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WP1 Development of regional registries and ICTUSnet platform

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This document describes the interoperability aspects of the ICTUSnet registry, with special detail on international and local standards used.

Revision history			
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V1	10/01/2019	Initial proposal	AQuAS
V2	25/02/2019	Adding contributions from all the partners	All
V3	27/05/2019	New version focusing on Semantic interoperability	AQuAS
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ABBREVIATIONS AND ACRONYMS

ERDF	European Regional Development Fund
ICTUSnet	"Excellence R&D network towards the successful development and implementation of innovative models of stroke care strategies"
Interreg	European Territorial Co-operation
Sudoe	Southwestern Europe

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EXECUTIVE SUMMARY

The present interoperability framework tackles the semantic and technical aspects of the central ICTUSNet registry and aims to help different stakeholders involve in the development of stroke registries, mainly those related with the endovascular procedures, to follow international recommendations (SNOMED-CT) and technical aspects once they consider to be part of the ICTUSnet network.

In this document, there are also a brief description of the stroke epidemiology and some aspects that were taking into account for every region to develop their stroke registry.

There is also a table with the list of variables that are part of the ICTUSnet registry, with their corresponding definition, SNOMED-CT code, values and labels to prepare a csv files ready to be interoperable with the central registry.

1. INTRODUCTION

The objective of the ICTUSnet registry, one of the main products of ICTUSnet project, is to create a South Western European repository of episodes of hospital admission due to ischemic stroke following a mechanical thrombectomy procedure. This repository will initially contain information of episodes from 6 regions of 3 different countries: Portugal (North), France (Occitania) and Spain (Aragon, Navarre, Balearic Islands and Catalonia); but it will be designed to allow its scalable evolution including more information about the episodes (i.e., more procedures) and the integration of the information coming from any European country. In this approach, defining an interoperability common strategy for the exchange of information is a must.

An interoperability framework has the objective to solve a concrete interoperability scenario, using already existing international standards. In this framework, reference standards are selected and particularized to the concrete needs of the considered project, starting from the description of the current situation of each agent involved in the scenario.

This document has the objective to define the Interoperability Framework for the ICTUSnet project, which is structured in the following sections:

- **ICTUSnet project:** General description of the ICTUSnet project, with the main related information: partners, calendar, etc.
- **SUDOE regional situation:** Description of the relevant characteristics of each participant region.
- **Definition of interoperability and its layers and Interoperability framework of the ICTUSnet registry:** general description of interoperability and specific characteristics of the ICTUSnet registry.

As part of ICTUSnet Work Package 1 (Development of regional registries and ICTUSnet platform/PortalWeb), ICTUSnet members are entitled to develop the present framework that will try to guide, not only partners responsible of the associated tasks, but other stakeholders interested in be part of the ICTUSnet registry.

2. ICTUSnet PROJECT

ICTUSnet has the mission of promoting collaboration in research and innovation to improve the integrated care and quality of life of patients affected by a stroke. The project is supported on new data analysis technologies and the creation of a network of excellence agents, sharing information, experiences and good practices using interoperability methodologies.

ICTUSnet project has three specific objectives:

1. Use of **innovative big data technologies** available to extract and analyse information and explore new perspectives on stroke care strategies.
2. **Analysis of collected information** and stroke care strategies on patients, with attention to the different health and profile characteristics. Study, agree and plan measures to enhance effectivity in stroke care strategies on severe stage and post-evaluation procedures to reduce impact on stroke consequences.
3. **Foster international and regional cooperation** by exchanging good practices, peer learning among the different regional initiatives, and implementing a common advanced training programme.

The project is based on the management and shared use of data related to the stoke care process in the participating regions, covering geographical areas with a total population of approximately **20 million inhabitants**.

As part of the project, the WP1 leading partner institution (AQUAS) has the objective to develop a South Western European repository including data from episodes of hospital admissions due to ischaemic stroke that underwent mechanical thrombectomy. The clinical information about these episodes will be transmitted from 6 different regions (regional registries) to the ICTUSnet registry (central registry).

3. SUDOE REGIONAL SITUATION

The ICTUSnet project involves 6 regions from 3 different countries: Portugal (North Region), France (Occitanie) and Spain (Aragon, Navarre, Balearic Islands and Catalonia). The following image geographically locates these different European regions:

Figure 1. Location of the regions involved in the project.

Markers in the map also identify the partners of the project (involved in the exchange of information) as it is detailed in the table below:

Marker	Location and partner	Country
	Balearic Islands: Fundación de Investigación Sanitaria de las Islas Baleares	Spain
	Aragon: Instituto Aragonés de Ciencias de la Salud	Spain
	Navarre: Navarrabiomed	Spain
	Catalonia: AQUAS (Agència de Qualitat i Avaluació Sanitàries de Catalunya)	Spain
	North Portugal: Administração Regional De Saúde Do Norte	Portugal
	Occitania, Montpellier: Centre Hospitalier Universitaire	France
	Occitania, Toulouse: Centre Hospitalier Universitaire	France

Table 1. ICTUSnet partners identification.

The following subsections summarize the present main characteristics of each of these partners, as well as their organization:

3.1. Catalonia

The current situation of the Catalonia Autonomous Community, in Spain, is presented in the following table [1]:

Category	Item	Current situation
General information	Population:	7.518.913 citizens
	Number of hospitals:	71 hospitals
	Number of healthcare professionals:	130.000 professionals
	Health system:	Public Health System called "SISCAT (Sistema sanitari integral d'utilització pública de Catalunya)"
ICT characteristics	Use of standards:	Use of HL7, DICOM, IHE Use of ICD-9 and ICD-10 to encode diagnosis and procedures (hospital and primary care datasets, respectively) Use of LOINC for laboratory test Use of SNOMED CT as reference terminology for the EHR
	EHR situation:	20-30% of hospitals have the same EHR system but the remaining 80-70% use different EHR systems
Stroke related information	Regional stroke program:	A regional Stroke program and a code stroke network exist
	Reference stroke hospital:	27 hospitals in Catalonia are part of the so-called Code Stroke network (6 Comprehensive Stroke Centres, 8 Primary stroke Centres, and 13 Community Hospitals with Telestroke)
	Number of stroke cases per year:	>13,000 episodes per year, of which just over 800 involve treatment with Mechanical Thrombectomy
	Stroke registry:	A centralized stroke registry exists, called CICAT, but it is not integrated with the different EHR systems
	Stroke structured information:	The information is structured in the register but not in the different EHR systems, with the exception of hospitals sharing a common HER system

[1] Information complemented with 2017 General Report of the Catalan Health System.

Approach for ICTUSnet	Next steps:	Improving the existing registry to facilitate the recording process by professionals and integration of this information in the different EHR systems
	Publication of information:	Directly from the regional registry
	Data sources:	27 hospitals
	Possible use of FHIR and SNOMED CT:	They think that the use of FHIR and SNOMED CT for the ICTUSnet project is assumable and possible
	Piloting centres:	Directly from the regional registry (27 hospitals)
Other considerations and comments		

Table 2. Stroke summary of the current situation in Catalonia

3.2. Aragon

The current situation of the Aragon Autonomous Community, in Spain, is presented in the following table[2]:

Category	Item	Current situation
General information	Population:	1.308.750 citizens
	Number of hospitals:	12 hospitals
	Number of healthcare professionals:	16.659 professionals
	Health system:	Public Health System called Servicio Aragonés de Salud (SALUD)
ICT characteristics	Use of standards:	Use of HL7 Developed their own data model based on 13606 Use of ICD-10-CM to encode diagnosis (2016/01 onwards). This refers only to diagnosis and procedures registered during the hospital episode. Diagnoses at other instances of the healthcare system (i.e., Primary care or Emergency wards within the hospital) are coded using other standards (i.e., CIAP-I for primary care and CIE-9MC ES

[2] Information complemented with the official statistics webpage of the Aragon's government.

		for emergency ward services). Experience in SNOMED CT to structure the EHR information
	EHR situation:	All the hospitals have the same EHR system with an integrated data base (with integration of the Stroke registry from January 2019 onwards)
Stroke related information	Regional stroke program:	A regional Stroke code network exists from 2009 onwards (Código Ictus Aragón)
	Reference stroke hospital:	Thrombectomy treatments: Multihospital unit involving neurologist from both Hospital Miguel Servet and Hospital Clínico Lozano Blesa located in Hospital Miguel Servet Fibrinolysis treatment: Performed in all hospitals of Aragon. Neurological clinical service: 24x7 service by the multihospital unit at Miguel Servet Hospital
	Number of stroke cases per year:	>2000 episodes per year and 90-130 of them involving a thrombectomy treatment
	Stroke registry:	A unique and centralised registry exists for all the region (maintained and supported at Hospital Miguel Servet, as centre of reference within the Regional Health Service (SALUD)
	Stroke structured information:	They have it but it is not structured using an international controlled vocabulary
Approach for ICTUSnet	Next steps:	The development of the Stroke registry module in the HER has already concluded and it has been deployed and is piloted by neurologists at Royo Villanova and Alcañiz hospitals.
	Publication of information:	They are evaluating the use of a middleware to send the information to the ICTUSnet platform with a fix periodicity. This is an operative and organisational requirement as participant partner is Instituto Aragonés de Ciencias de la Salud, not Servicio Aragonés de Salud thus data from the registry should be handled previously de-identified at

		origin to the IACS in order to enable their transformation to the ICTUSnet common data model and interoperability standards and transferred to the ICTUSnet registry.
	Data sources:	2 possible strategies: obtain the information from the central registry or from the HER. There is only one common EHR covering all health system in Aragón. Preferred strategy accounting for a prospective registry would be to extract all information from the Stroke module of the EHR.
	Possible use of FHIR and SNOMED CT:	They think that the use of FHIR and SNOMED CT for the ICTUSnet project is assumable and possible
	Piloting centres:	Directly from the regional registry (9 hospitals)
Other considerations and comments		

Table 3. Stroke summary of the current situation in Aragon

3.3. Balearic Islands

The current situation of the Balearic Islands Autonomous Community, in Spain, is presented in the following table[3]:

Category	Item	Current situation
General information	Population:	1.115.999 citizens
	Number of hospitals:	7 hospitals
	Number of healthcare professionals:	14.289 professionals
	Health system	Public Health System called “Servei de Salut Illes Balears”
ICT characteristics	Use of standards:	Use of HL7 Use of ICD-10 to encode diagnosis Experience in SNOMED CT to structure the

[3] Information complemented with the official webpage of the Balearic Islands government.

		EHR information
	EHR situation:	There are 3 different EHR platforms in the Public Health System: Primary Care use ESIAP, Hospital Son Espases use Cerner-Millennium and rest of Hospitals use HCIS.
Stroke related information	Regional stroke program:	A protocol "code stroke" exists at a clinical level
	Reference stroke hospital:	Thrombectomy treatments: Hospital Son Espases Palma de Mallorca
	Number of stroke cases per year:	>2000 episodes per year and 130-200 of them involves a thrombectomy treatment
	Stroke registry:	They have 2 different stroke specific registries, one in Son Espases Hospital and another one in Son Llàtzer Hospital. The registries are not integrated nor structured using an international controlled vocabulary
	Stroke structured information:	In the EHR system, they have structured all the data set considered in ICTUSnet project, but currently not using international controlled vocabularies (working in mapping with SNOMED-CT)
Approach for ICTUSnet	Next steps:	To decide the publication strategy
	Publication of information:	They are evaluating the use of a middleware to send the information to the ICTUSnet platform with a fix periodicity
	Data sources:	Data from Hospital Son Espases Palma de Mallorca (because it is the unique hospital that performs thrombectomy)
	Possible use of FHIR and SNOMED CT:	They think that the use of FHIR and SNOMED CT for the ICTUSnet project is assumable and possible
	Piloting centres:	1 centre: Hospital Son Espases Palma de Mallorca
Other considerations and comments		

Table 4. Stroke summary of the current situation in Balearic Islands

3.4. Navarre

The current situation of the Navarre Autonomous Community, in Spain, is presented in the following table[4]:

Category	Item	Current situation
General information	Population:	643.234 citizens
	Number of hospitals:	3 hospitals
	Number of healthcare professionals:	10.277 professionals
	Health system	Public Health System called "Servicio Navarro de Salud-Osasunbidea"
ICT characteristics	Use of standards:	We use HL7 with some products Use of ICD-10 to encode diagnosis in hospital Use of ICPC2 to encode diagnosis in primary attention Experience in SNOMED CT to structure the EHR information of allergies
	EHR situation:	All the hospitals have the same EHR system with an integrated data base
Stroke related information	Regional stroke program:	A protocol "code stroke" exists
	Reference stroke hospital:	1 hospital with stroke unit Complejo Hospitalario de Navarra, in Pamplona
	Number of stroke cases per year:	900 episodes per year: 86% correspond to ischemic strokes and 20% of these are treated pharmacological (fibrinolytic) intravenously and 4% benefit from thrombectomy treatments by catheterization
	Stroke registry:	There isn't a regional stroke registry
	Stroke structured information:	The stroke information is not structured in the EHR
Approach for ICTUSnet	Next steps:	They are working to create an structured centralized registry of stroke episodes
	Publication of information:	The information can be send directly from the new stroke registry
	Data sources:	Complejo Hospitalario de Navarra new registry

[4] Information complemented with 2017 General Report of the Navarre Health System.

	Possible use of FHIR and SNOMED CT:	They think that the use of FHIR and SNOMED CT for the ICTUSnet project is assumable and possible
	Piloting centres:	1 centre: Complejo Hospitalario de Navarra
Other considerations and comments	They have patients from La Rioja and they can consult their information but they don't have this information integrated in their EHR	

Table 5. Stroke summary of the current situation in Navarre

3.5. North Portugal

The current situation of the North region of Portugal is presented in the following table:

Category	Item	Current situation
General information	Population:	3.689.000 citizens
	Number of hospitals:	ARSN region: 25 hospitals, 11 of them receive stroke code patients (and do thrombolysis), of which 4 also do endovascular treatment
	Number of healthcare professionals:	35537 – professionals in all ARSN hospitals; 31317 – professionals in ARSN 11 hospitals with stroke code and thrombolysis treatment; 16035 – professionals in ARSN 4 hospitals with endovascular treatment
	Health system:	Public Health System called Serviço Nacional de Saúde
ICT characteristics	Use of standards:	Use HL7 V2.X in some projects and initiatives Use of ICD-10 to encode diagnosis and procedures Use of SNOMED CT in some projects and initiatives (not in stroke care)
	EHR situation:	All the hospitals have the same EHR system (SONHO / Sclínico) with an integrated data base, developed by the Ministry of Health of Portugal (Serviços Partilhados do Ministério da Saúde – SPMS)
Stroke related information	Regional stroke program:	yes
	Reference stroke hospital:	11 hospitals perform intravenous thrombolysis and 4 hospitals perform

		endovascular treatment in stroke patients
	Number of stroke cases per year:	About 7000 stroke episodes per year: 85% correspond to ischemic strokes and about 8% of these are treated pharmacological (fibrinolytic) intravenously and 4% benefit from thrombectomy treatments by catheterization
	Stroke registry:	In advanced preparation
	Stroke structured information:	Not yet. The stroke information is not structured in the EHR
Approach for ICTUSnet	Next steps:	They are creating a regional specific stroke registry and they think that it will be available in 2019. It implies to add the stroke variables in the structured EHR system
	Publication of information:	The information can be send directly from the new stroke registry
	Data sources:	Directly from the regional registry
	Possible use of FHIR and SNOMED CT:	They think that the use of FHIR and SNOMED CT for the ICTUSnet project is assumable and possible
	Piloting centres:	Directly from the regional registry
Other considerations and comments		

Table 6. Stroke summary of the current situation in North Portugal

3.6. Occitania Montpellier and Toulouse

The current situation of the regions of Occitania Montpellier and Toulouse, in France, is presented in the following table:

Category	Item	Current situation
General information	Population:	5.900.000
	Number of hospitals:	58
	Number of healthcare professionals:	27579
	Health system	Public health system called “Agence regional de santé”
ICT characteristics	Use of standards:	Don’t use HL7

		Use of ICD-10 to encode diagnosis
	EHR situation:	Montpellier and Toulouse have different EHR systems
Stroke related information	Regional stroke program:	National stroke plan 2010-2014
	Reference stroke hospital:	▪ 5 TSC ▪ 15 PSC ▪ 2 CSC (CHU Toulouse et CHU Montpellier)
	Number of stroke cases per year:	250 ischemic episodes per 100,000 inh per year:. Thrombolysis rate: 14.3% Thrombectomy treatments: NK
	Stroke registry:	There is a regional registry called PMSI but it contains sociodemographic data. There is a Endovascular treatment in ischemic stroke registry called ETIS. There isn't a specific regional stroke registry.
	Stroke structured information:	The stroke information is not structured in the EHR
Approach for ICTUSnet	Next steps:	They need to decide if they create a regional stroke registry (for example, enlarging the scope of ETIS) or if they create a specific registry per centre
	Publication of information:	It depend on the next steps decision
	Data sources:	It depend on the next steps decision
	Possible use of FHIR and SNOMED CT:	They think that it could be possible to use SNOMED CT to send the stroke variables to ICTUSnet They think that it could be so difficult for them to adopt FHIR or web services to it They propose to send a file like an CSV one
	Piloting centres:	2 centres: Centre Hospitalier Universitaire de Toulouse and Centre Hospitalier Universitaire de Montpellier
Other considerations and comments		

Table 6. Stroke summary of the current situation in Occitania Montpellier and Toulouse

3.7. Current situation summary

Currently, regional stroke registries are in different stages of development: Catalonia is the region that has the oldest stroke registry (since 2011), while ARSN, Aragon, Navarre and Balearic Island have their own regional registry in different stages. Unlike Catalonia, these regions have developed their registry with information integrated in the HER, except ARSN that is developing a form using Microsoft software within the public health network. Occitaine does not have a registry yet and it is going to develop its own registry during the course of the ICTUSnet project and will obtained the information through the French national registry (Endovascular Treatment in Ischemic Stroke, ETIS).

Regarding the approach for ICTUSnet, stroke information is not fully structure in all regions.

4. DEFINITION OF INTEROPERABILITY AND ITS LAYERS AND INTEROPERABILITY FRAMEWORKD OF THE ICTUSnet REGISTRY

Interoperability is the capability of components (like IT systems or devices) to exchange information without losing its meaning. This communication needs to be performed ensuring the coherent sharing of data between different departments, organizations, care levels or regions, like countries.

In our case, the primary objective of ICTUSnet registry is to compare the performance of the hospitals offering the mechanical thrombectomy procedure to patients admitted with an ischemic stroke, and generate new evidence.

Interoperability is not an ability that happens or not, as it has the following different levels:

- **Technical**: Makes focus on the communication's establishment in order to allow the exchange of information.
- **Syntactic**: Allows the exchange of information in this communication.
- **Semantic**: Ensures that the information that is exchanged doesn't lose its meaning.
- **Legal**: The exchange is done respecting law and ethical issues, also in a cross-border scenario.
- **Organizational**: The exchange is aligned with processes and workflows of all the organizations involved in the exchange of data.

Specific standards have been created to address each layer of interoperability. The Interoperability Framework described in this document makes focus on the **technical** and **semantic** layer for the purpose of ICTUSnet. For the legal and ethical issues, please, refer to Deliverable 1.2

4.1. Semantic interoperability

This kind of standards aims to normalize the meaning of the information according a conceptual model. Some of them are reference models itself and others use a subjacent conceptual model to organize and represent real concepts or ideas. International and standard controlled vocabularies are necessary to ensure that the meaning of heterogeneous data coming from different sources is not lost or altered, and that it can be exploited and analysed in a global way.

According their use in IS (Information Systems), the languages used in healthcare domains can be classified in natural language and controlled vocabularies. Natural language can't be used by IS to process automatically the information, it is necessary to structure the vocabulary before it. Controlled vocabularies are those specifically designed to represent information in IS and can be of three different types:

- **Interface (input) vocabularies**: Those used by healthcare professionals to record the information in IS performing the first level of formalization. They offer options to refine the concepts by adding more information to them.
- **Reference vocabularies**: They allow relate controlled vocabularies in order to compare and consider information obtained from different sources. This type of vocabulary has the maximum level of detail and should has concepts related to each other through different type of relationships. They are the vocabularies that allow us to achieve full semantic interoperability of contents and that can be used to represent the information to be used in Clinical Decision Support Systems.
- **Aggregation (output) vocabularies**: Those used to exploit the information to plan, statistics, reimbursement, population analysis, etc. It offers the possibility to interpret information from different points of view (e.g. clinical and financial).

There are different international controlled vocabularies used to represent and encode information of different healthcare domains. For the purpose of ICTUSnet project, we will use **SNOMED CT** (Systematized Nomenclature of Medicine Clinical Terms, a clinical terminology that contains concepts from different domains like procedures, diagnosis, substances, physical objects, etc. It also includes several non-strictly-clinical concepts like social problems, environmental information or wellness and fitness ones); **ATC** (Anatomical Therapeutic Chemical, a classification to group active ingredients of medicines); and **ICDs** (International Classification of Diseases, classifications to group diagnoses, with some of their editions also including procedures).

ICTUSnet's Consortium has elaborated a Glossary (see Deliverable 1.1.1 http://ictusnet-sudoe.eu/pub_type/deliverables/) that contained the consensus variables (54) related to reperfusion treatment in acute ischemic stroke, mainly endovascular treatment (EVT) to be shared in ICTUSnet registry. A process of codification using the aforementioned international controlled vocabularies has took place, with the collaboration of the Office of

Standards and Interoperability (OFSTI) of the TIC Salut Social Foundation (https://ticsalutsocial.cat/en/area/interoperability/). During the process, we have detected that some variables were not found in the current SNOMED-CT version, so a formal requirement to introduce these missing terms was sent to IHTSDO (pending response).

Here we present a figure with the final version of the dataset content and database structure:

Name	Description	Concept Id (SNOMED CT)	Term (SNOMED CT)	Format (text, data, numeric)	Values - Code	Values - Description	Units of mesure	Related information
Id event	**Id for every episode**	**non**	**non**	**numeric**	**random**	**None**		
Id region	Identification of the region of the stroke event: Occitania, North Portugal, Aragon, Balearic Islands, Navarre, Catalonia	223496003	Geographical and political regions of the world	Coded - fix value	FR-OCCEWEST	**Occitania west**		
					FR-OCCEAST	Occitania east		
					PT-RN	Portugal North Region		https://www.iso.org/obp/ui/#iso:code:3166:PT
					ES-AR	Aragon		
					ES-NC	Navarre		
					ES-IB	Balearic Islands		
					ES-CT	Catalonia		
Resident in the area	The case corresponds to a patient that has his/her residency in the same region where he/she is assisted, in order to distinguish tourists (included for population rates)	416647007	Country of residence	boolean	0	no		
					1	yes		
Sex	Sex of the patient	184100006	Patient sex		248153007	Male		
					248152002	Female		

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				Coded - single selection	82334004	Undetermined		
Age	Age of the patient in the stroke event moment	424144002	Current chronological age	Numeric			Years	
Previous mRS	Modified Ranking Scale, with its associated data and time. For the 3-month mRS, if the final value is 6 (which implies death), the data of death will also being indicated	273729003	Rankin scale	Numeric	0 to 5 or 99			
Comorbilities	Relevant history of diagnostics to consider: Past history of myocardial infarction (including angina) Past history of cerebrovascul	398192003	Co-morbid conditions	Coded - multiple selection	275526006	History of cerebrovascular accident		
					399211009	Past history of myocardial infarction		
					260413007	None		

	ar accident (considered all types, ischemic, haemorrhagic, TIA)						[redacted]
Risk factors	Relevant factors that increase patients' risk of stroke, and are present at the time of admission: Atrial fibrillation Hypertension: per physician diagnosis, use of medication, or evidence of at least two raised blood pressure measurements [systolic >140 mmHg or diastolic >90 mmHg] recorded on different days before stroke	80943009	Risk factor	Coded - multiple selection	49436004	Atrial fibrillation	[redacted]
					38341003	Hypertension	
					73211009	Diabetes mellitus	
					266918002	Tobacco smoking consumption	
					370992007	Dyslipidemia	[redacted]

	onset Diabetes mellitus: previous physician diagnosis or use of medication Current tobacco smoking consumption Dyslipidaemia: physician diagnosis, use of medication, serum cholesterol concentration >220 mg/dl, low-density lipoprotein cholesterol >130 mg/dl or serum triglyceride concentration >150 mg/dl in previous blood tests						[redacted]
					260413007	None	

Diastolic blood pressure	At time of admission in the emergency department (first measure) Measured in mmHg, with its associated date and time	271650006	Diastolic blood pressure	Numeric	integer		mmHg	
Systolic blood pressure	At time of admission in the emergency department (first measure) Measured in mmHg, with its associated date and time	72313002	Systolic arterial pressure	Numeric	integer		mmHg	
Blood glucose	At time of admission in the emergency department (first measure) Measured in mg/dl, with its associated date and time	434912009	Blood glucose concentration	Numeric	Integer		mg/dl	

INR	At time of admission in the emergency department (first measure) International Normalized Ratio	165581004	INR	Numeric	float (1) o 99			
Prior anticoagulation therapy	Active treatment prior to the episode	81839001	Anticoagulant agent		0	No		
					1	Yes		
Type of anticoagulation	Active treatment prior to the episode	PENDENT CODI ATC	Anticoagulant agent	Coded - multiple selection	B01AA07	acenocumarol		Conditional if "prior anticoagulation therapy" is 1 (YES)
					B01AA03	warfarin		
					B01AB01	heparin iv		
					B01AB	heparin group (subcutaneous)		
					B01AE07	dabigatran		
					B01AF01	rivaroxaban		
					B01AF02	apixaban		
					B01AF03	edoxaban		
prior antiplatelet therapy	Active treatment prior to the episode	108972005	Antiplatelet agent		0	no		
					1	yes		
type of antiplatelet therapy		PENDENT CODI ATC			B01AC05	ticoplidine		Conditional if "prior antiplatelet therapy" is 1 (YES)
					B01AC06	acetylsalicylic acid		

					B01AC07	dipyridamol		
					B01AC24	ticagrelor		
					B01AC04	clopidogrel		
Date time of onset of symptoms (or last time seen asymptomatic)	Date time of onset of symptoms (or last time seen asymptomatic)	409586006	Complaint	date time			[redacted]	Date YYYYMMDDTHHMM or 99
Date time of arrival to the hospital (receptor)	Date time of arrival to the first hospital. Corresponds to the date time recorded in admissions	32485007	Hospital admission	date time				Date YYYYMMDDTHHMM or 99
Initial NIHSS	NIHSS score at the arrival	450741005	National Institutes of Health stroke scale	Numeric	0 to 42 or 99			
Diagnostic	Initial diagnostic	439401001	Diagnosis	Coded - single selection	1386000	Intracranial hemorrhage		
					422504002	Ischemic stroke		
Type of 1rst imaging		71388002	Procedure	Coded - multiple selection	34227000	CT of brain		
					433111008	CT of brain perfusion		
					29567006	MRI of brain and brain stem		
					419059006	MRI cerebral perfusion study		

					426099006	CT of cerebral vessels		
					241664002	MRI of cerebral vessels		
					431648005	Transcranial doppler ultrasonography		
					394719009	Carotid artery doppler assessment		
					129118002	Arteriography		
					262008008	Not performed		
Date/time first imaging				date time				Date YYYYMMDDTHHMM or 99
ASPECTS score 1rst imaging		ASP1	Aspects score	Numeric	0 to 10 or 99			Requested to IHTSDO.
Vessel affected		20059004	Cerebral artery occlusion	Coded - multiple selection	260413007	None		
					261665006	Unknown		
					38917008	Right internal carotid artery		
					58379002	Left internal carotid artery		
					TICA_R	Right terminal portion of internal carotid artery		
					M1_R	Right middle cerebral artery M1 segment		

					M2_R	Right middle cerebral artery M2 segment	
					TICA_L	Left terminal portion of internal carotid artery	Requested to IHTSDO.
					M1_L	Left middle cerebral artery M1 segment	Requested to IHTSDO.
					M2_L	Left middle cerebral artery M2 segment	Requested to IHTSDO.
					369299002	Left anterior cerebral artery	
					369298005	Right anterior cerebral artery	
					369300005	Right posterior cerebral artery	
					369301009	Left posterior cerebral artery	
					369354007	Right vertebral artery	
					369355008	Left vertebral artery	
					59011009	Basilar artery	
Reperfusion treatment administered		276239002	Therapy	Coded - multiple selection	472191000119101	Thrombolysis of cerebral artery by intravenous infusion	

					21710002	Intracranial thrombectomy		
					230934004	Thrombolysis of intracranial vessel		
Date/time iv thrombolysis				date time				Date YYYYMMDDTHHMM or 99
Type of thrombolityc treatment		416608005	Drug therapy	Coded - single selection	387152000	Alteplase		conditional to Thrombolysis of cerebral artery by intravenous infusion
					127967007	Tenecteplase		
Transfer from another Centre for EVT	The Centre that enter the data is the Centre where EVT is done. In some regions, according to their Code Stroke protocol, patients are firstly taken to a primary centre where IVT is administered and then transferred to a comprehensive Centre. This variable seeks	439980006	Referral placed	Boolean	0	No		

	to collect information about that type of circuit.							
					1	Yes		
Date time of arrival to another Centre for EVT		183467009	Neurology emergency hospital admission	date time				Date YYYYMMDDTHHMM or 99
Following imaging		71388002	Procedure	Coded - multiple selection	34227000	CT of brain		
					433111008	CT of brain perfusion		
					29567006	MRI of brain and brain stem		
					419059006	MRI cerebral perfusion study		
					426099006	CT of cerebral vessels		
					241664002	MRI of cerebral vessels		
					431648005	Transcranial doppler ultrasonography		
					394719009	Carotid artery doppler assessment		

					129118002	Arteriography		
					262008008	Not performed		
Date/time following imaging				date time				conditional to Following imaging if diferent a "Not performed"
ASPECTS score following imaging		ASP2	Aspects score	Numeric	0 to 10 or 99			Requested to IHTSDO.
NIHSS prearteriography	NIHSS previous to the procedure	450741005	National Institutes of Health stroke scale	Numeric	0 to 42 or 99			
Date/time of arterial puncture		DTAP	Date/time of arterial puncture	date time				Date YYYYMMDDTHHMM or 99
Vessel affected by arteriography		20059004	Cerebral artery occlusion	Coded - multiple selection	260413007	None		
					261665006	Unknown		
					38917008	Right internal carotid artery		
					58379002	Left internal carotid artery		
					TICA_R	Right terminal portion of internal carotid artery		
					M1_R	Right middle cerebral artery M1 segment		
					M2_R	Right middle cerebral artery M2 segment		
					TICA_L	Left terminal portion of internal carotid artery		Requested to IHTSDO.

					M1_L	Left middle cerebral artery M1 segment		Requested to IHTSDO.
					M2_L	Left middle cerebral artery M2 segment		Requested to IHTSDO.
					369299002	Left anterior cerebral artery		
					369298005	Right anterior cerebral artery		
					369300005	Right posterior cerebral artery		
					369301009	Left posterior cerebral artery		
					369354007	Right vertebral artery		
					369355008	Left vertebral artery		
					59011009	Basilar artery		
Initial mTICI score		mTICI_Initial	modified treatment in cerebral ischemia	Text	0 or 1 or 2a or 2b or 2c or 3 or 99			Requested to IHTSDO.
EVT modality					0	Mechanical thrombectomy		
				Coded - single selection	1	pharmacological		Revisar valors

					2	both		
Device model		49062001	Device	Text				
Number of passes		447754009	Number of procedure attempts	Numeric			passes	Integer
Use of balloon		86768006	Balloon pump	Boolen	0	No		
					1	Yes		
Stent		65818007	stent	Coded - single selection	360046005	Arterial stent		
					413766009	Carotid stent		
					705639000	Intracranial vascular stent		
					260413007	None		
Embolization to new territories?		EMB	Embolization to new territories?	Boolen	0	No		Requested to IHTSDO
					1	Yes		
Final mTICI score		mTICI_Final	modified treatment in cerebral ischemia	Numeric	0 or 1 or 2a or 2b or 2c or 3 or 99			Requested to IHTSDO. Used to represent: initial and final (diferenciated by associated date-time)
Date/time of revascularization/end of procedure		DTRP	Date/time of revascularization/end of procedure	date time				Date YYYYMMDDTHHMM or 99
Neuroimaging <=36 h post-EVT		183616001	Follow-up arranged	Boolean	0	No		
					1	Yes		
SICH		SICH		Boolen	0	No		Requested to IHTSDO

			Secondary intracraneal hemorrage		1	Yes		
3 month mRS	Modified Ranking Scale, with its associated data and time. For the 3-month mRS, if the final value is 6 (which implies death), the data of death will also being indicated	273729003	Rankin scale	Numeric	0 to 8			
Death date		419099009	Died	date time				Date YYYYMMDDTHHMM or 99. Required if "3 month mRS" is 6

Figure 2. Dataset content and databased structure of the ICTUSnet Registry

4.2. Technical Interoperability

Our first approach was to be aligned with the international standard protocols like HL7 (Health Level Seven International) with FHIR (Fast Healthcare Interoperability Resources), as they are newest standard of HL7 to exchange healthcare information based on REST (Representational State Transfer) web services. It includes both XML and JSON (JavaScript Object Notation) formats definition and it has been design to facilitate the adoption of the standards within newest technologies and mhealth environments. A Web Service was initially design to send the information from local registries to AQuAS (where the ICTUSnet central registry is going to be located) using these standards. However, due to security problems detected, an intermediate platform was designed to proceed with the sending of information.

4.2.1. Information System architecture

The following is a description of the different technologies used:

- Java 8 virtual machine: It is the "translator" between Java and the operating system, the basic functionalities of the language are found.
- Different standard Java technologies are used, as:
  - Java Persistence API (JPA) 2 .1 for data persistence.
  - Java Transaction API (JTA) 1.2 in charge of database transactionality. It is implemented by Hibernate.
  - Context Dependency Injection (CDI) 1.1 for dependency injection. Implemented by Weld.
  - Bean Validation 1.1 for the validation of Java classes, is understood with JAX-RS and JSF for the validation of the forms. Implemented by Hibernate Validator.
  - Logback 1.1.7 with SFL4j 1.7.21 for log generation.
  - Apache Commons 3.4 for basic utilities of numbers, strings, reflection, etc.

4.2.1.1. Features

- Log: Ability to generate logs for the application.
- Audit: Audit tables of application processes.
- Validation: Screen components, before being persisted are validated to verify that the data types are correct; in addition there are validations at the level of logic.
- Exceptions and control of errors: Control of all possible errors offering the maximum information to the user and technicians. In order to avoid system crashes by controlling all possible casuistry.
- Multi language: Internationalization to allow applications to be in different languages.
- Environments: Using a variable at the start of the application you can choose one or other configuration parameters.

- Configuration files: management of the different configuration files, commonly “properties” or “xml”.
- Security: Different rules and protocols to ensure the security of the application.
- Navigation: Control of navigation between the different screens.
- Session control: Control of the different objects of the session, such as the disconnection of the user in case of inactivity.
- Application management:
  - Users, Roles and Menus
- Authentication: Application access control.
- Master table - detail: Table of tables for the different configuration parameters of the application or entities with few records and interaction.

4.2.1.2. Definition of the framework

This section describes the design rules and standards that are applicable in the development of the platform:

1) Tools

For the development of the application:

- Eclipse Oxygen: As a development interface in Java, XHTML and CSS.
- WildFly 10.0.0.Final: As an application server for the web application.
- SQLServer: As a database manager.
- Maven: It is a software tool for the management and construction of Java projects.
- Postman: For testing and development of REST services. Does not apply to ICTUSnet.
- Continuous development integration:
  - Gitlab as a Git version controller.
  - Gitlab CI as a continuous integration engine.
  - Artifactory as a library repository.
  - SonarQube for code analysis.

2) ECB (Entity, Control and Boundary)

When identifying the elements present in a scenario to be analyzed, each type of behavior found can be aligned with one of the following three main perspectives: Entity, Control or Boundary (Boundary). Although the final design may be altered by the characteristics of the language used and other quality elements, a first approach that covers the required system behavior can always be coupled with elements from these three perspectives.
This pattern is similar to the Model Vista Driver pattern, but ECB is not used to define user interfaces. An entity is a passive element of the system, responsible for some significant part of the information. You can also manage this information with some associated behaviour.

A control element manages the interaction within the scenario, from end to end, or within a subset of elements. Behavior and business rules related to relevant information should be assigned to entities, while the controller is solely responsible for the flow within the scenario.

A Boundary element is located on the periphery of the system, but within it. Depending on the structure of the scenario, some of these elements will be of the "front-end" type, which accept inputs from the outside, for example from a user interface. They can also be of the "back-end" type, managing the communication and support of elements outside the system or subsystems. This pattern can be easily modeled using a UML robustness diagram (Figure 3).

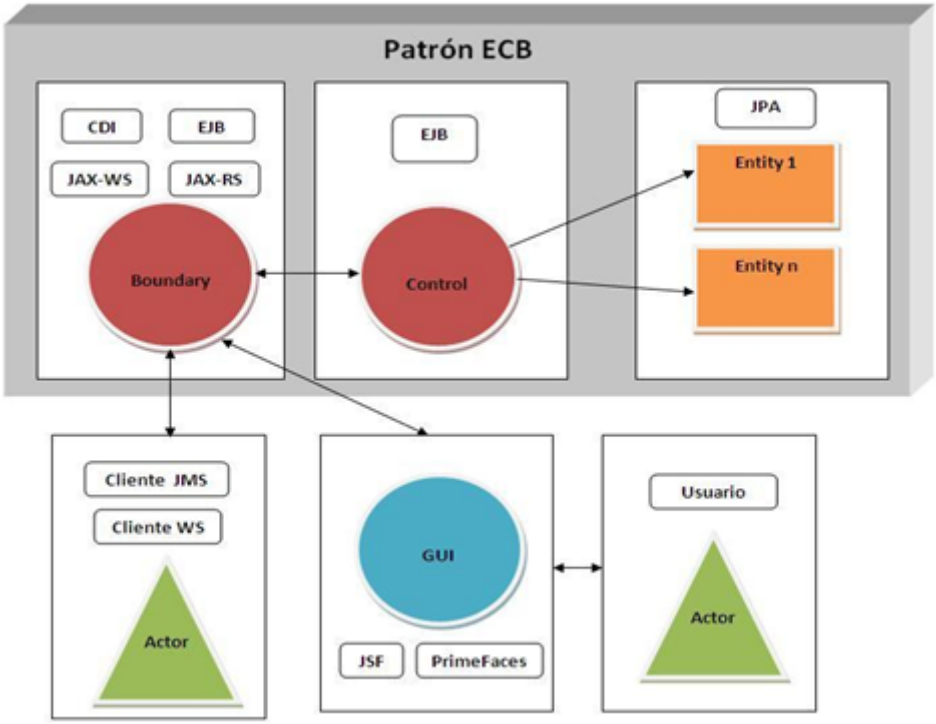


Figure3. ECB pattern

3) Definition of Technological Environments

- Production: This environment provides the real exploitation capacity of the information system. Stability and security are maximized. The implementation in this environment must be performed by systems personnel, without any contact with the application development tasks, based on the implementation instructions provided by the development teams.
- Pre-production: It is an exact replica of the production environment. Any abnormal behavior of the system that occurs in Production may be reproduced in this environment. The development team will not access this environment.
- Development: The testing environment aims to provide an environment to run unit, integration, and acceptance testing.

4.2.1.3. Physical Data Design

This section describes everything related to the persistence of the Information System.

1) Specification of the DBMS and basic design and architecture characteristics

Specification of the Database Management System to be used by the Information System. Definition of the necessary configurations and the necessary architecture for the operation.

2) Optimized physical data design

Based on the class model in the previous section (Figure 3), the optimized physical data design and database model diagram is performed (Figure 4).

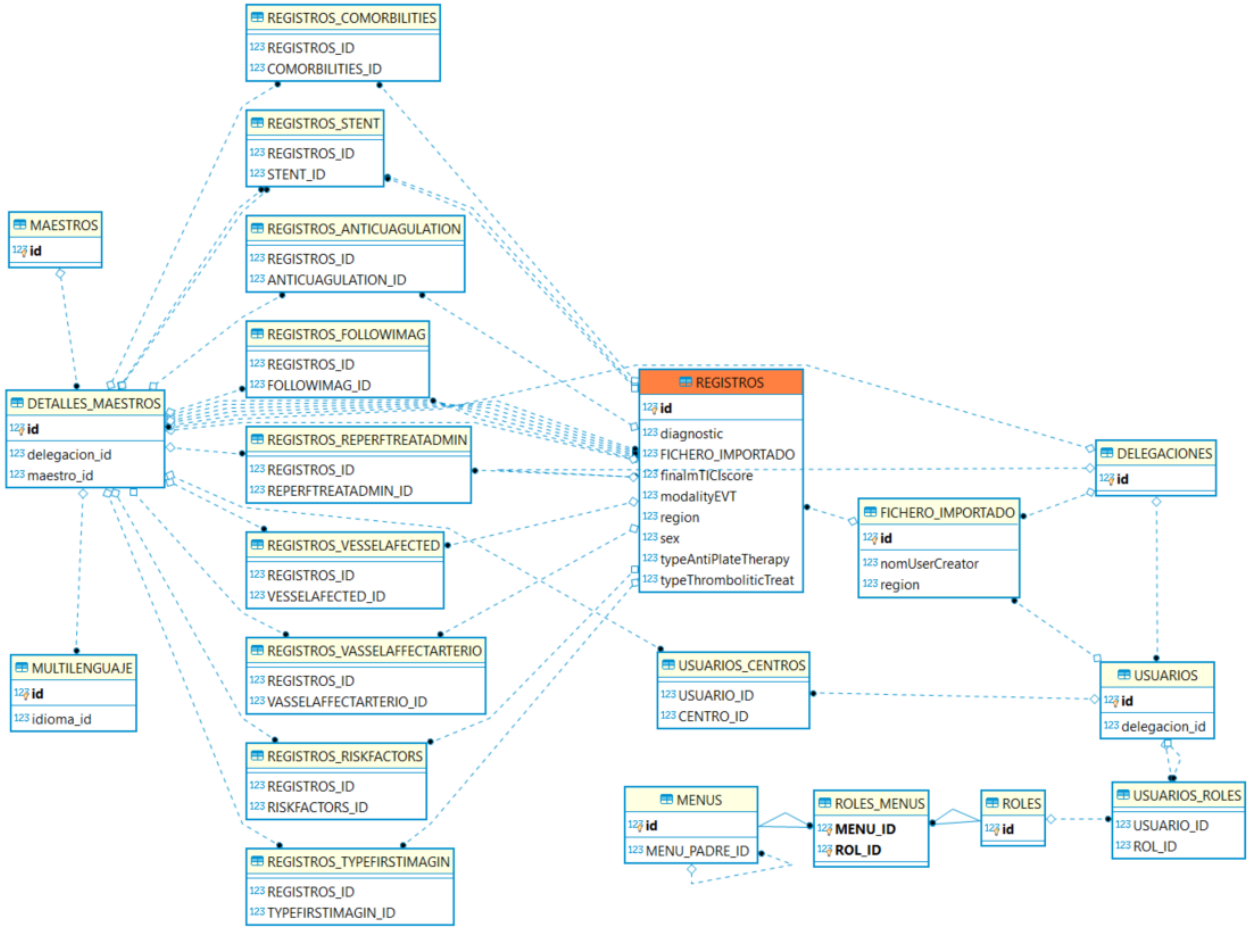


Figure4. BASE scheme

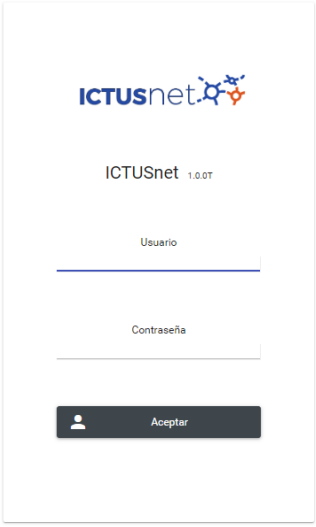
4.2.2. How to send information to the ICTUSnet registry

Users of regional registries (members of the ICTUSnet Consortium) must prepared an excel file following the structure and content explained in the Semantic interoperability section. Once it is filled with the full information (meaning that every case entered has to have the 3 month follow-up already done), a csv file has to be uploaded in the ICTUSnet registry platform following the instructions (Box 1)

The authorized user has to login login the platform designed (Figure 5) and follow the indications.

Box 1. (1) consider every row is a case; 2) every case has to have a unique Id (that it would be reconverted once uploaded the file); 3) choose properly your region code; 4) the character "|" must appear 47 times: the excel file has 48 fields that have to be (all) filled up as follows: all the variables are mandatory except those in orange. Those variables in green are conditional to the values of the variable above; 5) if there are unknown values for mandatory variables, put 99 only in places permitted; 6) if there are unknown values for non-mandatory or conditional variables, leave a blank space between pipes (||).

Figure 5. ICTUSnet registry login



Data Manager at AQuAS will be the administrator of ICTUSnet registry.

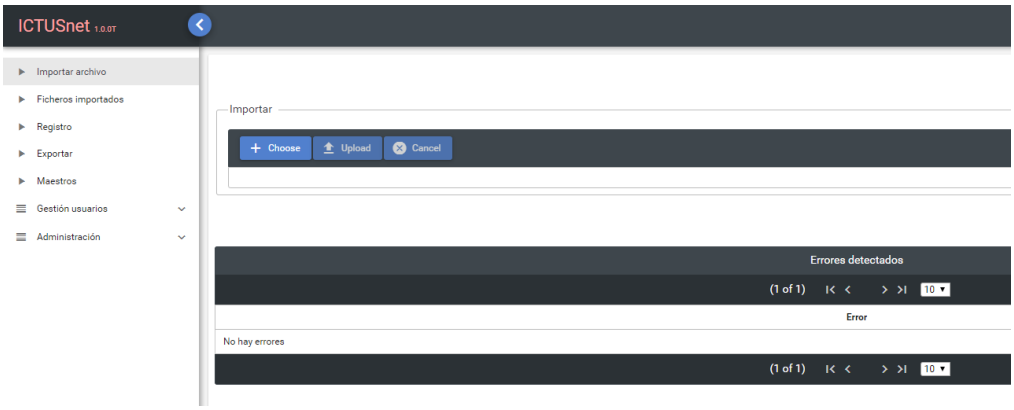


Figure 6. ICTUSnet registry platform

(The csv file that I sent you is just a model and the “new” information has to be sent following the next instructions:

- Every row is a case.
- Every case has to have a unique Id (that we reconvert once we upload the file).
- Your region code for CHUM is FR-OCCEAST. Once the programm is ready, we, as administrator, give you a login and password to upload only information of CHUM. If you put another value in the variable “region”, it will be impossible to upload the file.
- The character "|" must appear 47 times: the excel file has 48 fields that have to be (all) filled up as follows: all the variables are mandatory except those in orange. Those variables in green are conditional to the values of the variable above (there is an explanation in the last colum of the excel file "20191002_Variables_ICTUSnet_appweb.xlsx"). If there are unknown values for mandatory variables, you must put 99 only in places permitted. If there are unknown values for non-mandatory or conditional variables, you must leave a blank space between pipes (||).