ADOPT
BBMRI-ERIC®
gateway for health

Rare Diseases Working Group - BBMRI RD WG

EuroBioBank webinars

Date 16.07.2018

Rare Diseases Working Group -RDWG

We set up a **working group on rare diseases** to reduce fragmentation and work jointly to optimize the results of various infrastructures and projects which are currently working on rare diseases

The first **TC 'BBMRI Rare Diseases Working Group'** was held on **November 15th 2016.** The Rare Diseases Working Group is active since few years, but the work, at the beginning, was difficult and fragmented. This TC was set up to begin a continuous work on rare diseases.

We proposed to have a TC every 3 months, in order to give continuity to WP7 activities and Rare Diseases WG. The WG efforts aim to avoid any duplication of work on overlapping activities between ERNs, ADOPT, RD-CONNECT and ELIXIR.

Rare Diseases Working Group TC

- **November 15th 2016**
- **February 6th 2017**
- **May 10th 2017**
- **July 5th 2017**
- **September 27th 2017**
- **February 1st 2018**
- **April 23th 2018**

RD Working Group Participants

in order sustain the continuous work on activities related to rare diseases. The WG teleconferences have involved regular representatives from BBMRI-ERIC, and representatives from RD-CONNECT project. The WG also enables the involvement of the BBMRI National Nodes within the RD activities.

Representatives/contact person for ***BBMRI-ERIC***

Representatives/contact person for ***National Nodes***

Representative/contact person for ***Spain Biobanks***

Telethon Network of Genetic Biobanks - ***TNGB***

Member

- *Austria (at)*
- *Belgium (be)*
- *Estonia (ee)*
- *Finland (fi)*
- *Germany (de)*
- *Italy (it)*
- *Malta (mt)*
- *Netherlands (nl)*
- *Poland (pl)*
- *United Kingdom (uk)*
- *Czech Republic (cz)*
- *France (fr)*
- *Greece (gr)*
- *Norway (no)*
- *Sweden (se)*
- *Switzerland (ch)*
- *Latvia (Lv)*

Observer

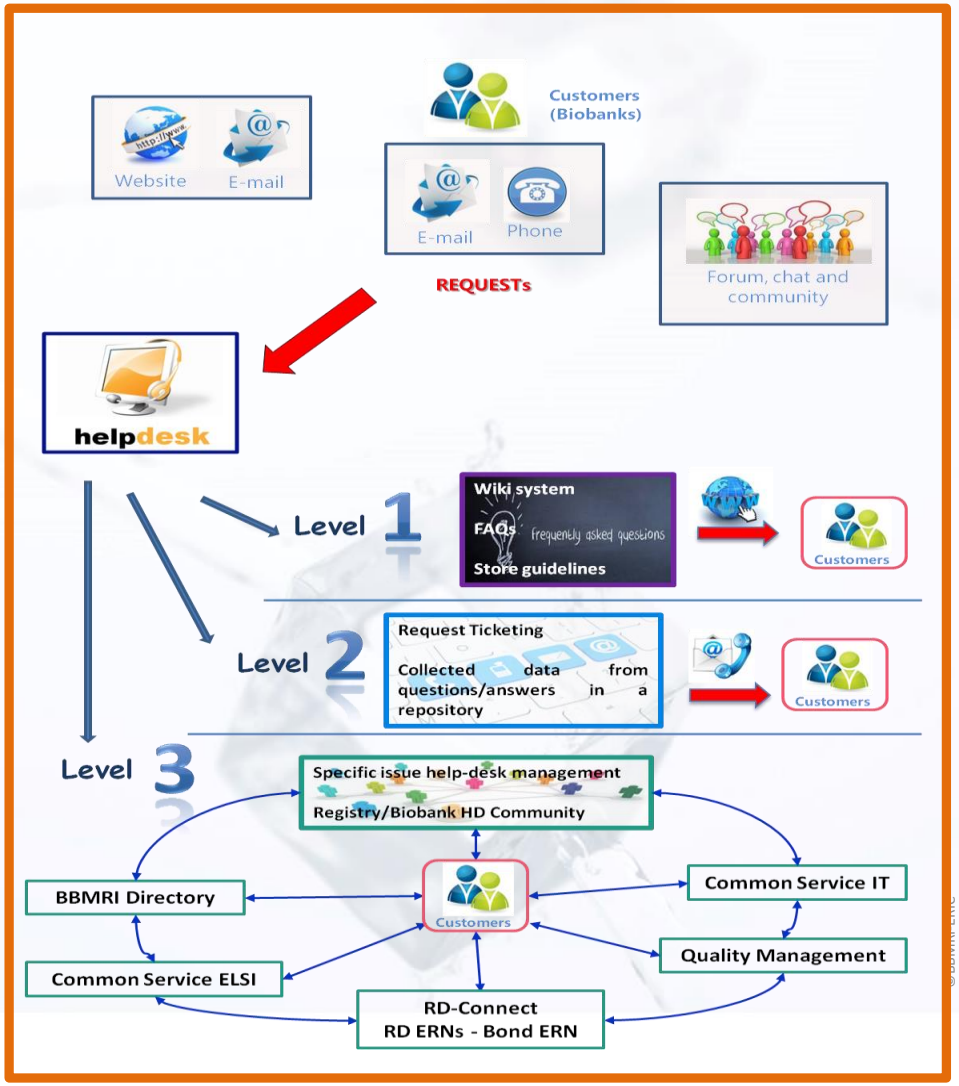
Switzerland (ch)
Turkey (tr)
Cyprus (Cy)

Objectives and progress, Networking and Synergies

Registry/biobank Help-desk HD facility

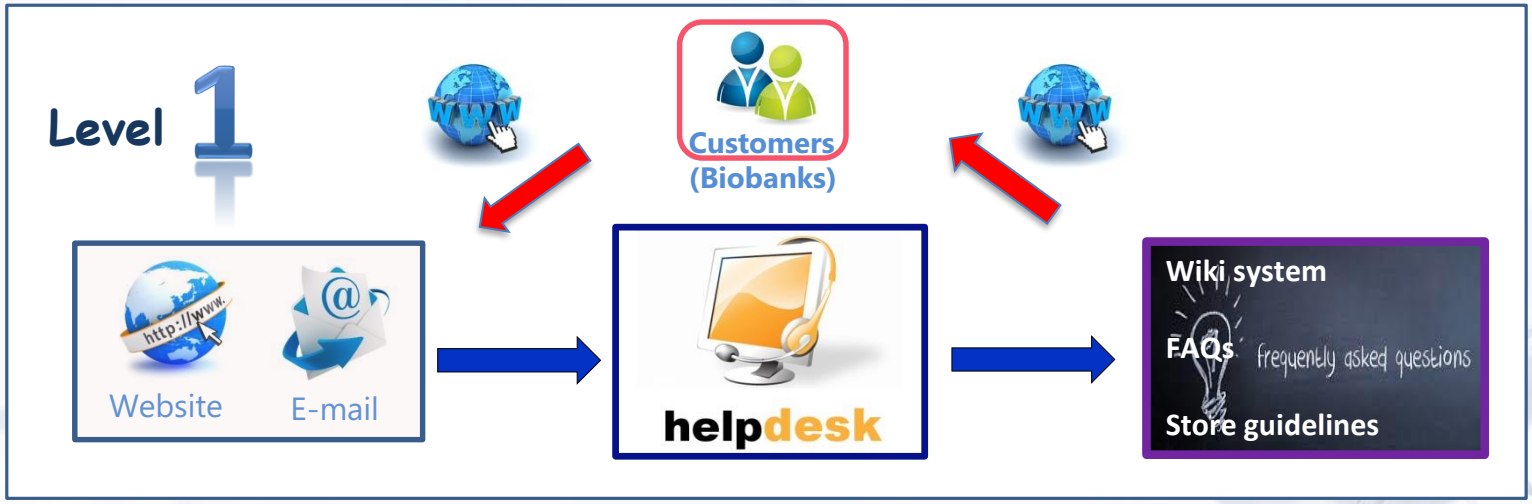
*Establish a **Help-desk facility** to provide real-time support to RD biobanks and/or registries to meet requirements for participation to BBMRI-ERIC.*

- ✓ Model with requests to three possible levels, and ***three possible levels*** of assistance:
  - ↘ 1 - Wiki system, FAQs and Guideline Repository
  - ↘ 2 - Ticketing
  - ↘ 3 - On particular aspects the HD aims to manage directly the site or service interest



The Help Desk model was proposed and disseminated among the participants of ADOPT and the Rare Disease Working Group (RDWG) for contribution in specific issues and for further development then we will revised, and we harmonize contributions

HD model version was revised and we have harmonized contributions, proceeding with the implementation of a preliminary version of HD in collaboration with the WP3, built by the Common Service IT



✓ Web wiki for HelpDesk: https://helpdesk-wiki.bbmri-eric.eu/

in collaboration with RDWG we are implementing Wiki and FAQs

WIKIs' examples

Rare diseases

Rare diseases are diseases which affect a small number of people compared to the general population and specific issues are raised in relation to their rarity. In Europe, a disease is considered to be rare when it affects 1 person per 2000. A disease can be rare in one region, but common in another. This is the case of thalassemia, which is rare in Northern Europe, but it is frequent in the Mediterranean region. There are also many common diseases whose variants are rare. [1]

Informed Consent: the informed consent is a document composed of an Information Sheet and a Consent Form. The Information Sheet aims to explain the consent and to inform the participants and must be described to patients/participants. The Consent Form is the effective certificate of consent capable to record the agreement and must be accepted/signed by patient/participant.

Biobanks

Biobank: an organized collection of human biological material and associated information stored for one or more research purposes[2]

Genetic Biobanks: The Genetic Biobanks are service units which operate according to the high-quality standards with the aim to collect, process, store, distribute human biological material (hereinafter referred to as "sample") from individuals affected by genetic diseases. [3]

Biobanks FAQs' examples

Could a rare disease biological sample collection become to a biobank?
It could be but it will depend on the type of rare diseases, the lack of similar collections and the characteristics of that collection in terms of quality, traceability and ethical issues (type of informed consent signed by donors/depositors)

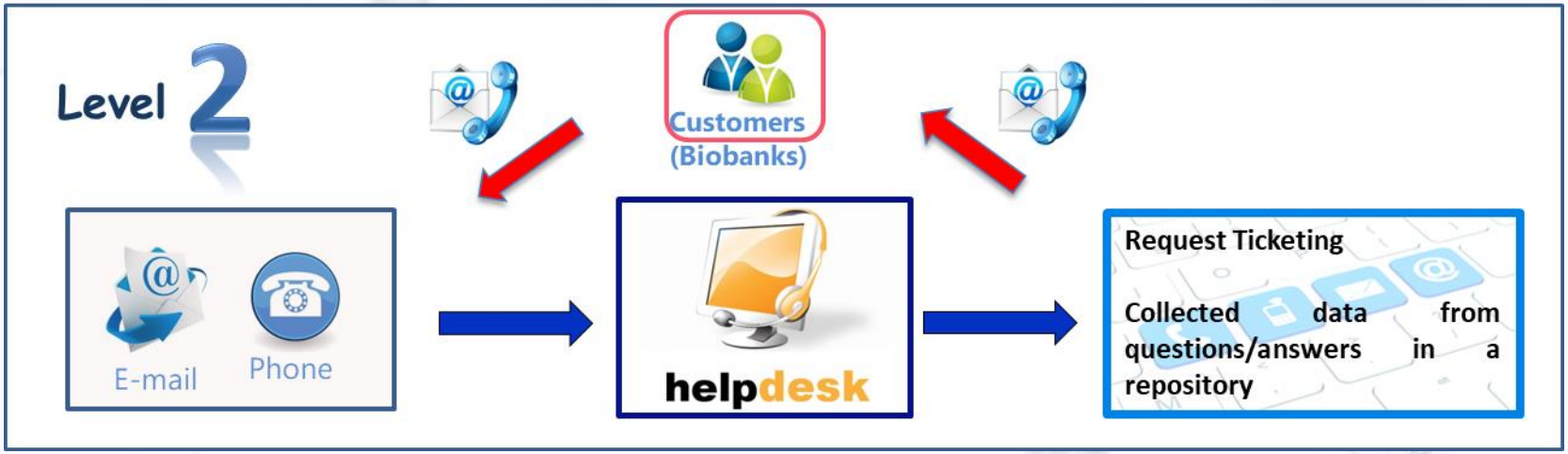
How many biological samples are needed to constitute a rare diseases biobank? Is there a threshold of samples?
There is not a threshold of samples, which differentiate between a collection and a biobank. Rare diseases are rare in terms of data and also of good biological samples collection. A small collection for an ultra-rare disease is welcome, if they have other questions solved such as traceability, appropriate informed consent and samples are reusable for future projects out of the responsible organization of that collection

Could add my rare diseases collections of biological samples to another existing biobank? What organization is working on rare diseases biobanks?
Yes, of course. EuroBioBank (EBB) is the main organization working in the rare diseases biobanks since 2001. You can either send your own proposal to become a member of EBB or collaborate with an existing biobank near to your center.

What kind of criteria should be applied to my collection to be a good biobank?
A biobank is a system well organized which collect and donate both samples and disease data according with ethic codes and governance to improve the rare diseases knowledge.

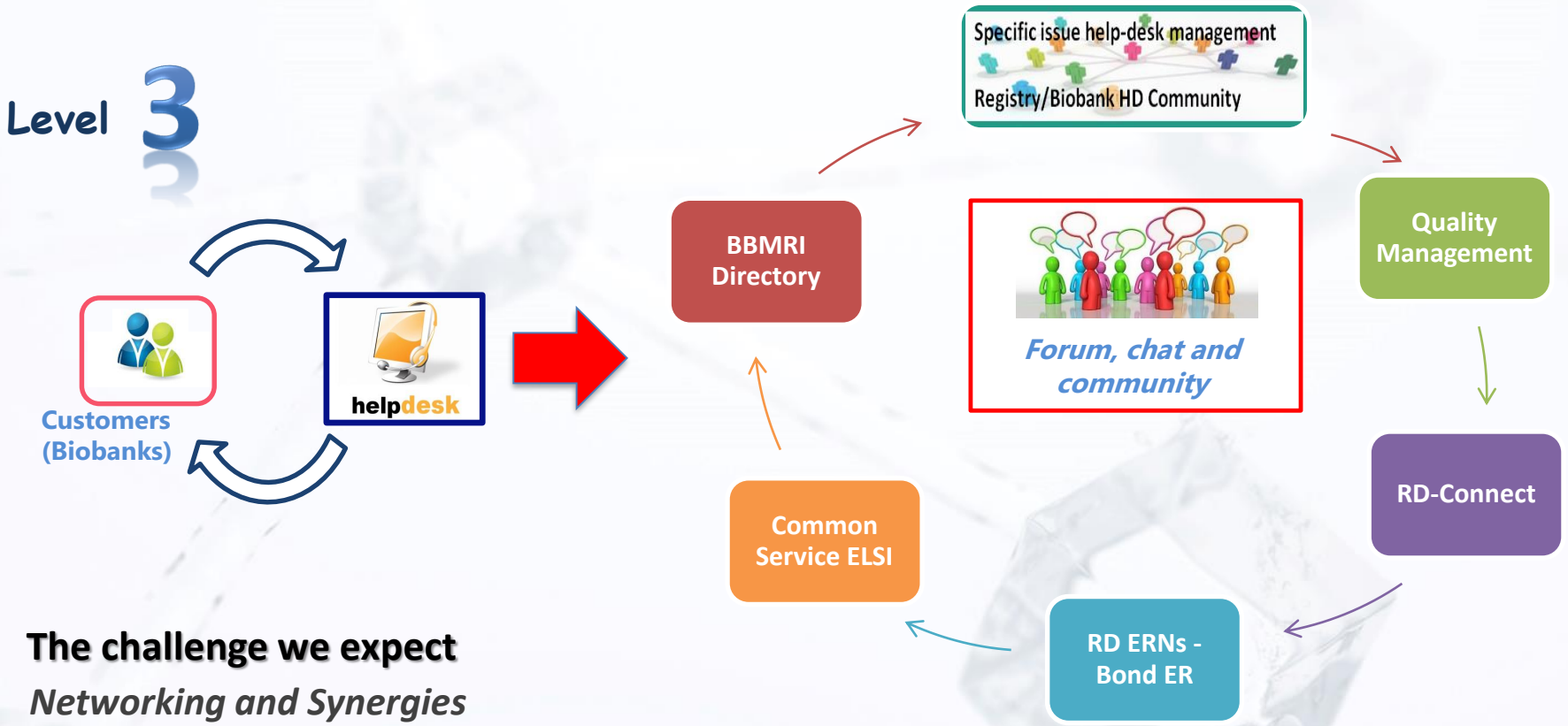
How can competing requests for scarce samples be managed?
The samples stored in Rare Disease (RD) biobanks are precious owing to their rarity, in particular samples such as tissues, blood and its derivatives (e.g. plasma/sera and DNAs/ RNAs) are limited and could run out shortly. Therefore, competing requests concerning limited amounts of sample need to be carefully evaluated. In order to sort out potential conflict of interest and to avoid sample misuse the RD biobanks are recommended to implement a devoted approval procedure which involves an external access committee composed by relevant and impartial legal, ethical and technical experts. In general, RD biobank should

↘ A webinar - tutorial was organized that shows how to use the Request Tracking system (RT), which is the basis for the rare disease helpdesk. The tutorial focused on how to send a request (then how to create a "ticket"), how to manage the ticket and also how to manage the ticket queues within the RT (*Petr Holub IT & Data Protection Manager @ BBMRI-ERIC)*.



- ✓ Help Desk Request Tracker accessible by the administrators at the address: https://helpdesk.bbmri-eric.eu/
- ✓ To send a request to the Help Desk <rd@helpdesk.bbmri-eric.eu>

Registry/biobank support service/ Help-desk facility
implemented of a web service composed of 3 support level in collaboration with WP3 and RDWG .



- **The challenge we expect**

Networking and Synergies

The HD will finally be tested as a transversal service on ERN on Rare Bone Diseases: *as a common service of BBMRI-ERIC involving RD- Connect*.

Help Desk Service for European Reference Networks

Osteogenesis imperfecta Pilot Study

ERN FAIR: to test the principles of FAIR data to support European reference networks through greater interoperability of clinical and biomedical data, test case: Osteogenesis imperfecta "

Osteogenesi Imperfetta, as a model of rare disease
This pathology has been selected because: a) it is well known; b) is well defined at the molecular and biochemical level; c) has a different degree of severity; d) is clinically complex; e) there are possible treatments

The idea of the project is to make the ***data of the biobanks and OI registers Findable, Accessible, Interoperable and Reusable (FAIR)*** - a system developed at the University of Leiden - and to test this type of approach and test its effectiveness also in the ERNs

Findable

Accessible

Interoperable

Reusable

↘ make data linkable,
↘ possibility of linking data to specific outcomes,
↘ test interoperability

We have shared data collection models within the RD Working Group.

LegacyCode	FamilyNumber	Gender	Proband	Phenotype	Genotype	O_Mutation	DateDiagnosis	DiagnosisType	DiagnosisKind	OmimNumber	Icd10	OrphanetNumber	RelationType	ProbandLegacyCode

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SERVIZIO SANITARIO REGIONALE EMILIA - ROMAGNA

CLINICAL OBSERVATION FORM

Patient Date of visit .....

Institution .....

Patient ID .....Unique identifier .....

Date of birth ..... Country of birth .....

Gender ☐ M ☐ F

Age of first manifestations.....

Age at diagnosis.....

Nationality .....

Clinical diagnosis.....

Type of OI (international classification).....

Family history

Family ID.....

Familiarity: ☐ Yes ☐ No ☐ Unknown

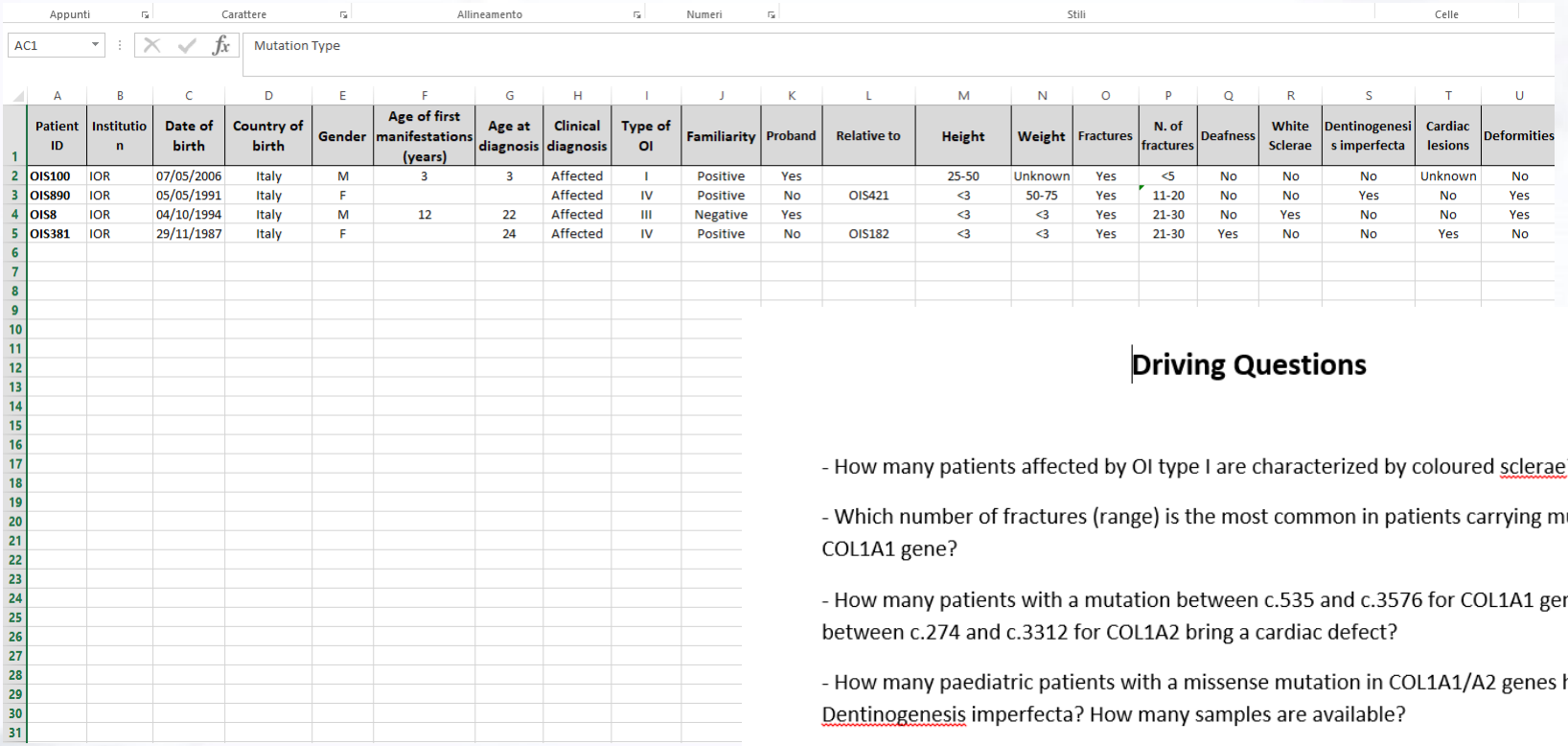
☐ proband ☐ relative to (patient ID).....

Clinical features:

Height..... Weight.....

- Osteogenesis Imperfecta Form for clinical information
- Sample minimum data set

- Defined together and shared the main vocabularies and ontologies
- Defined together and shared the data and file to be used



Appunti | Carattere | Allineamento | Numeri | Stili | Celle

AC1 | Mutation Type

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
1	Patient ID	Institution	Date of birth	Country of birth	Gender	Age of first manifestations (years)	Age at diagnosis	Clinical diagnosis	Type of OI	Familiarity	Proband	Relative to	Height	Weight	Fractures	N. of fractures	Deafness	White Sclerae	Dentinogenesis imperfecta	Cardiac lesions	Deformities
2	OIS100	IOR	07/05/2006	Italy	M	3	3	Affected	I	Positive	Yes		25-50	Unknown	Yes	<5	No	No	No	Unknown	No
3	OIS890	IOR	05/05/1991	Italy	F			Affected	IV	Positive	No	OIS421	<3	50-75	Yes	11-20	No	No	Yes	No	Yes
4	OIS8	IOR	04/10/1994	Italy	M	12	22	Affected	III	Negative	Yes		<3	<3	Yes	21-30	No	Yes	No	No	Yes
5	OIS381	IOR	29/11/1987	Italy	F		24	Affected	IV	Positive	No	OIS182	<3	<3	Yes	21-30	Yes	No	No	Yes	No

Driving Questions

- How many patients affected by OI type I are characterized by coloured sclerae?

- Which number of fractures (range) is the most common in patients carrying mutation on COL1A1 gene?

- How many patients with a mutation between c.535 and c.3576 for COL1A1 gene and between c.274 and c.3312 for COL1A2 bring a cardiac defect?

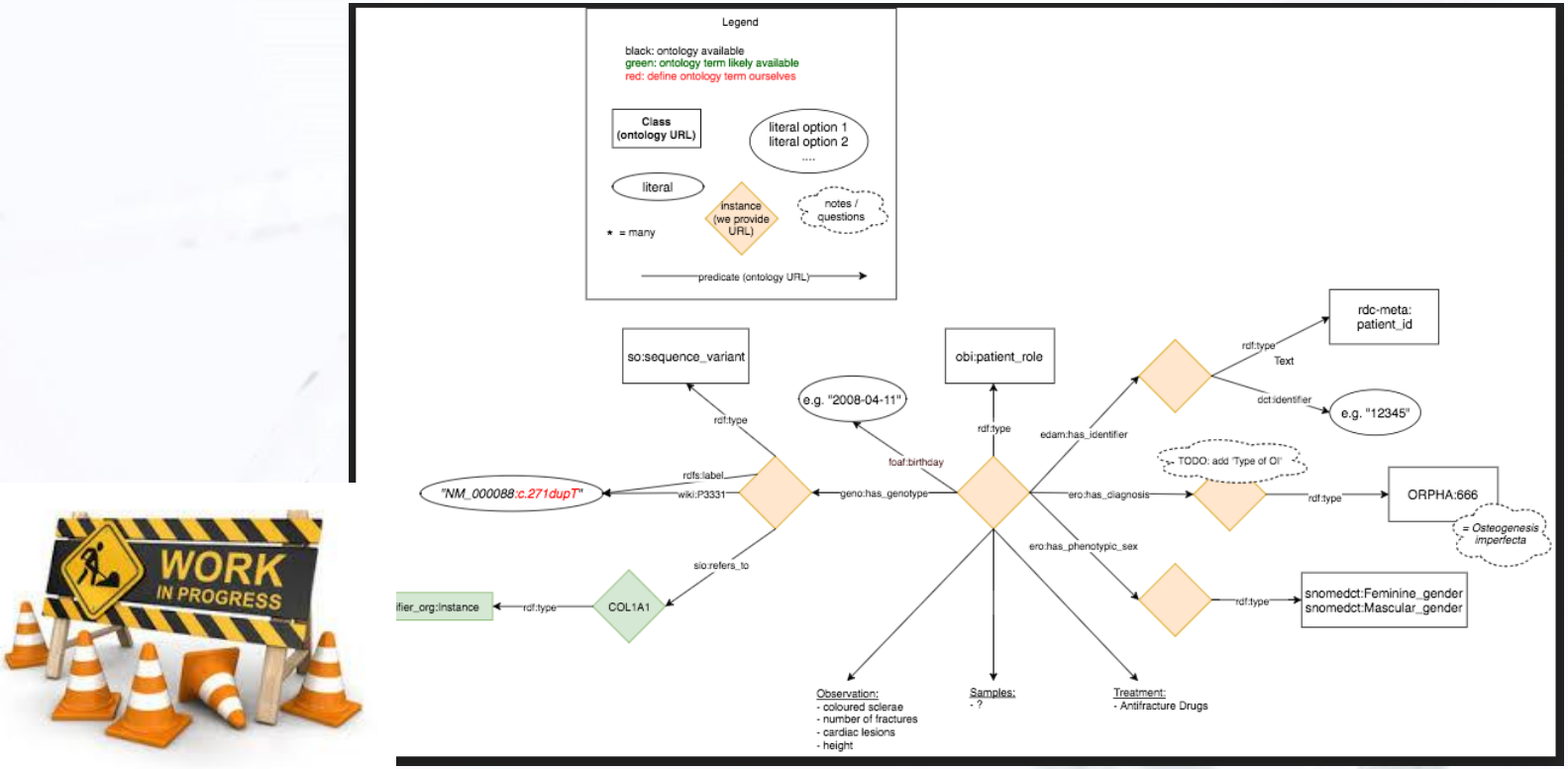
- How many paediatric patients with a missense mutation in COL1A1/A2 genes have a Dentinogenesis imperfecta? How many samples are available?

- Among all adults, which OI type is characterized by higher height? How many of them are males?

- For each type of OI, how many familiar cases with splice site mutations are present in the dataset?

- Provided excel with genetic clinical data and samples of interest i
- Definition of Driving questions

- LUMC generates an OI data model



Pilot OI ongoing

Thank you for your attention!

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