FP7 RESEARCH INFRASTRUCTURES

CP-CSA

DELIVERABLE D1.1.3
SUSTAINABILITY PLAN

ORGANISATION NAME: GARR

Project co-funded by the European Commission within the 7th FP		
Dissemination Level PU		
PU	**Public**	**X**
PP	**Restricted to other programme participants (including the Commission Services)**	
RE	**Restricted to a group specified by the consortium (including the Commission Services)**	
CO	**Confidential, only for members of the consortium (including the Commission Services)**	

Document Identifier:	**DECIDE-D1_1_3.doc**
Date:	**01/01/12**
Work Package:	**WP1: Management**
Lead Partner:	**GARR**
Document Status:	**Final**
Document Link:	**-**

Abstract:

The document sets out strategies and next steps for the sustainability of the DECIDE e-Infrastructure and service beyond the project lifespan. Chapter 2 identifies what are the "activities" and the "resources" which the project has to offer, namely the key assets that make the project results appealing to the "outer world", or "stakeholders" at large. Chapter 3 discusses what are the stakeholders, which specific project activities and resources may be relevant to them, and at the same time which of the stakeholder's "activities" and "resources" are possibly of interest to the project itself. Some commonly used business models, and their applicability to the case of DECIDE are presented in Chapter 4. Chapter **Errore. L'origine riferimento non è stata trovata.** introduces an estimate of the expected costs to be incurred to keep the infrastructure and service alive, and some of the ways by which the project may meet such costs: the same chapter also discusses the organizational model for handling revenues. Chapter 6 draws the conclusions and recaps the overall strategy.

Document log

Issue	Date	Comment	Author

Document change record

Issue	Item	Reason for change

CONTENTS

1. EXECUTIVE SUMMARY

This document sets out strategies and next steps for the sustainability of the DECIDE e-Infrastructure and service beyond the project lifespan (i.e. how to find the resources to ensure the maintenance of the DECIDE e-Infrastructure along time).

Firstly, we defined the "activities" and the "resources" which the project has to offer. These are the key assets that make the project results appealing to the "outer world", or "stakeholders" at large. This part is described in Chapter 2 "Project Activities and Resources".

Then, we defined the stakeholders, and the specific project activities and resources of interest to them. Furthermore, we specified the stakeholder's "activities" and "resources" of interest to the project itself. This part is discussed in Chapter 3 "Identification of Stakeholders".

Next, we discussed some commonly used business models and tried to assess their applicability to the case of DECIDE: this part is presented in Chapter 4 "Existing e-service business models and their applicability to DECIDE".

The costs expected for sustaining the infrastructure and service were estimated in Chapter 5 "Sustainability Roadmap": the same chapter introduces how we planned to meet such costs, and discusses the organizational model for handling revenues.

Finally, Chapter 6 "Conclusions" summarizes, also in graphical way, the overall strategy which is expected to ensure the maintenance of the DECIDE e-Infrastructure after the end of the project.

2. PROJECT ACTIVITIES AND RESOURCES

2.1. Scenario

The diagnosis of neurodegenerative pathologies such as Alzheimer's disease (AD) is changing dramatically. For the first time after 25 years, medical experts have proposed a major change in the criteria for the diagnosis of AD, to detect and treat the disease earlier and earlier, even before the overt dementia. Specifically, the new diagnostic guidelines (Sperling RA et al 2011) state that new imaging technologies such as PET and structural MRI scans can be used to detect the disease even before there are remarkable deficits of memory or of other cognitive functions.

Development of these guidelines, by panels of experts convened by the National Institute on Aging and the Alzheimer's Association, began since 2010 because, with a new understanding of the disease and new ways of detection, it was clear that the old method of diagnosing AD was sorely outdated. Today, researchers are convinced that AD is active a decade or more before dementia. Their thinking has changed considerably and now they view dementia as a late stage in the process. The new guidelines include criteria for three different stages of the disease: (I) preclinical disease, (II) mild cognitive impairment due to AD and, lastly, (III) Alzheimer's dementia.

Under the new guidelines, for the first time, diagnoses aim to identify AD as it is developing by using results from biomarker tests like brain scans, MRI scans and spinal taps that reveal telltale brain changes. The biomarkers were developed and tested only recently and, for this reason, none had been previously formally approved for AD diagnosis. One of the newest methodologies, the PET scan, shows plaque in the brain that is a unique sign of AD brain pathology. The others provide strong indications that AD is present, even when patients do not yet have dementia or even much memory loss. AD scientific community has welcomed the new criteria. In fact, adding these biomarkers to the diagnosis is a big improvement. More concretely, the diagnosis of AD in the next 10-20 years would be increasingly carried out with multimodal approaches using 1 biological (e.g.: Aβ42 or Tau protein in CSF) and 3 neuroimaging markers (e.g.: PET amyloid imaging, ^{18}FDG-PET and MRI). This is a giant step forward in the right direction because it moves us closer to the brain underpinning of the disease rather than just looking at clinical symptoms as done in recent years.

In the present innovative framework, only the last two neuroimaging biomarkers (^{18}FDG-PET and structural MRI) lend themselves to be implemented in a distributed infrastructure. MRI enables detailed visualization of structures implicated in the diagnostic feature of AD. ^{18}FDG-PET has been approved for diagnostic purposes and it is sensitive and specific in detecting AD in early stages. Growing evidence about these new AD/dementias biomarkers allowed us to incorporate them into the DECIDE diagnostic e-infrastructure.

Furthermore, the scientific community increasingly supports the idea that AD targets specific and functionally-connected neuronal networks and that oscillatory electromagnetic brain activity might be a hallmark of the disease. In this line, digital electroencephalography (EEG) allows non-invasive analysis of cortical neuronal synchronization, as revealed by resting state brain rhythms. A bulk of studies on resting state eyes-closed EEG rhythms recorded in amnesic mild cognitive impairment

(MCI) and AD subjects support the idea that spectral markers of these EEG rhythms, such as power density, spectral coherence, and other quantitative features, differ among normal elderly (Nold), MCI, and AD subjects, at least at group level. Regarding the classification of these subjects at individual level, most previous the studies showed a moderate accuracy (70-80%) in the classification of EEG markers relative to normal and AD subjects. A recent study by the DECIDE Consortium tested the accuracy of resting state EEG markers in the discrimination of 82 Nold and 96 AD individuals towards clinical applications. Results showed 80.2% of mean sensitivity, 61.8% of mean specificity, and 71.8% of mean accuracy of the EEG markers. Area under ROC curve was of 0.78. These results suggest that the combination of the above low-cost and non-invasive EEG makers allows a moderate classification of Nold and AD individuals. Such classification is potentially useful for the preliminary screening of large populations of elderly patients at risk of AD.

Noteworthy, DECIDE is the first integrated platform able to predict progression to AD in preclinical phase, to establish and support the diagnosis based on the new criteria suggested by a well-known international groups of researchers (Jack et al 2011). More specifically, to meet the new criteria for AD diagnosis, DECIDE offers reliable quantitative volumetry of the hippocampi, referenced to a well-characterized population with age norms, acquired by MRI. Moreover, an innovative specific pattern recognition algorithm is included in the DECIDE suite for the analysis of functional imaging (PET) acquisitions of the brain too. This new method allows clinicians to extract diagnostic factors from functional imaging data showing typical AD patterns. On the whole, the DECIDE diagnostic service is based on a model suited for the daily diagnostic routines and compliant with new criteria and with consistent clinical/imaging data and high computing power to be used for early diagnosis and care. The DECIDE diagnostic service offers to clinicians a rich e-infrastructure suited to perform single case diagnosis in the field of AD. A powerful brain analysis suite of tools is available to carry out analyses using the web-grid-service, which represents an opportunity to improve the power of single case analysis investigations and better understanding of the prognosis. All this is possible through the evidence coming from cross-system sophisticated processing analysis of MRI and PET.

The interest of the DECIDE e-infrastructure is not only in the use of well established neuroimaging diagnostic markers for AD such as ^{18}FDG-PET and structural MRI. The DECIDE e-infrastructure also offers opportunities to validate and use for scientific purposes EEG diagnostic markers. Although they have not been reported in the revised diagnostic criteria, they are under evaluation as one of the cheapest, less invasive and largely available candidate biomarkers for AD diagnosis, at least as a first screening methodology. In line with a modern social and clinical trend, we need a feasible screening test particularly cost-effective to select patients with suspected AD who might enter more expensive and invasive (and more precise) diagnostic path. The DECIDE e-infrastructure includes the most promising resting state EEG markers including those reflecting the cortical sources of EEG power density and the functional coupling of EEG rhythms (spectral coherence and direct transfer function, DTF).

2.2. DECIDE assets and resources

The DECIDE e-infrastructure and e-service, currently in a pilot phase, has mobilised a number of resources that can be maintained after the end of the project with limited costs (see Chapter 5 for an estimate) and are regarded as key assets to support the

sustainability after the end of the project. They are listed in the following:

- Reference databases: these are databases storing data (^{18}FDG-PET scans, structural MRIs, and resting state EEG data) relevant to groups of Nold, MCI and/or AD subjects, , which can be used for the statistical comparison with the individual dataset under analysis. For some kind of data, like ^{18}FDG-PET scans, due to the lack of public databases such datasets are extremely difficult to acquire, for both ethical and financial issues. Even a large university hospital would take several years before it could build a dataset large enough to fully exploit the statistical power of the processing algorithms.
- Computing/storage infrastructure: this is a remarkable resource not only for the ensemble of computing and disk-storage resources, but most importantly due to the innovative way these resources are made easily and effectively available to users: we refer to the ScienceGateway, the handling of Robot Certificates, the way databases are exposed to applications via AMGA and gLibrary, and the secure storage brought about by the KeyStore.
- Algorithms: the DECIDE service offers the unique opportunity to access a powerful suite of tools, to get in contact with the most advanced research activities in the field neuro-degenerative diseases, and to possibly correlate different analyses from single or multi modality methods.
- Experts: another significant asset is the availability, in the DECIDE Consortium, of experts on the algorithms for diagnostic marker extraction and related applications.

Nowadays only few specialised excellence centres can afford to have in-house the above resources and expertise, the remainder being prevented from using the innovative approach proposed by DECIDE.

In order to achieve sustainability, the project aims at addressing this large and diverse poll of potential users by providing them with a production-quality e-service for the computer-aided extraction of quantitative disease markers for clinical diagnosis and scientific use.

The DECIDE service will be available to users through the project web portal, subject to qualification in a specific test, in order to determine the user's skills to correctly use one or more algorithms and understand its results and their implications in the diagnostic procedure.

The service offer will be completed by technical support, training and expert consultancy.

As the service is not intended for emergencies, but for diagnostic use, a reasonable initial hypothesis of Service Level Agreement (SLA) would include:

- Availability guaranteed in working days,
- Support offered during office hours;
- Average incident handling time: 48 hours;
- Average time to get expert advice: 72 hours;

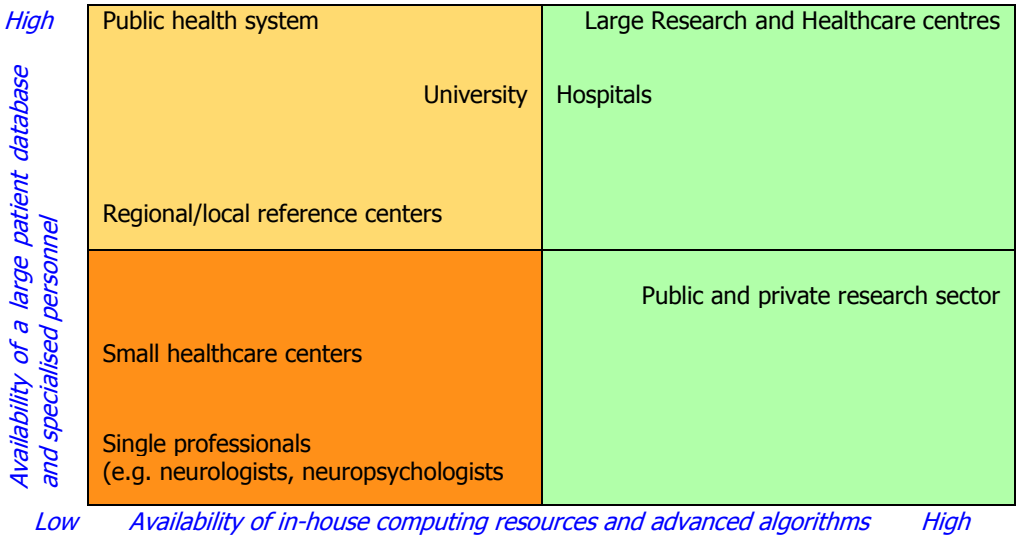
In addition to these assets, in order to provide a real, usable, production service, the project Consortium will need mobilise resources aimed at:

- Maintaining/upgrading the computing and storage infrastructure and ensuring its availability with production-level SLAs over the network;
- Maintaining/updating software packages, for compatibility with updates of generic software in use in the infrastructure (operating systems, Java, Apache, Grid middleware,…)
- Supporting users in the case of technical malfunctioning and faults;
- Maintaining/updating the reference databases, ensuring their availability and the security of the stored data;
- Maintaining the users' database, enrolling new users and ensure the security of credentials;
- Training new users and answering to common questions;
- Supporting users in the correct interpretation of the algorithms' outcome.

Last, but not least, the DECIDE architecture is extensible to further algorithms, so additional effort could be required in order to port promising applications on the e-infrastructure. Although the evolution of the DECIDE resources is important for the future of the e-service, this activity could however be funded separately, i.e. on a project basis.

2.3. DECIDE potential users

The table below shows the potential users of the DECIDE e-service and their position in relation to the following items: (1) the availability of advanced quantitative algorithms and the computing power and storage to exploit them; (2) the personnel needed to maintain the service and to provide technical support; (3) the availability of large, standardised databases of quality patient data; (4) the scientific expertise to exploit it in the diagnostic/research work.



In the table, the colours indicate the different levels of readiness in adopting the DECIDE approach: green for relatively high level of readiness, yellow for an intermediate one, and red for a lower level. It is important to highlight that the DECIDE project could in principle bring added value to all segments, although key

levers (i.e. cost-effectiveness, availability of quality data, exploitation of new diagnostic markers etc.) for each segment to adopt the service are different. For this reason, in order to achieve sustainability, DECIDE could either focus on one or few segments and stress the appropriate lever(s), or aim at hitting all of them with a good mix of different levers, and using targeted strategies.

- Advanced public and private healthcare centres (including university hospitals) could easily adopt the approach, having both the expertise, the occasion and human resources needed to fruitfully use the service. A minority of these clinical centres may have internal computing resources/databases for the extraction of PET, MRI, and EEG markers. This would lower the motivation in adopting the service. To make the adoption of DECIDE attractive to this segment, the service should either provide scale economy benefits if compared to the in-house approach, or additional advanced algorithms that are not yet used in the centre – or both.
- The situation is similar for the Public and Private Research sector, which could also easily adopt the service. Besides offering highly valuable algorithms and a cost-effective service, key to this segment could be the availability of large quality patients' and normative databases (as the acquisition costs of such data can be high and impact on the overall budget of the research) and of peculiar algorithms for marker extraction in which the scientist can change the parameters for the data analysis.
- The public health system as well as the regional and local reference centres for the diagnosis of AD and other dementias would have a high motivation in adopting the DECIDE diagnostic service, which would offer an important tool to improve the diagnostic confidence at the early stages of the disease and, in a longer term perspective, offer new opportunities to perform low-cost, non-invasive screenings on the normal population (e.g. thanks to the use of the EEG toolset). This segment currently does not have access to computing power and ICT-aided extraction of quantitative markers, and may lack the technical expertise needed to set up and maintain them. As a potential obstacle to the penetration of the DECIDE diagnostic service, personnel of the more peripheral public health centres may be not familiar with the exploitation of quantitative neuroimaging/neurophysiologic markers for AD diagnosis. To make the adoption of DECIDE attractive to this segment, the project should provide effective training programs for an extensive exploitation of the e-service.
  Noteworthy, these subjects have access to the patient's data, which are thus immediately usable with the tool, while on the contrary a single neurologist depends on an external medical centre to perform diagnostic tests such as a MRI.
- The latter is one of the main reasons why the last segment, which includes single professionals and small healthcare centres is expected to be the most difficult to outreach. In several countries, the existing laws on patients' data protection and privacy could prevent the DICOM data from being used outside the hospital's premises and made available to the single neurologist. In addition, the latter could lack the skills needed to manipulate the data (i.e., data entry and analysis with DECIDE resources). Although this can be tackled delivering appropriate training, it is clear that single persons or small

organizations may lack the motivation, time and/or resources to afford the training. Furthermore, the dissemination to this segment is made more complicated by the high degree of fragmentation. To partially overcome this problem, we will disseminate the features and opportunities of the DECIDE service to professional associations or public bodies (e.g. regional/municipal governments etc). Although adoption barriers are higher for this segment than for others, it can be speculated that the motivation to adopt an e-service such as the one proposed by DECIDE is very high for this group, which has no direct access to large normative databases nor to advanced ICT tools. Key levers would in this case be an affordable costs, easy and widespread training processes, and ease of use.

3. IDENTIFICATION OF STAKEHOLDERS

Value-creating and sustainable e-Health systems involve the development and implementation of business models where processes and stakeholders' interactions are identified and mapped. In addition, unlike other commercial environments, identifying value creation and sustainability in e-Health requires taking financial and non-financial factors into consideration.

The DECIDE project is clearly concerned with the sustainability aspects of the development, maintenance and support of the overall e-infrastructure used by the biomedical communities to access and manage data. The DECIDE long-term sustainability is intertwined with the capacity to deploy a mature e-Health system, which has overtaken the pilot phase and is fully operational for early adopters to try it out and assess its overall performance.

The present chapter details the interactions and interdependencies among all stakeholders, and how their interests are represented in the DECIDE model, and reflected in its appropriate operational elements.

3.1. Infrastructure

DECIDE infrastructure is built on two pillars: network and Grid infrastructures.

3.1.1. Network

It has emerged from a European survey[1] on e-Health benchmarking that all hospitals are connected to broadband (92%), although half of them have a bandwidth of below 50Mbps (52%). Thus, there is still room for improvement, with the transition to next generation broadband (>100Mbps). High bandwidth could prove useful in advancing digital imaging and telemonitoring. There is a clear focus on investment in broadband and in next generation networks in the strategy set out towards 2020 in the EC's Digital Agenda for Europe. However, attention should be paid to the considerable differences among the countries regarding the quality of broadband speed provided.

In the DECIDE infrastructure, very high bandwidth network connectivity is required for pre-production and production Grid sites, and especially for sites storing and producing images/data, which need to be accessed by the applications, but not necessarily for end-user sites (although of course very poor network performances could affect the user experience). As a matter of fact, according to DECIDE service model, applications generate most network traffic while getting data (in encrypted form) from Grid storage sites, and will only contact the sites owning the data (hospitals and research centres) to retrieve the cryptographic keys.

The analysis presented in deliverable D2.2.2 shows that most DECIDE sites (with the exception of maatG) are presently interconnected by the NRENs and the GÉANT network. The same study also shows that the network requirements for applications users are not extremely stringent: the most demanding operation from the user's point of view is the patient's image upload, and even this operation can be dealt with

[1] http://ec.europa.eu/information_society/eeurope/i2010/docs/benchmarking/ehealth_benchmarking_3_final_report.pdf

rather easily via the default network connection of the hospital or research centre or, in the worst case, via 3G connectivity.

Nowadays hospitals and research centres are connected to ultrafast network infrastructures or at least have Internet connections at lower bandwidth, and include connectivity-related costs in the institutional operating costs. Furthermore, the always decreasing connectivity costs compared to the increase of capacity would allow other partners and new users to easily adopt a network connection performing enough to access DECIDE infrastructure, applications, data and resources.

From the project's point of view, to have data owners and data processing sites inter-connected by the NRENs and GÉANT is an optimal configuration, because of the quality of service the network providers guarantee, and the opportunity to exploit tailored services they can offer: however, it is not a necessary condition, as both the NRENs and GÉANT are open networks which are interconnected to the general Internet and can of course be reached also from commercial providers.

GÉANT interest in DECIDE is not strictly related to the project's activities: rather, it is of indirect sort, since DECIDE is a representative of the medical/research user community which is using the network. In this respect, DECIDE fits in GÉANT vision[2] for 2020 of extending its user base to any public sector where economies of scale can be achieved.

DECIDE will maintain stable relationships with NRENs and GÉANT, as these can be important vehicles to establish contacts at a policy level.

3.1.2. GRID infrastructure

The DECIDE Grid layer is a distributed storage and computing infrastructure interconnected through the high-bandwidth network provided by GÉANT and the NRENs. The DECIDE Grid infrastructure enables access to distributed resources to process data and perform the automatic extraction of biomarkers. The DECIDE Grid infrastructure is interoperable and integrated with the EGI (computing and storage resources) and EMI (middleware) European flagship initiatives, strengthening the reliability and manageability of the services and establishing a sustainable model to support, harmonise and evolve the service itself. The integration with the largest DCIs (Distributed Computing Infrastructures) will assure the DECIDE service to be accessible and usable by the widest European biomedical community. The principal Grid stakeholder of the Project are:

- Core Project Partners (COMETA, GARR, UNIFG, UWAR for the production environment and CNR, ICL, FbF, Maat-G, SDN and UNIGE for the testing environment)
- National and European Grid initiatives

MoUs have been signed with EGI, EMI and other Grid projects and initiatives, to ensure computational capacity and operational support. In particular, as agreed in the context of the MoU signed with EGI, DECIDE representatives will seat in the EGI User Community Board, thus establishing a strong and effective channel to communicate requirements and solve possible issues.

[2] http://cordis.europa.eu/fp7/ict/e-infrastructure/docs/geg-report.pdf

With very limited exceptions, DECIDE is using standard Grid services, which are in the official service portfolio developed by EMI and are of widespread use within EGI. The exceptions are represented by:

- KeyStore service: this is currently provided as a virtual machine, set up and maintained by INFN. A KeyStore service will be hosted by each site owning data to be shared in the infrastructure, e.g. by hospitals sharing their scans of normal subjects: the service will be contacted, in a secure manner, by applications in order to obtain the cryptographic key needed to decrypt data files stored in Storage Elements.
- gLibrary: this is a tool developed by INFN in close collaboration with COMETA, whose aim is to offer a robust, secure and easy-to-use system to handle digital assets stored as grid files. It is currently used also in the context of other projects related to different domains as well as e-health.

As a consequence, these services are the most critical Grid components in terms of sustainability. For both components, DECIDE will leverage on the MoU's already signed with EMI and EGI to push for their adoption in the official portfolio of services being developed (in the case of EMI) and deployed (in the case of EGI). In fact, the availability of such components as off-the-shelf components is an obvious sustainability driver for DECIDE, going in the direction of decreasing the development and maintenance costs.

Turning now to individual Grid infrastructure providers, two categories can be identified.

In the first category fall those Grid sites (third parties external to the Consortium) offering only computing capacity. From the Grid site perspective, this implies accepting the VO vo.eu-decide.eu. Supporting a VO on one's own site implies a one-time re-configuration of the batch system (Computing Element and Worker Nodes) requiring, more or less, just a couple of hours: re-configuration can be scheduled during a downtime declared for other reasons, so as not to affect the site's availability. Supporting a VO is a site-level decision, hence it is fully voluntary, however there is a number of reasons why a site would like to activate support for a new VO: adhering to directions given by the relevant NGI, liaisons with personnel involved in DECIDE project, or simply the willingness to make the best use of free CPU cycles. The only possible concern is connected with the job turnaround time, if it is too long it will affect the user experience and perceived quality of the service. To limit this risk, the project will take two actions:

- Monitor each site and possibly exclude non-optimal ones from topBDII;
- Prepare a specific MoU requesting a minimal level of support for the VO: this can range from the setup of a dedicated queue with guaranteed share of resources, to the definition of a policy to give higher priority to jobs based on their anticipated maximum duration.

From DECIDE perspective, such sites are important because the relevant extra resources improve the overall reliability of the service as they increase the chance that a job will find a suitable slot to run. The fact that the computing power provided by third parties external to the consortium is for free, on one hand cuts the e-infrastructure costs and allows for a wide scalability of the e-infrastructure even in the event of a widespread uptake of the service across multiple public health systems

across Europe, but at the same time it also poses some limitations to the possible business models for DECIDE: in particular, it implies that the project cannot bill users on the basis of, e.g., the number of jobs executed, but can only ask to cover the expenses of user support, training etc (see Chapter 4 for a detailed discussion on business models) and strongly suggests that the access to resources should remain free for some user categories, e.g. researchers, who have limited need for these items.

The second category of Grid sites comprises those offering storage space. For these sites, the voluntary approach is not a viable solution as they are more closely connected to the quality of the service DECIDE is offering to its users. To assure that adequate performances are offered, these sites need to be dedicated and, at least in an initial phase after project end, they will coincide with the sites maintained by project partners, who will formally commit to offer a reasonable amount of storage and the needed manpower free of charge for some amount of time. However, the sustainability model will need to include costs related to the provision of physical disk space and its maintenance, which are estimated in Chapter 5, and the incremental costs involved in enlarging the storage infrastructure.

Other sustainability drivers in the domain of Grid infrastructures are the enlargement of the users base, and the synergy with other projects. For example, a project aiming at enlarging the DECIDE application portfolio will definitely provide some resources to keep the infrastructure alive, and this will effectively turn into covering some of the infrastructural costs.

3.2. Users

3.2.1. Research and Clinical Groups

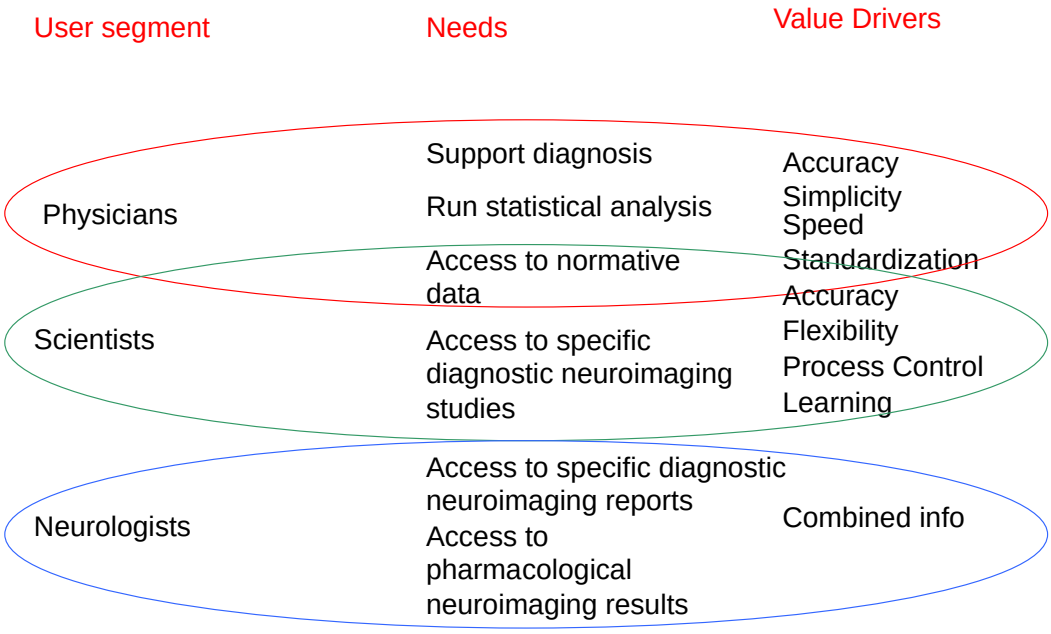
DECIDE service is targeted to specific biomedical research and clinical groups and could be represented in a specific biomedical Virtual Research Community devoted to the development and/or use of new diagnostic tools relying on imaging facilities. Three main profiles may be distinguished in such community:

a) Neurologists and Geriatrists as users of Life-science and biomedical communities, acting along the whole data management process, taking care of all the related medical, ethical and privacy issues associated to the clinical management and decisions on the elderly patients with cognitive decline;

b) Clinical physicians, acting at a specific stage of clinical process, as Clinical Neurophysiologists, Radiologists, Nuclear Medicine physicians who provide diagnostic information from PET, MRI and EEG exams, relative to the specific test of competence, reporting changes in the diagnostic and therapeutic data under study;

c) Scientists, dealing with advanced algorithms for data processing/integration and extraction of markers, including Physicists, Mathematicians, Statisticians, Engineers who collaborate with Neurologists and Clinical Physicians to provide knowledge and comprehension of the methodology used to support medical diagnostic or therapeutic decisions.

The picture below summarises the principal needs and related value drivers for each of these profiles.



The three groups of potential users match the "user profiles" which have been defined within DECIDE project.

As an important value driver towards these users, DECIDE has taken actions to explicitly address their interests while designing and implementing the service. Potential users have been involved very early in the project lifetime, and their feedback has been (and will continue to be) duly taken into account. Having a service tailored to user needs (in terms of usability as well as in terms of algorithmic performance) is obviously a key element to ensure service adoption after the pilot phase, eventually supporting the service sustainability.

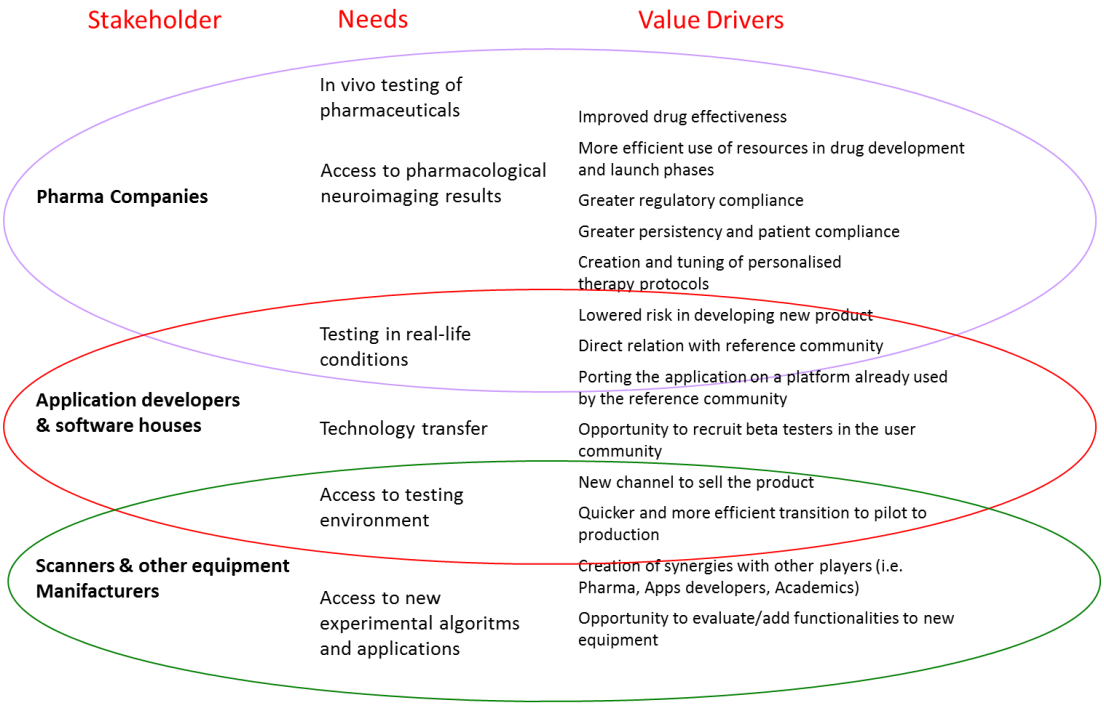
An additional value driver is the training and qualification of users. Competence tends to be a matter of particular concern when assessing some professional disciplines, such as in medicine, health, teaching and social work. In the framework of DECIDE, high competence and many innovative skills, integrating different know how and experience will be required, by all users needing to learn how to work with those innovative services.
Specific training programmes devoted to specific user profiles have been put in place to allow that kind of competence to assure the service adoption by scientists and physicians as described in D3.3.6 and D3.3.7.
Training can play a key role in the success of a service such as the one offered by DECIDE, where ease of use and accuracy are important requirements, and this should be reflected in the development of a suitable business model. In addition, training costs are relevant cost item. These two aspects strongly suggest that the new users' participation in training and qualification programmes should be on a fee basis.

3.3. Private Companies

Developing an innovation-driven economy is crucial for competitiveness. The Commission's broader innovation strategy highlighted the necessity to use consistently and strategically tools and instruments in support of innovation, with a

demand-driven approach. The report "Creating an Innovative Europe", the EU 2006 Competitiveness report, and stakeholder consultations also concurred in concluding that Europe must seek to develop innovation-friendly markets in a more targeted way, decisively facilitating the marketing of innovations. SMEs and enterprises would benefit from support such as activities to facilitate the knowledge-transfer to be used in some market segments like software development, equipment vendor (e.g. Grid and network equipment), scanner manufacturing. Private stakeholders are closely involved in issues relating to interoperability, integration, and standardization. This group of stakeholder is also represented in the Lead Market Initiative[3], for which eHealth has been selected as one of the markets.

The picture below summarises the principal needs and related value drivers for each of the categories which will be discussed in the following sub-chapters.



Private stakeholders would develop new technical solutions and tools and, generally speaking, "products" dedicated to different biomedical market segments, after an experimental and testing phase carried on the DECIDE infrastructure. This collaboration will give back DECIDE new products, tools and equipment built on specific requirements basis.

3.3.1. Application Developers

The DECIDE infrastructure is hosting tools to detect biomarkers, thus targeting the biomedical application developers' community. From this perspective, DECIDE is an application provider infrastructure, making tools available to the clinical and research biomedical community. The DECIDE environment is devoted to research and diagnostic service activities: validated tools will be exploited to obtain markers to be used in the daily clinical activities, while experimental tools and biomarkers would be

[3] http://ec.europa.eu/information_society/activities/health/policy/lmi_ehealth/index_en.htm

validated and run using the testing infrastructure. Once a tool has been validated, it could be offered as service in the ScienceGateway infrastructure. The DECIDE environment is flexible and able to host applications both validated and open to research and development. This structure is expected to attract stakeholders from the research and industrial sectors who would test or use the DECIDE algorithms or infrastructure to develop new tools.

It is envisaged that the business model of DECIDE includes strict relationships with private Companies (i.e. Software houses) to exchange or have access to technologies for diagnostic services either on a fee or on joint venture basis. Specifically, it will be also possible to have software packages developed on a free basis under agreements between DECIDE and Software Houses involved in biomedical activities: in this case DECIDE Consortium could use new developed tools on top of free available tools providing new services.

3.3.2. Scanner Manufacturers and Pharmaceuticals Producers

Stakeholder interest in this area is different with respect to the kind of markers included into the DECIDE service such as MRI, ^{18}FDG-PET, and EEG markers.

MRI and ^{18}FDG-PET markers

What is common to hippocampal atrophy as measured from MRI and temporo-parietal hypometabolism as measured from ^{18}FDG-PET is that there is no currently formal requirement (e.g.: Practice Guidelines from scientific societies) to use quantitative metrics for the diagnosis with the new clinical criteria. Although new data acquisition methods and sophisticated image-processing algorithms are poised to make a substantial impact on our ability to make precise quantitative measurements of the structure and function of regions within the human brain, this practice is left at the discretion of individual neurologists and neuroimaging academic clinical centres.

Intuitively, there is value in providing physicians quantitative data regarding regional structural atrophy or regional hypometabolism in the brains. However, the use of MRI and PET in clinical practice still faces many hurdles. These include technical challenges to obtain precise measurements and barriers to the acceptance of new clinical data and procedures in daily practice, such as the lack of information about sensitivity and specificity in real- world clinical practice and some logistical challenges for incorporating the techniques into daily workflow. For these reasons, still the majority of physicians prefer to make a diagnosis by observing and evaluating qualitatively the MR and PET images with their own expert eyes.

This implies that until predicaments from scientific societies will be issued, the inclusion of quantitative metrics in the diagnostic process will chiefly be of interest to organizations and centres where research and clinical praxis are deeply intertwined, i.e. research and healthcare centres, university hospitals, etc. The DECIDE infrastructure has already solved many of the technical hurdles reported above through clinical based studies guiding the use of the technology and has avoided inappropriate uses of the infrastructure. Nevertheless, at this stage it is still unclear whether these players would be prepared to pay for the access to an e-service as the one proposed by DECIDE.

As far as the hippocampal atrophy on MR is concerned, the major scanner manufacturers are currently investing on the development of automated hippo

segmentation algorithms. Hippocampal volumetry is the most widely studied quantitative magnetic resonance imaging measure in Alzheimer's disease, and thus represents the most rational target.

Currently, the biggest effort is to fine-tune the magnetic transfer (MT) contrast making it much more sensitive to subtle histological changes, and improving the capability of automatic algorithm to segment the correct hippocampal region. In addition to sensitivity, reliability and precision are crucial for any non-invasive imaging quantitative parameters in assessing disease substrates for both cross-sectional and longitudinal studies. In this context, various magnetic transfer measurements (e.g.: histogram metrics, mean magnetic transfer ratios, etc..) are under evaluation and comparison. All major scanner manufacturers (e.g.: GE, Siemens and Philips) are launching on the market right now scanners with already integrated advanced neurology imaging software (Table 1).

	GE	Philips	Siemens
MRI	Dynamic VUE: display, analyze and process sets of dynamic PET images. The main apps available today for neurology are: 1) Integrated Registration 2) Brain-Wave	Extended MR eXplore WorkSpace (EWS)	Syngo MultiModality Applications for post-processing and Intelligent Computer-Aided Drafting (CAD)
PET	Dynamic VUE: display, analyze and process sets of dynamic PET images. The main apps available today for neurology are: 1) Integrated Registration 2) Cortex ID	Extended MR eXplore WorkSpace (EWS) with NeuroQ app	Syngo MultiModality Applications for post-processing and Intelligent Computer-Aided Drafting (CAD)

Table 1 Summary table of the algorithms available today for clinical use by the 3 main Scanner Manufacturers. For the time being, none has an algorithm for automatic segmentation of the hippocampal region. Same consideration goes for the voxel-based analysis (VBM) of the brain regions to assess temporo-parietal hypometabolism.

In this light, hippocampal segmentation algorithm for single subject analysis may be available in the next 2-3 years and when this happens, applications will be built into the scanners allowing flexible quantitative measurement of valuable data supporting early disease detection and diagnosis. It will enable fast routine analysis and simplify the hippocampal border segmentation study thanks to automatic or semiautomatic tools. These algorithms characterized by the ability to generate accurate contouring should enable clinicians to process more cases in less time as well as in a standardized way.

Until that time, the ADABOOST application in the DECIDE platform will have a place in academic clinical practice, but after that time, it might be of interest to researchers only. In fact, the latters will continue to use hippocampal segmentation algorithms to constantly characterize and understand better the evolution of the Alzheimer's disease and its pathogenic mechanisms.

With reference to the study of the PET imaging biomarkers, the DECIDE

infrastructure is practically not interested in the study of the amyloid imaging, mainly because the scanner manufacturers have already monopolized the development of advanced integrated tools capable of analyzing and quantifying reliably the results directly from the seat of the radiologist.

Although PET is still comparatively limited in terms of diffusion, the Temporo-Parietal hypometabolism on ^{18}FDG-PET scans is instead a promising marker. Despite its first commercial appearance in the late 1970s, positron emission tomography (PET) did not gain widespread acceptance as a viable clinical technology until the mid-1990s.

This change is largely due to the inclusion of PET among diagnostic tests eligible for reimbursement by the public health system, and of radiopharmaceuticals among eligible medicaments.

The diffusion of PET, which is still growing, may help pharmaceutical companies developing new drugs to try to attack the disease much earlier than today. So far, there are no drugs altering the course of Alzheimer's disease and, in this context, the adoption of the SPM Grid and DECIDE platform by Pharma industry will provide a formidable spur to test the efficacy of new candidate drugs.

Moreover, as reported in table 1, even if all the PET manufacturers are currently developing ^{18}FDG-PET applications built into the scanners, all these are mainly focused to facilitate the use of PET scanners, streamlining the visualization and analysis of data through the provision of specific viewer applications. Conversely, none of the major scanner manufacturers is currently investing money on the development of automated algorithms for the detection of the "classical pattern" of temporo-parietal hypometabolism via Voxel-Based-Morphometry (VBM). Hence, this scenario opens to business opportunities for the exploitation of the DECIDE GridSPM algorithm in this field and suggests that pharmaceuticals may become a key user of the DECIDE platform, and/or establish joint ventures with the project.

The DECIDE consortium is aware that the algorithms developed within this project are not the only ones in use for processing structural and functional data. As a matter of fact, in recent years a number of software have been developed allowing the comparison of an individual ^{18}FDG-PET study to an age matched normal database. Three of the most popular automated programs for estimating the hypometabolism are (I) PMOD/PALZ (II) 3D-SSP/NEUROSTAT (III) SPM8.

PMOD/PALZ implements the automatic Alzheimer discrimination method developed by Herholz, which is based on the outcome of a vast multi-centre trial. It is characterized by a very good sensitivity and specificity for differentiation of patients with suspected Alzheimer's disease from the controls (100% and 83% respectively). PMOD/PALZ is commercially available.

The program called 3D-SSP/NEUROSTAT, developed by Professor Satoshi Minoshima, is available free-of-charge. This software is used for the discovery of posterior cingulate hypometabolism in AD.

Last but not least, the original SPM8 program, from which has been gemmed the SPM Grid tool, should also be mentioned. It allows VBM analysis although it is a bit too complex for physicians. Upon successful completion of a mandatory training programme (paid by the user), user is granted free use the software, which however requires the commercial license of Matlab to run.

All these tools have been available since 2000s but, apparently, were not of any

interest for the scanner manufacturers, since they have never been integrated in any PET scanners.

This said, it is clear that competitors are currently present, but they are not particularly rooted in academic clinics.

Therefore, the lifetime of SPM Grid seems to be reasonably longer than ADABOOST's. In fact, SPM Grid offers three key points that are able to strengthen itself and are represented by: (1) the availability of a substantial number of control PET studies suitable for statistical comparison with patients, (2) the use of a platform equipped with specific commercial licensed software, and (3) the set up of the SPM statistical design for clinical neurological single-subject comparisons. Meeting the first requirement is very complex, due to ethical issues and to the costs; the second one implies additional costs as well as maintenance; the third one limits the use to nuclear medicine centres with great expertise in statistical methods. All these points can be answered thanks to the DECIDE support center and the technical solutions adopted in the project.

EEG markers

The use of EEG markers in clinical practice requires a final experimental validation to overcome the barriers to the acceptance of new clinical data and procedures in daily practice. We need more information about sensitivity and specificity in real-world clinical practice, and there are of course some logistical challenges for incorporating the techniques into daily workflow to be tackled. However, there is a growing interest of the AD community towards EEG markers (see for example Alzheimer research forum; http://www.alzforum.org/new/detail.asp?id=2977). As a result, there is a strong interest of private Companies in the field of biomedical instruments and Pharma Companies to the validation of EEG markers for the diagnosis of AD. For example, EEG markers for AD are investigated in all experimental work packages of the bigger European project on AD such as "PharmaCog", which includes all most important European Pharma Companies such as GSK, Lundbeck, Janssen, Roche, ESAI, Eli Lilly, UBC and was granted for more than 20 million of Euro (IMI Undertaking Neurodegenerative disease; http://www.alzheimer-europe.org/Research/PharmaCog).

The mentioned interest is not surprising. In the last years, several studies of DECIDE partners have shown that quantitative analysis of resting state eyes-closed EEG rhythms is a low-cost, easy to perform, and widely available neurophysiological approach to the study of AD and MCI. Indeed, resting state EEG markers are virtually not affected by metalearning relative to task processes, anxiety for performance, emotional variables, skillfulness, and subjects' social compliance. Furthermore, recording of the resting state EEG rhythms can be repeated countless times along the AD progression with negligible repetition effects on EEG markers used for therapy monitoring. Finally, resting state EEG rhythms seem to provide -at least at group level- useful markers/end points to evaluate disease progression and pharmacological intervention in amnesic MCI and AD subjects. Specifically, previous studies of some DECIDE partners have shown the following results on resting state eyes closed EEG rhythms in AD, MCI, and normal elderly (Nold) subjects: (1) dominant alpha frequencies (8-10 Hz) of EEG rhythms were specifically abnormal in AD subjects when compared to Nold and cerebrovascular dementia (VaD) subjects; (2) delta (2-4 Hz) and alpha rhythms are related to attention and global cognitive status in both MCI and AD subjects; (3) alpha rhythms were more altered in MCI and AD subjects

with ApoE-4 (i.e. genetic risk factor for AD) than non-ApoE4 carriers; (4) haplotype B of CST3 (i.e. genetic risk factor for AD) was related not only to alpha rhythms, but also to delta rhythms (2-4 Hz) in MCI and AD subjects; (5) brain white-matter atrophy and delta rhythms were related to each other in MCI and AD subjects; (6) long-term (1 year) cholinergic therapy (i.e. Donepezil) was just able to slow the decline of alpha rhythms in AD subjects; (7) combined power and linear functional coupling of EEG rhythms predicted conversion from MCI to AD after about 1 year; (8) non-linear functional coupling of EEG rhythms was abnormal in MCI and AD subjects; (9) delta and alpha rhythms were related to neuropsychological measures of immediate memory based on focused attention in MCI and AD subjects; (10) serum 'free' copper (i.e. a typical biomarker of AD) was related to alterations of EEG rhythms in AD subjects, namely an increase of the pathological delta rhythms; (11) delta rhythms were related to the amount of blood serum homocysteine, an amino-acid with neurotoxic effects; (12) power and directionality of functional coupling of EEG rhythms were abnormal in MCI and AD subjects as a function of white matter vascular lesions; (13) hippocampal atrophy was related to the decline of alpha rhythms in MCI and AD subjects; (14) damage to the cholinergic system was associated with alterations of alpha EEG power and functional global coupling in MCI subjects; (15) alpha rhythms were altered in subjects with subjective memory complaints (no objective memory deficits) compared with MCI and Nold subjects; (16) alpha rhythms was related to stability of clinical condition in MCI subjects; (17) delta and alpha rhythms did not deteriorate with the increase of white-matter vascular lesion in MCI and AD subjects; (18) the decrease of alpha rhythms was higher in AD than Parkinson's disease subjects. In general, these mentioned data suggest that resting eyes-closed EEG rhythms can provide reliable neurophysiologic information on AD and MCI subjects, which would be related to neurodegenerative processes as indexed by brain atrophy and biological markers of neurodegeneration. As mentioned above in this document, a recent study of the DECIDE Consortium showed 80.2% of mean sensitivity, 61.8% of mean specificity, and 71.8% of mean accuracy of the EEG markers. Area under ROC curve was of 0.78. These results allow a moderate classification of Nold and AD individuals, which is potentially useful for the preliminary screening of large populations of elderly patients at risk of AD. Therefore, Public and private stakeholders in the field of AD diagnosis are interested in the development of cheap and largely available EEG markers for a preliminary screening of elderly subjects with cognitive decline and suspect to progress to AD. DECIDE service represents the first example of an experimental use of EEG markers in clinical practice.

The conclusion of the present survey is that, in a short term perspective, the adopters of the DECIDE platform will tend to be a small segment of academic clinical centers and a more plentiful group of researchers in the public and private sector.

3.4. Public Institutions

European healthcare systems are the pillars of Europe's social infrastructure. Although they differ in terms of operational and financial structure, they share common goals and priorities such as universality, access to good quality care, equality and solidarity. More importantly, EU states also share common challenges. The funding of healthcare among EU Member States varies; however, they all rely on a combination of resource funding, with the majority of funds directly or indirectly

controlled by national state administration.

Member States have been taking a complementary and pro-active approach to e-Health. Council Conclusions adopted on 1st December 2009 called upon the European Commission to update the 2004 e-Health Action Plan. This has been followed up by the creation of the "e-Health Governance Initiative", driven by Member States and jointly supported by DG INFSO and SANCO[4]. The overall objective of the initiative is to actively contribute to shape the e-Health political agenda at EU level, with a specific focus on interoperability.

The technological advancements in electronic healthcare, also, are creating heightened public policy concerns about patient privacy and information security. These challenges can be addressed through advancements in technical standards for e-Health. The standardization process creates the necessary interoperability among healthcare systems, while minimizing the risks involved in new technology development and preventing single vendor lock-in.

This second e-Health action plan (eHAP)[5] provides an opportunity to consolidate the actions which have been addressed to date, take them a step further where possible and provide a longer term vision for e-Health in Europe, in the context the EU 2020 Strategy, the Digital Agenda for Europe as well as Innovation Union and its associated European Innovation Partnership on Active and Healthy Ageing (EIP-AHA)[6].

This vision is in line with the DECIDE approach and it represents an opportunity to attract policy support and funding from the EC and the member states (see Chapter 4 for a discussion).

[4] http://ec.europa.eu/information_society/activities/health/policy/ehealth_governance_initiative/index_en.htm

[5] http://ec.europa.eu/information_society/activities/health/ehealth_ap_consultation/index_en.htm

[6] http://ec.europa.eu/research/innovation-union/index_en.cfm?section=active-healthy-ageing

4. EXISTING E-SERVICE BUSINESS MODELS AND THEIR APPLICABILITY TO DECIDE

In the following, five typical business models applicable to e-services, i.e. "subscription", "manufacturer", "utility", "advertising" and "infomediary" models, are briefly discussed, with their pros and cons, in relation to their applicability to DECIDE. In addition to those, other models which are not specifically related to e-services, but are typically applied to non-for-profit and public utility activities, i.e. the "educational", the "central funding" and "NGO" should be also taken into account. Given the intended European dimension of the service and the differences between EU countries' public health systems, however, it is quite unlikely that one of these models alone will be capable of sustaining the service across borders. It is more likely that a blend of two or more can more adequately address the sustainability issue, accommodating different sources of funding and different kinds of users/subscribers into a common framework.

1. Subscription model

In the subscription model, users are charged a periodic (daily, monthly or annual) fee to subscribe to a service. It is not uncommon for those who apply this model to combine free contents and services with "premium" (i.e., subscriber- or member-only) ones. Subscription fees are incurred irrespective of actual usage rates.

PROS: This model can answer the need for different service levels (e.g. Researchers Vs Clinicians, with the former who can live with a free, best effort service and the latter that need a "premium" service, with support and even expert consultancy for difficult or dubious cases), and is flexible enough to offer different subscription types to different kinds of users (e.g. single professionals Vs small clinical centers Vs large hospitals or even local/regional/national health systems) and adjust the pricing accordingly. In addition, being not connected to actual usage rates, it does not require any overheads in order to manage the usage accounting (as for the utility model, see below). Another important advantage of this model is that it can be easily integrated with other models (i.e. advertising, donation/sponsorship which could be beneficial in order to keep subscription fees low, or central funding, which could grant free access to certain subjects).

CONS: the main con is the fact that the subscription fee can be a significant barrier to the initial adoption of the service, and thus prevent many prospective users to actually try it; in this as in other models, it is not always clear who should buy the service (the public health system, the single hospital, etc), and in any case, if we exclude the case of single professionals (for whom, however, other barriers such as the dependence from third parties to perform the diagnostic tests and the need for the professional to access the DICOM data), the subject who uses the service and can be motivated to adopt it is not the same who pays for the service.

2. Manufacturer model

The manufacturer or "direct" model, is based on the opportunity, for the "manufacturer" (i.e., a company supplying products or services) to reach buyers directly through the web channel, and thereby to compress or avoid the distribution channel. This model can leverage on cost-effectiveness, and on the direct relation with the customer/user for delivering an efficient, tailored customer service, relying on the knowledge of the user behavior and preferences. For the DECIDE purposes, the sale of the service in this model could be offered under a license agreement. In

the license model, which is typically adopted for software, the sale involves only the transfer of usage rights to the buyer, in accordance with a "terms of use" agreement, while ownership rights remain with the manufacturer (e.g., with software licensing).

PROS: the model is very simple and flexible enough to allow for different sorts of licenses (i.e. single subject, groups, educational,…); it is a well-known model and understandable by prospective buyers.

CONS: the main problem with this model is that not all applications deployed on the DECIDE e-infrastructure are owned by project members: as a matter of fact, two of them –and those of proven diagnostic value, are by third parties, which makes of course impossible to license them without prior agreement with the third parties who produced the software. This would in turn make the whole governance much more complicated, unless these third parties are interested in joining the consortium on a peer basis.

3. Utility model

The "utility" or "on-demand" model is based on metering usage, or a "pay as you go"/"pay per performance" approach. Thus, metered services are based on actual usage rates. Billing can be based either on Metered Usage (measures and bills users based on actual usage of the service) or Metered Subscriptions (allows subscribers to purchase access to content in metered portions, e.g., numbers of patient studies processed).

PROS: this model shares most of its pros with the Subscription model, adding an even finer-grained billing system, which could be in principle more comfortable for the prospective users in order to try the service. It could allow different payment methods (e.g. micro-payments via credit card or paypal etc, i.e. per single patient processed Vs periodical billing), which could also be a factor of success.

CONS: this model shares the cons of the subscription model, adding a significant one: the overhead needed to manage the accounting and billing procedure, which can be significant in the event of a large and widespread number of users across different countries.

4. Advertising model

The web advertising model is an extension of the traditional media broadcast model. The "broadcaster", in this case, a web site, provides content and services mixed with advertising messages. The advertising messages (e.g. by banners) may be the major or sole source of revenue for the broadcaster. The broadcaster may be a content creator or a distributor of content created elsewhere. The advertising model works best when the volume of viewer traffic is large or highly specialized.

PROS: the model is very simple and offers a very significant advantage in comparison with the previous ones, i.e. the opportunity for qualified users to access the service for free. In this way one of the most significant access barriers for the first adoption of the service is removed; it should be highlighted that this barrier is irrespective of the access costs being low or high, as buying something, being it a service, a software etc, implies in many organizations, and namely in the public sector, a procedure which can be slow and complicated, and may entail tendering etc. In addition, the absence of fees or bills simplifies much the user management.

Although in a short-to-medium term perspective the volume of users for the service is not likely to be very large, it will be very specialized, so it is expectable that

companies interested in addressing neurologists, neuropsychologists, imaging experts etc (typically pharmaceuticals, medical equipment vendors, etc) could be interested in this kind of exposure, which could as well be complemented with targeted communication with users, also on the basis of their preferences (see also next point).

CONS: Even if it simplifies the user management, billing, and accounting procedures, in order to be efficient this model requires a well-focused publicity sales activity, which is not part of the core activities of any of the DECIDE partners, so the adoption of this model would require adding new competences in the consortium, and solely for the DECIDE purposes (this would not be a problem if the consortium decides to go for a new legal entity but would otherwise complicate the governance).

Furthermore, given the limited number of users involved, at least in the first phases of the service, it is extremely unlikely that advertisers, although interested, are prepared to cover the whole costs of the service, which makes this model unrealistic if used alone. On the other hand, it could be useful if integrated with the subscription, utility or manufacturer model, to allow for sponsored free access periods (or licenses), promotions, etc, or simply to cover part of the costs and keep the fees/bills/license prices to a minimum. Promotions can be also used to further induct new users to try the service if one of the three non-for-free models is adopted.

5. Infomediary model

This model is based on the assumption that data about users and their consumption habits are valuable, especially when that information is carefully analyzed and used to target marketing campaigns. Independently collected data about producers and their products are useful to users when considering a purchase. Some firms function as infomediaries (information intermediaries) assisting buyers and/or sellers understand a given market and their need.

PROS: this model shares with the previous one its two main pros, i.e. the opportunity to offer free access to the service, and the very specialized user community.

CONS: it is unlikely that this model can be applied to the DECIDE service as such, because of course it cannot be lightly applied to the patients' data for obvious privacy reasons, and although it could be in principle applied on the user's behavior, the information on this subject does not seem to be attractive enough for some company to spend to acquire it. This is not just connected to the limited numbers involved, which would make the collected information not so much statistically relevant; at the moment the user interaction with the platform is designed to be the most simple possible, which makes it not much informative from the point of view of a company interested in buying information on the users' behavior. In the future, with more functionalities added, and possibly with the further integration of the prognostic process, this could become an additional option (for instance, to correlate information about the diagnosis, the medications adopted for the patient, etc.

6. Educational model

The educational model is not specifically applied to e-services, and it is mainly adopted in the freeware and open source software sector, as an alternative to the license-based model, often integrated with the subscription model (for support) and with the next one (to ensure additional fundraising). In this model, the software is licensed for free, upon the acceptance of a term of use, but the user pays for training and qualification.

PROS: this model suits very well the DECIDE approach, where a user needs be qualified in order to access one or more algorithms and exploit them for diagnostic purposes, and it is used in the medical environment for similar software.

CONS: even so, it is unlikely that this model alone is capable of sustaining all costs connected with the e-service, as the users pay once for the course, but can keep using the service, and the user support for years and years. Furthermore, a single professional could qualify and process all patients of a large hospital, which is of course allowed by the model, but would make the costs for this hospital equal to those of a single professional or a small centre. This model should hence be integrated and corrected with others.

7. "NGO" model

This model bases on the assumption that the DECIDE service is of public utility and provides added value to the society as a whole and, because of its societal value, there are individuals, companies, foundations, and other subjects that are prepared to sustain it through donations and sponsorships.

PROS: as for the advertising and infomediary ones, the main pro of the model is that it provides free access to the service.

CONS: the problem with this approach is that it is unsure and falls largely out of control of the project partners, while the competition for getting donations and sponsorships, especially in times of austerity, should not be underestimated and many charities and foundations can count on a much higher visibility, a greater understandability of their objectives and immediate outcomes etc. In principle, it is not impossible for a service such as DECIDE to create a foundation and attract donations etc, with a sharp, widespread and well-focused dissemination and fund-rising strategy, although it seems very unlikely that this would cover all the costs involved in delivering a production-quality service.

8. Central funding model

The model is based on the assumption that DECIDE provides a scalable, cost-effective, innovative and easy to use solution to perform the early diagnosis of AD and that this early diagnosis is valuable for some subject- because it allows to save money, improve the patients' life, impact on the medications selected for slowing down symptoms and hopefully, in the future, to cure the disease- and that, because of this, this subject is prepared to pay for the service. Potential funding agencies in this perspective could be the EC, national governments, and even large pharmaceuticals. The EC generally demands member states to cover the production phases of e-infrastructures, and it is unlikely that this will change in Horizon2020. For this reason, the EC could be an additional source of funding (typically, on a project basis e.g. for widening the infrastructure or to add new algorithms or functionalities), but not the only one. Member states are of course a good option, and AD is for sure one of the key health priorities in many member states. However it is unlikely that all member states will adopt promptly the service centrally, unless it becomes a European standard (a process that could take years even in the best case), nor that there won't be differences in the funding models of different states, in the procedures needed to obtain the funds, and in the timelines to get funded. For this reason, although convincing one or more governments to pay for the service would be a major step towards sustainability and the actions aimed to achieve this are at the top of the DECIDE agenda, this model should not be considered as exclusive, lest

the risk of losing the European dimension of the service.

Central funding from a large pharmaceutical may be the only option to keep the European (or even wider) dimension while avoiding to multiply the funding sources, procedures and agencies. However, to achieve this, the project should focus on strengthening the bonds between early diagnosis and the therapy.

PROS: central funding can ensure a constant budget over several years, thus making a major step towards sustainability. It also would imply a widespread diffusion of the service in one or more countries, hitting virtually all the relevant users – a result which would never be accomplished in the medium period addressing single organizations.

CONS: the main con for this model is that it is not "central" enough, as the most likely source of funding is not at the European, but at the national level (and in some countries it could also go down to the regional one), which would make a simple model much more complicated and risk to lose the European dimension.

5. SUSTAINABILITY ROADMAP

In view of achieving a long term sustainability, the project consortium must:

1. Establish DECIDE operating costs in terms of incremental hardware, human resources, training the user-communities. The costs may change as the dimensioning of the service varies, although this aspect could be more relevant for certain cost items (i.e. for instance the user support or the training, which is directly dependent from the number of users) than for others (i.e. for instance the hardware needed). These costs are estimated later in this chapter.
2. Identify a sustainable business model that will allow partners to cover the service costs, and appropriate sources of funding. In order to do so, an assessment of existing business models that can be applied to e-services is given in previous chapter, where the applicability of the models to the DECIDE service is also discussed.
3. In close connection with the previous point, the project Consortium will decide about the service and e-infrastructure governance after the end of the project, as the project Consortium is not a legal entity, and the Consortium Agreement that regulates the relation among project partners will most likely terminate with the project itself. The discussion on this important point, that in a longer term perspective could bring to the creation of a novel legal entity, or to empowerment of one of the partners as the service provider, has already started and it is briefly summarised below in Chapter 5.3. A shorter-term solution could be either extending and widening in scope the operating Consortium Agreement or to sign a new MoU. In any case, the solution should also cover (a) the rights and obligations of partners who decide to withdraw from the agreement and not to support the service anymore and (b) the policy to allow new partners to join.
4. Perform a market analysis in order to determine: (a) the approximate size of the potential users' pool, (b) the existence of potential competitors (e.g. similar services, software performing similar functions, algorithms embedded in vendors equipment) and (c) the projects' positioning in relation to potential competitors. This market analysis will complement the stakeholders' survey discussed in Chapter 3 and the potential users description given in Chapter 2.3 and will allow to refine the selected business model, and, if applicable, determine appropriate pricing policies.

5.1. Timeline

The project is bound to end on August 2012. However, following the recommendations emerged as an outcome of the 1st year review, the project Consortium is applying for a 6 months extension at constant budget, the (likely) approval of which would set the end of the project in February 2013.

All above analyses should be available by that time, while it is unlikely that either the governance or the business model will be fully in place, especially in case that Partners opt to go for the new legal entity option. However it is clear that, in order to avoid gaps in the service provision, the project Consortium will have a very clear plan and timeline to translate the selected strategy into practice by August 2012 or February 2013 at the latest, lest the early adopters and beta testers who are being enrolled at date should abandon the service. Despite the relatively small number of

early adopters (inside and outside the DECIDE Consortium), this would prove a serious risk for the project, as many of them are decision leaders in their community and thus considered a key to further extend the user base.

5.2. Costs Estimate and Streams of Revenues

Costs can be categorized as follows:

- Costs related to the infrastructure
- Costs related to service provisioning
- Costs related to user training and assistance
- Costs related to extending the application portfolio

5.2.1. Infrastructure costs

In this category fall all costs related to maintaining, operating and upgrading the network, computing and storage infrastructure, and with ensuring the availability of the infrastructure with production-level SLAs.

As per the discussion in paragraph 3.1.1, network costs can be neglected as they are generally "hidden", both in the case of hospitals and research centres and in the case of Grid sites.

However, some costs may be involved in case of new centres/facilities extending the core infrastructure that where not previously connected to their NREN or have not a high performance link, as they would need larger bandwidth to be effectively accessed. These cases are expected to be comparatively limited in number and will be tackled on a case by case basis. Anyway, the cost of the link is not expected to fall in the DECIDE infrastructure costs, but would be most likely covered by the entering partner or through specific agreements with the local NREN or other relevant parties (e.g. Ministries or other funding agencies, sponsors, etc.), which DECIDE may seek to favour.

Grid sites offering only computing resources do not expose any cost to the Project, hence can too be neglected: to first approximation, having such sites supporting the DECIDE VO can lead us to neglect the cost of computing resources tout-court.
On the hand, storage capacity is a real cost which is composed by several elements:

- The bare hardware cost: based on a survey among DECIDE partners, this currently amounts to some 150 €/TB;
- Infrastructural costs, to account for RAID redundancy, chassis and controllers cost, a fraction of other LAN equipment (FC and Ethernet switches, routers), air conditioning system, etc.: these can be estimated as to be roughly equal to the bare hardware cost, 150 €/TB;
- Operational costs, accounting for electric power for both the hardware and the air conditioning: assuming a storage system with 16 disks per chassis, powered by a 0.7 kW supply, and assuming a reasonable efficiency for the data centre (PUE=1.5) one can estimate 80 €/TB/year

To get the unit yearly cost for storage, one should also consider that:

- hardware is often acquired with a 3-year warranty, which is the period of time on which to average fixed and recurring costs;

- to ensure high data availability, data should be replicated in at least three instances: as a consequence, the unit cost grows by the same factor.

Summarizing, the estimated cost for disk space is of the order of 500-600€/TB/year. On top of this, the site will need to invest some manpower to cover the specific needs of the DECIDE VO: for example, to setup a monitoring system, to react to alarms, to setup and maintain the StorageElement. Such cost is expected to be small, since we are talking about sites which are already part of a production Grid infrastructure, and roughly independent of the DECIDE storage capacity, at least as long as we are dealing with storage sizes of the order of tens of TBs. Only the differential costs may be charged to DECIDE: as a rough guess we may estimate 0.05 FTE for an intermediate technical profile (assumed equal to 40k€/year) for each site. In total, this would amount to some 6k€/year.

5.2.2. Service provisioning costs

These include costs to setup, maintain and update the Grid infrastructure as well as the applications and the relevant databases. Specifically, the project will need to mobilise manpower resources to perform the following tasks:

- VO management: monitor sites' availability/reliability, handle VO tickets, install software packages, etc.;
- Reference database management: ensuring their availability and the security of stored data;
- ScienceGateway management: maintain the users' database, enrolling new users and ensuring the security of the credential;
- Application management: maintain and update software packages for example for compatibility with updates of generic software in use in the infrastructure (operating systems, Java, Apache, Octave, Grid middleware, etc.);
- User support: in case of technical malfunctioning and faults.

It is envisaged that the needed manpower will be of the order of 0.4-0.5 FTE, to be most probably provided by more than one actor. The required profile will be of rather high level, for a cost which can be assumed equal to 50 k€/year.

The overall cost would thus be in the range 20-25 k€/year.

5.2.3. User training and user assistance costs

The format for training differs for each application. As an example, the format which is being finalized for application GridSPM foresees:

- the availability of training material to be used before, during and after the training course;
- the setup of a 2-day (or 3-days, for the advanced) training course: the course will be held using virtual-presence systems like AdobeConnect. One application expert and one clinical expert will be available for the full duration of the course;
- the setup of a training qualification session, lasting one full day: again, one application expert and one clinical expert will be available the full day.

Assuming 4 courses will be held each year, and the hourly costs reported by partners for the needed manpower, one can estimate a total cost of 6 k€/year per application.

In this simplified model, costs related to the update of the training material have been neglected: a reasonable assumption is that the material would need minor revisions at least twice per year and possibly a deeper revision yearly.

As far as user assistance is concerned, the relevant cost critically depends on the number of users and may change with time as users get more acquainted with the applications. Initially, one can estimate that one expert for each application will be sufficient, who will devote to user support 0.1 FTE (or half a day each week, in two sessions, so as to meet the anticipated SLA to get expert's advice within 72 hours). If this is the case, the relevant cost would be of the order of 6 k€/year per application.

5.2.4. Extending the application portfolio costs

The probability to incur these costs depends on the actual availability of new algorithms which are deemed of interest to the project. Moreover, it is obvious that the exact costs will depend on the specific algorithm. As an estimate, we can consider the figures presented in DECIDE "Description of Work" for porting one of the algorithms to GRID (WP6: 3 months) and for middleware interfacing (WP7: 10 months for all four applications). Of the latter component, only a fraction much smaller than one fourth should be considered, since, by design, it can be expected that a lot of the work already done on the ScienceGateway may be reused with little effort. Moreover, it can also be expected that the new application developer will be interested in porting her algorithm to the DECIDE infrastructure, and thus would be willing to contribute effort to this aim.

Overall, one can assume 0.3-0.4 FTE from a high level technical profile, corresponding to an estimate of 15-20 k€.

5.2.5. Costs Summary and possible streams of revenues

On the basis of the above estimates, the overall cost of the DECIDE e-infrastructure to be fully operative ìs in the range of 20-25 k€/year, including maintenance, training and clinical services and update of the software procedures. Most of these costs (about 50%) are related to manpower for the maintenance of the infrastructure and training/technical assistance of new users. In addition, further resources (again, chiefly manpower) would be needed for awareness-raising activities, to induct new users to adopt the infrastructure, and to approach partners, funding agencies etc.

In principle, to mobilise these resources is in the capacity of the DECIDE consortium, which is prepared to allocate resources in order to avoid the interruption of the DECIDE service after the end of the project, expected for February 2013. To this end, a formal agreement is under study that will regulate the allocation of qualified human resources to the maintenance of the infrastructure and training/technical assistance of new users for at least one year after February 2013. This agreement should be regarded as a short-term solution in the case the project consortium should prove unable to collect external resources to maintain and expand the DECIDE service (i.e. National and international grants, contracts with Public and private entities interested in the technology or clinical services by DECIDE) in the next year.

5.3. Organisation Issues

Connected to the choice of a business model and the definition of a realistic business plan to ensure the longer-term sustainability of the DECIDE infrastructure is the organizational and legal framework. In simple terms, this issue can be summarised as: who will be the legal subject(s) to implement the selected business plan, sustain the costs hypothesized in previous paragraph, collect revenues?

This problem has also important governance implication, including: rights and obligations of partners, IPRs, decision-making process, distribution of costs and income, etc.

The DECIDE Consortium is not a legal entity and the Consortium Agreement, which is currently covering most of the above issues, is bound to end with the project itself. A decision about the form that the collaboration will take after that moment will be taken before the February 2012 project review, in order to start the needed steps to implement the selected solution.

Basically, the choice is to either delegate the management of the e-infrastructure to one of the partners, on behalf of the consortium, regulating this proxy with a private agreement (MoU or similar) among the partners, or to create a new legal entity.

Although the proxy solution could be preferred as a lightweight option, limiting the financial risk incurred by partners, it can be difficult to ensure to represented partners an adequate level of representation. Moreover, this solution has some intrinsic limitations, as it relies on a chosen organization with pre-existing purposes, priorities and procedures, which could be not fully in line with the most suitable model for DECIDE, or not enough flexible to fully implement it. Ideally, the partner selected to act as a proxy should have lightweight organization and procedures, in order to timely implement agreed actions (e.g. hiring new personnel, or signing an agreement with a sponsor or partner), a fact that could limit the capacity of larger parties, whose administration generally relies on more bureaucratic procedures, to play this role, although these would otherwise be good candidates because of their relative solidity.

The legal entity option is currently under evaluation by the Consortium. In particular, a study on possible legal forms and their implications for partners is ongoing and will be completed for PM24 with the support of APRE, the Italian Agency for the Promotion of European Research.

Most likely legal forms of such an organization would include:

- European Research Infrastructure Consortium (ERIC)
  An ERIC is an European instrument specifically developed for the operation of Research Infrastructures and it provides legal personality recognised in all EU Member States. An ERIC can benefit from exemptions from VAT and excise duty in all EU Member States and it may adopt its own procurement procedures, which have to respect the principles of transparency, non-discrimination and competition but are not subject to public procurement procedures.
- Research Spin-off
  A research spin-off is a company established by one or more public research organizations in order to facilitate the transfer of research results to the market. Being a driver of innovation in society, in many countries, these

companies enjoy special fiscal and legal conditions, and a lightweight process to be established. Many large research organizations, including some of the DECIDE partners, e.g. CNR, have specific regulations for establishing research spin-offs and dedicated personnel that can offer support to applicants.

- Foundation
  The term "Foundation" includes a wide range of legal entities, often set up for charitable or collective purposes, which are nevertheless characterized by some common structural elements.
  Unlike companies, foundations have no shareholders, although they may have a board, an assembly and voting members. Foundations are regulated by the purposes set out in their constitutive documents, rather than fiduciary principles. They have a distinct patrimony independent of its founder(s). As companies, foundations follow diverse regulations depending on the jurisdiction where they are created. In some countries, they are eligible for tax-exemption or enjoy favourable tax conditions.

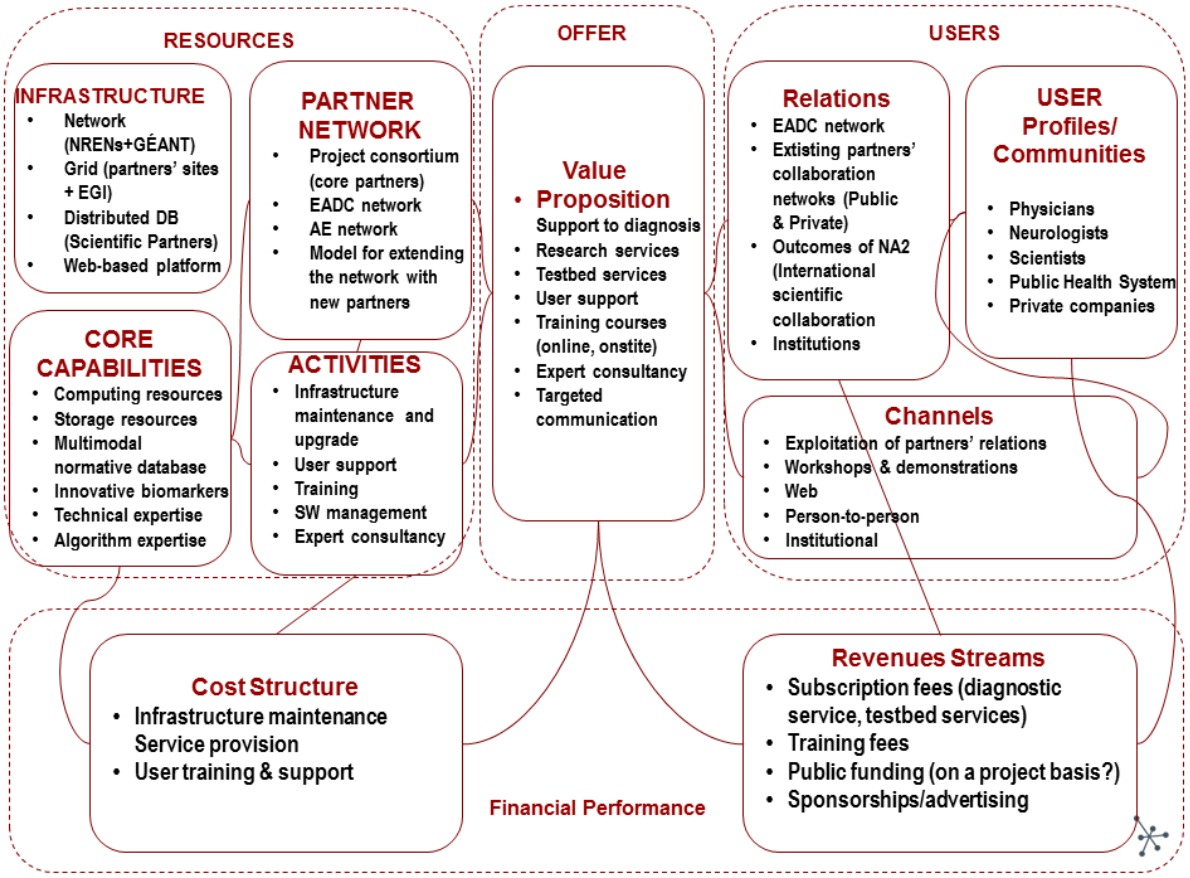
- Non-for-profit consortium or other form of association or company
  Under this label are included a number of diverse legal entities, all of them characterised by two elements: 1) the non-profit status, which implies that the organization uses surplus revenues to achieve its goals, rather than distributing them as profit or dividends, and 2) some direct form of representation of the shareholders. Also in this case, the new legal entity has a distinct patrimony.
  NPO regulations can significantly vary depending on jurisdiction, however as for foundation they are in many countries eligible for tax exemption or favourable tax conditions.

As highlighted above, the jurisdiction under which the new organization is created can make a difference in terms of legal steps to be taken for establishing the legal entity, tax status, etc. For this reason, alongside the study about possible legal forms to be adopted, some thoughts should be devoted to the place where the new legal entity should be incorporated.

6. CONCLUSIONS

The document described the plans for the DECIDE project to sustain the e-Infrastructure and service after project end.

The road to sustainability runs through understanding what are the resources which make the project appealing to users/entities outside the project Consortium, identifying what these users/entities are and (a) the best ways to reach them, (b) the most appropriate levers to stress in each case and (c) the possible sources of revenues to meet the anticipated costs. The picture below summarizes, in a graphical way, the outcome of the present study.



The project has taken several actions in line with the present plan and is already confident it will manage to sustain itself at least in the immediate term (1 year) after project end. The remainder of the plan is being defined in its details and implemented. The business model report, due by PM24, will report on the successes of the strategy, the challenges encountered and the actions taken to ensure DECIDE can play an important role in the European e-Infrastructure and service scenario.