in this case authorisation following Regulation 428/2009 would be required. Such publications will not be pursued; if such publications take place, it will be examined whether Regulation 428/2009 is applicable and in the affirmative, declarations or statements or export licenses will be requested from the respective partners. Considering the above, the Project does not have a military, but only civilian character.

5.1.9 Exclusive Focus on Civil Applications

Our research focuses exclusively on civil applications.

5.1.10 Potential misuse of research findings

The technologies, methods and knowledge used in the project will not physically harm humans, animals or the environment. However, CLINTOS is aware of the fact that some of the project's outcomes may be misused for unethical purposes. A brief assessment of the risk for the misuse of research findings will be conducted if necessary and appropriate measures to prevent it will be implemented. The Ethics Advisory Board (EAB) and the DPO will be monitoring the relevant deliverables throughout the project to avoid the potential for misuse.

5.1.11 Other Ethics Issues

The CLINTOS partners do not foresee that our research may raise any other ethical concerns.

SECTION 6: SECURITY

CLINTOS will not involve EU classified information[4] either as background or as results of the project. The project DOES NOT interact with organizations that are involved in activities dealing with national and/or European Security, nevertheless we do not foresee at the proposal stage any project deliverables identified as "classified".

Moreover, the technologies to be developed during the project are not classified. The data that are planned to be processed, will be first anonymised before being published and shared with the EU clinical trial repository. The use of the CLINTOS developments in the future by partners might be subject to IPRs, patents, etc. and become classified, but this is clearly outside the scope of this project.

In the event that the CLINTOS project proposal receives a security recommendation under Model Grant Agreement Article 37 Security Related Obligations, or its sub-clauses, the appropriate measure shall be taken to comply. Last, but not least, it is worth mentioning that all practitioners, Industrial partners and most academic research institutes in the consortium are used to handling security sensitive information and have the proper protocols and security clearances in place.

Activities or results raising security issues:	**YES**
'Classified information' as background (i.e. use of already classified documents/information at EU or national level) and/or results (i.e. production of documents/information that need to be EU classified):	**NO**

The CLINTOS Consortium therefore:

- will utilise a limited dissemination list (refer to section 6.1)
- establish a Project Security Officer (PSO) (refer to section 6.3.1).

[4] Article 37.1 of the Model Grant Agreement: Before disclosing results of activities raising security issues to a third party (including affiliated entities), a beneficiary must inform the coordinator — which must request written approval
from the Commission/Agency. Article 37.2: Activities related to 'classified deliverables' must comply with the 'security requirements' until they are declassified. Action tasks related to classified deliverables may not be subcontracted without prior explicit written approval from the Commission/Agency. The beneficiaries must inform the coordinator — which must immediately inform the Commission/Agency — of any changes in the security context
and — if necessary — request for Annex 1 to be amended (see Article 55)

In addition, it is worth mentioning that many of the CLINTOS members: practitioners, industrial partners, academic researchers and institutes are already handling security sensitive information and as such they had already implemented the required security protocols.

6.1 Limited dissemination

The following table presents the CLINTOS deliverables that can be disseminated/communicated only on a limited basis (confidential within the Consortium):

Table 6.1: Limited Dissemination Table

	Deliverable Name	WP	Lead	Type	Dissemination Level	Delivery Month
D1.1	Project Handbook - Quality Assurance Plan	1	UTB	R	CO	M2
D1.2	CLINTOS Data Management Plan (DMP) Handbook V1	1	SST	R	CO	M6
D1.3	Midterm Project Progress Report	1	UTB	R	CO	M18
D1.4	CLINTOS Data Management Plan (DMP) Handbook V2	1	SST	R	CO	M32
D1.5	CLINTOS Social Impact Plan (SIP) Handbook	1	UTB	R	CO	M2
D1.6	Final Project Progress Report	1	UTB	R	CO	M36
D1.7	Ethics Impact Assessment Report	1	EMA	R	CO	M36
D2.1	CLINTOS Tech Specs & Architecture Documentation	2	SST	R, Other	CO	M2
D2.2	CLINTOS Device Specs, Architecture Documentation	2	BC5	R, Other	CO	M3

D2.3	Critical Review Report of CLINTOS Specs & Architecture	2	SST	R, Other	CO	M3
D2.4	Online Access to CLINTOS Architecture & Specifications Documents	2	SBA	R, Other	CO	M3
D3.1	Complete CLINTOS Framework	3	BC5	DEM	CO	M9
D3.2	Manufacture 50 units of CE Marked CLINTOS SmartHub devices (Smart T Shirt included)	3	AFL	DEM	CO	M12
D4.1	Acquire 200 units of CLINTOS SmartHub devices	4	BC5	Other	CO	M16
D4.2	Acquire 200 units of Redoxer ORIB devices for testing	4	AFL	Other	CO	M18
D4.3	Obtain revised CE Marking of CLINTOS SmartHub wearable device	4	BC5	Other	CO	M18
D4.4	Ethical Votum for field trials (FT-1, FT-2 FT-3)	4	ISS	R	CO	M18
D4.5	Obtain CE marking for Redoxer wearable device	4	AFL	Other	CO	M20
D4.7	IPR- Patent Filing	4	BC5	DEC	CO	M20
D6.5	Business Plan & Sustainability	6	BC5	R	CO	M34

Nevertheless, and to ensure no doubts arise as to the character of the information used and produced, the project will appoint a Security Officer who will review all project deliverables with the purpose of identifying sensitive information. Initially, should the need to deal with classified material arise during project execution the consortium is well equipped to address this.

6.2 EU classified information

In case any information or material is marked as EU classified, CLINTOS will comply with the Commission's security rules and standards (Commission Decision 2015/444) when handling any EU classified information (EUCI). All EUCI provided or generated under this grant agreement will continue to be protected if the agreement is terminated. In case that the dissemination of deliverables needs to be reclassified, it will be done with the approval of the European Commission. A security scrutiny check may clarify whether information/material (as background or results) under the CLINTOS project needs to be marked and treated as EUCI. Security scrutiny may lead to 'security requirements'. If applicable, these will be included in the grant agreement as a Security Aspect Letter (SAL) and the Security Classification Guide (SCG).

6.3 Security Staff

CLINTOS will appoint a qualified individual from the consortium to undertake the role of Project Security Officer (PSO). The responsibilities of PSO will be to advise and review all security and sensitive material and matters of the project and to supervise and check compliance during the project lifespan. The PSO will closely coordinate with the project coordinator and Ethics Advisory Board (EAB) and the Data Protection Officer (DPO).

6.3.1 Project Security Officer (PSO)

Dr. Edgar Weippl has been appointed as Project Security Officer (PSO) for the CLINTOS project.

6.3.2. Security Advisory Board

There is no need for a Security Advisory Board (SAB). If such a need arises, then a SAB will be formed by the PSO and two more security experts coming from the consortium with knowledge of security issues. SAB will be chaired by the PSO. It will be the role of the SAB to assess the sensitivity of input and deliverables prior to publication and to assess the sensitivity of the information handled by the consortium during the lifecycle of the project. The two members of SAB will be decided at the latest during the Grant Agreement preparations.

6.4 Other project-specific security measures

- Members of the consortium must comply with the Commission's security rules and standards (see Commission Decision 2015/444) when handling any EU classified information (EUCI).
- EUCI is information that has been classified and marked or its equivalent under a national classification system. • All EUCI provided or generated under this grant agreement will continue to be protected if the agreement is terminated.
- In handling and filing those parts of the grant agreement referred to by the Security Classification Guide, one must abide by the following security rules:

1. obtain a facility security clearance, so they can handle EUCI;
2. inform all other parties to whom they give access to EUCI that they are responsible for its security (Commission Decision 2015/444);
3. take all the measures to safeguard EUCI that are prescribed by their National Security Authority/Designated Security Authority (NSA/DSA);
4. appoint a Facility Security Officer;
5. keep in touch with their NSA through the appropriate local channels;
6. keep a record of those of their employees taking part in the project who have been cleared for access to EUCI;
7. submit any information they generate in the course of this project for EU classification and marking;
8. obtain the approval of the contracting authority before starting talks on contracting out work;
9. allow the Commission's Security Directorate to inspect their facilities (in coordination with the NSA/DSA) to check whether they meet the security rules on handling EUCI;
10. report all cases of unauthorised disclosure or loss of EUCI to their NSA/DSA, the Commission's Security Directorate and the Contracting Authority;
11. not use the EUCI provided or generated for any purpose other than that of carrying out the grant agreement;
12. follow all other relevant instructions on handling and filing classified information (unless none are required under the work programme).

The CLINTOS consortium will strictly follow the aforementioned security rules and all specific project-related needs and obligations that will be addressed timely by the Project Security Officer and the Security Advisory Board from the beginning and during the evolution of the project.