

DMP and Open Data training

Session 3: Metadata



Life science standards and ENA submission

helene.chiapello@inrae.fr & thomas.denecker@france-bioinformatique.fr

Metadata & standards in life sciences

Metadata standards help describing data

How do you
describe
the data?

With a set of
metadata

A	B
1 Titre	
2 Auteur	
3 Date	
4 Résumé	
5 Mots-clés	
6 Identifiant	
7 Format	
8 Contexte de création	

How do you
ensure you don't
forget certain
metadata?

With a
**metadata
standard**

Disciplinary
standard



General
standard



Source: <https://www.pasteur.fr/fr/file/20615/download>

Definition of a standard

In essence, a standard is an **agreed way of doing something**.

A standard provides the **requirements, specifications, guidelines or characteristics** that can be used for the **description, interoperability, citation, sharing, publication, or preservation** of all kinds of **digital objects** such as data, code, algorithms, workflows, software, or papers.

source: <https://fairsharing.org/educational/>

Example of standard in biology : Gene Ontology

The standards concern both data and metadata

Why do I have to use a **data standard**?

- to analyse, compare and exchange data
- to publish datasets in international resources

And a **metadata standard**?

- To describe data richly and accurately, with the same vocabulary as the rest of your scientific community
- To make your metadata interoperable and to allow other systems to exploit them

The Gene Ontology is a **metadata standard**

Question: Do you know any standard in life sciences ?

5 minutes to find an example (one for data and one for metadata) and write a note in

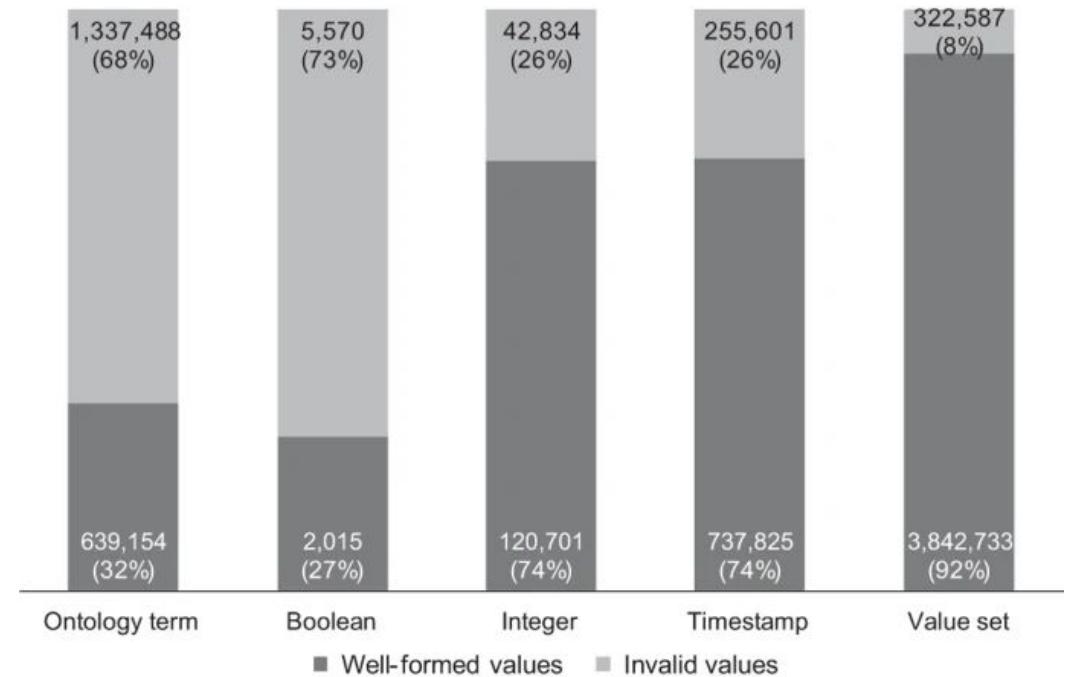
<https://scrumblr.ethibox.fr/standard>

Metadata exhibit questionable quality in biology

Submission in public resources is often a complex task

Submission procedures are heterogeneous

Metadata are often incomplete, inconsistent, redundant or not enough informative



Quality of dictionary attributes in NCBI BioSample according to their type, in [Gonçalves et al., 2019](#)

Standard adoption and perenity

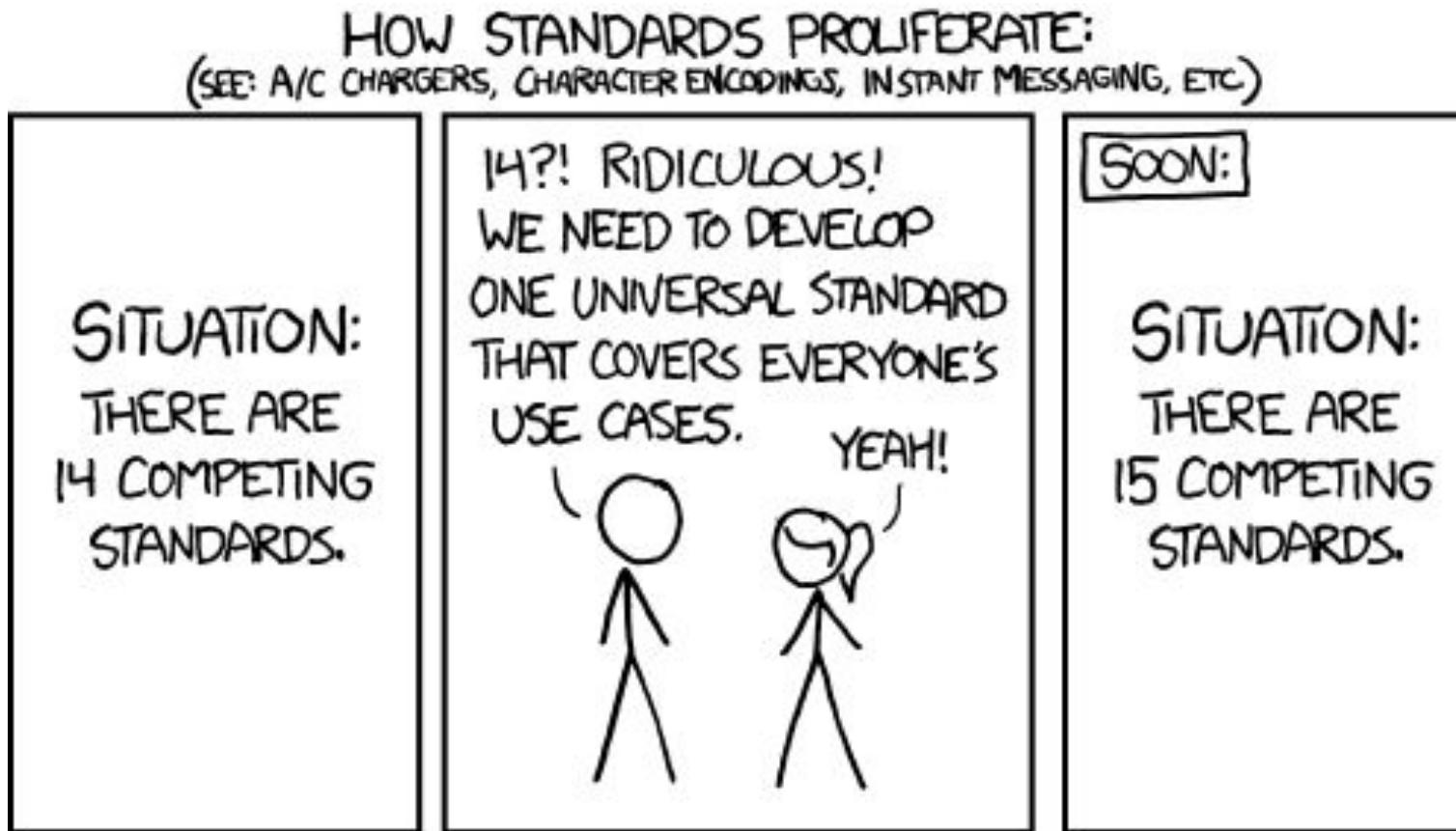
- There are thousand of databases, softwares and resources in biology with **unequal level of standard adoption**
 - Is is not always easy for Life scientists and bioinformaticians to identify and use the most appropriate standards



1641 databases in NAR Database 2021

Rigden et al., 2021

Standard adoption and perenity



Source: <https://xkcd.com/927/>

How do I find the standard I need?

The FAIRsharing portal

Sansone, *et al.* FAIRsharing as a community approach to standards, repositories and policies.

Nat Biotech. 2019

<https://doi.org/10.1038/s41587-019-0080-8>



A screenshot of the FAIRsharing.org website. The header includes the site's name, a search bar, and navigation links for Standards, Databases, Policies, Collections, Add/Claim Content, Stats, and Log in or Register. A main heading states: "A curated, informative and educational resource on data and metadata standards, inter-related to databases and data policies." Below this is a section titled "HOW CAN WE HELP?" with a sub-section for "Research data facilitators, librarians, trainers". It features an illustration of a person sitting at a desk with a computer monitor displaying a database interface, surrounded by icons representing documents, databases, and other resources. The page also includes sections for Researchers, Developers & Curators, Journal Publishers, Librarians & Trainers (which is currently selected), Societies & Alliances, and Funders. At the bottom, there are three boxes labeled Find, Discover, and Learn, each with a sub-section like Recommendations, Collections, and Educational. A footer bar contains a search bar, Advanced Search, Search Wizard, and a "Ask FAIRsharing" button.

<https://fairsharing.org>

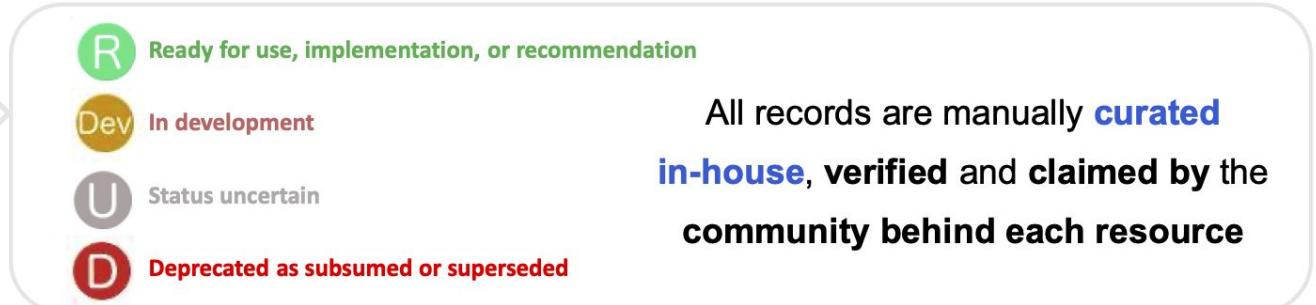
The FAIRsharing portal

Citable DOI for all records

Accessible via API or web interface

Curation

RECORD STATUS



<https://fairsharing.org>

The FAIRsharing portal: record status



R Ready for use, implementation, or recommendation



Dev In development



U Status uncertain

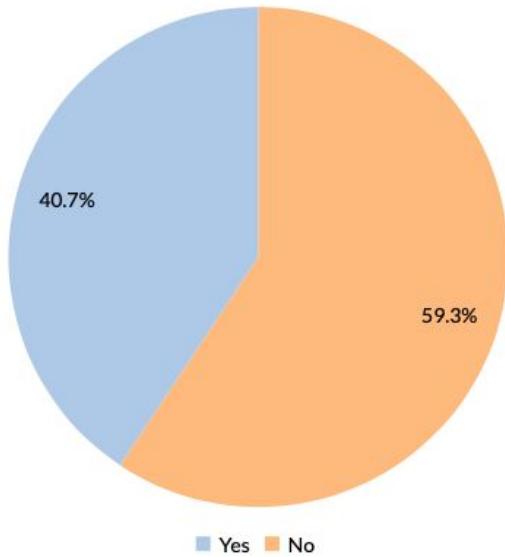


D Deprecated as subsumed or superseded

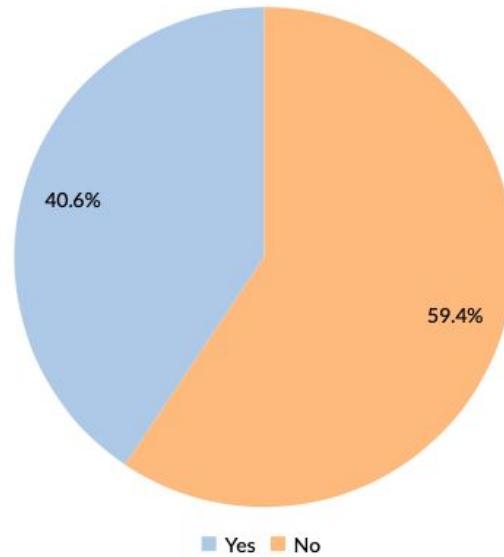
Please don't use “Uncertain” or “Deprecated” standards

Standard maintenance is a key point

Standard records that have maintainers



Standards that have a publication



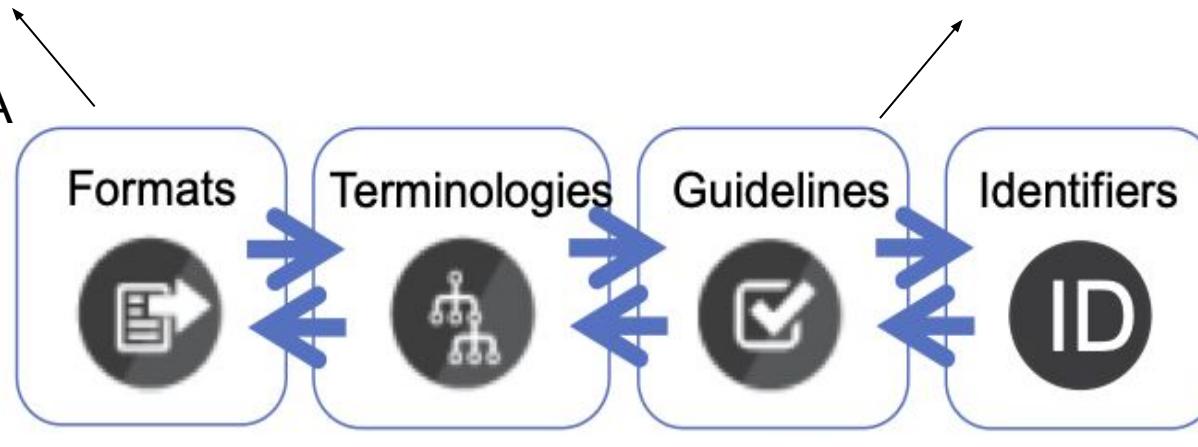
59.3 % of standards have no maintainer

59.4% of standard has no publication

<https://fairsharing.org/summary-statistics/?collection=standards>

Types of data standards

Conceptual model, schema, exchange formats, etc...
e.g. SBML, FASTA

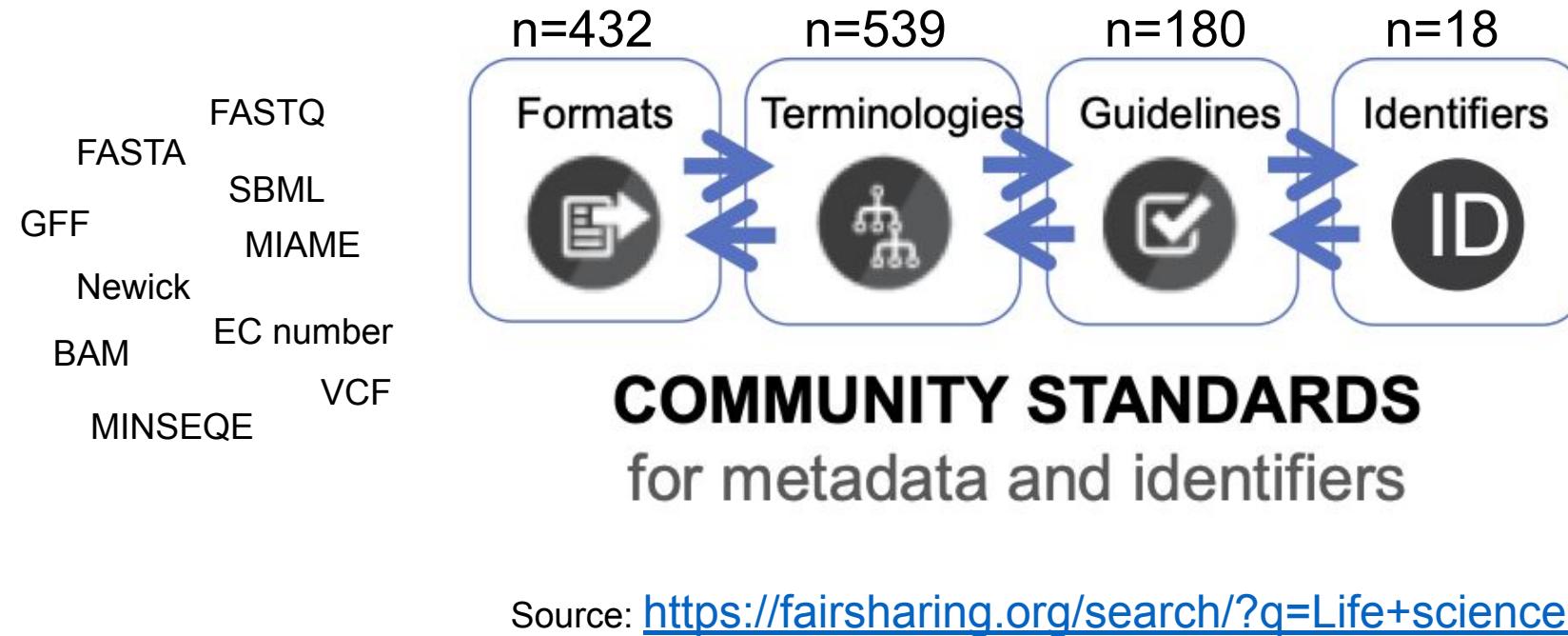


Controlled vocabularies, taxonomies, ontologies...
e.g. Gene Ontology

Minimum information reporting requirements, checklists...
e.g. MIAME guidelines

Formal systems for resources and digital objects that allow their identification
e.g. DOI

The landscape of standards in life sciences



 **genomic**
STANDARDS *consortium*

 **isatools**

 **GENEONTOLOGY**
Unifying Biology

 **Crop Ontology**
for agricultural data

 **DISEASE
ONTOLOGY**

Collections in the FAIRsharing portal

A *collection* include standards and/or databases grouped by *domain, species or organization*

Graph view to visualize relationship links between resources

<https://fairsharing.org/collections/>

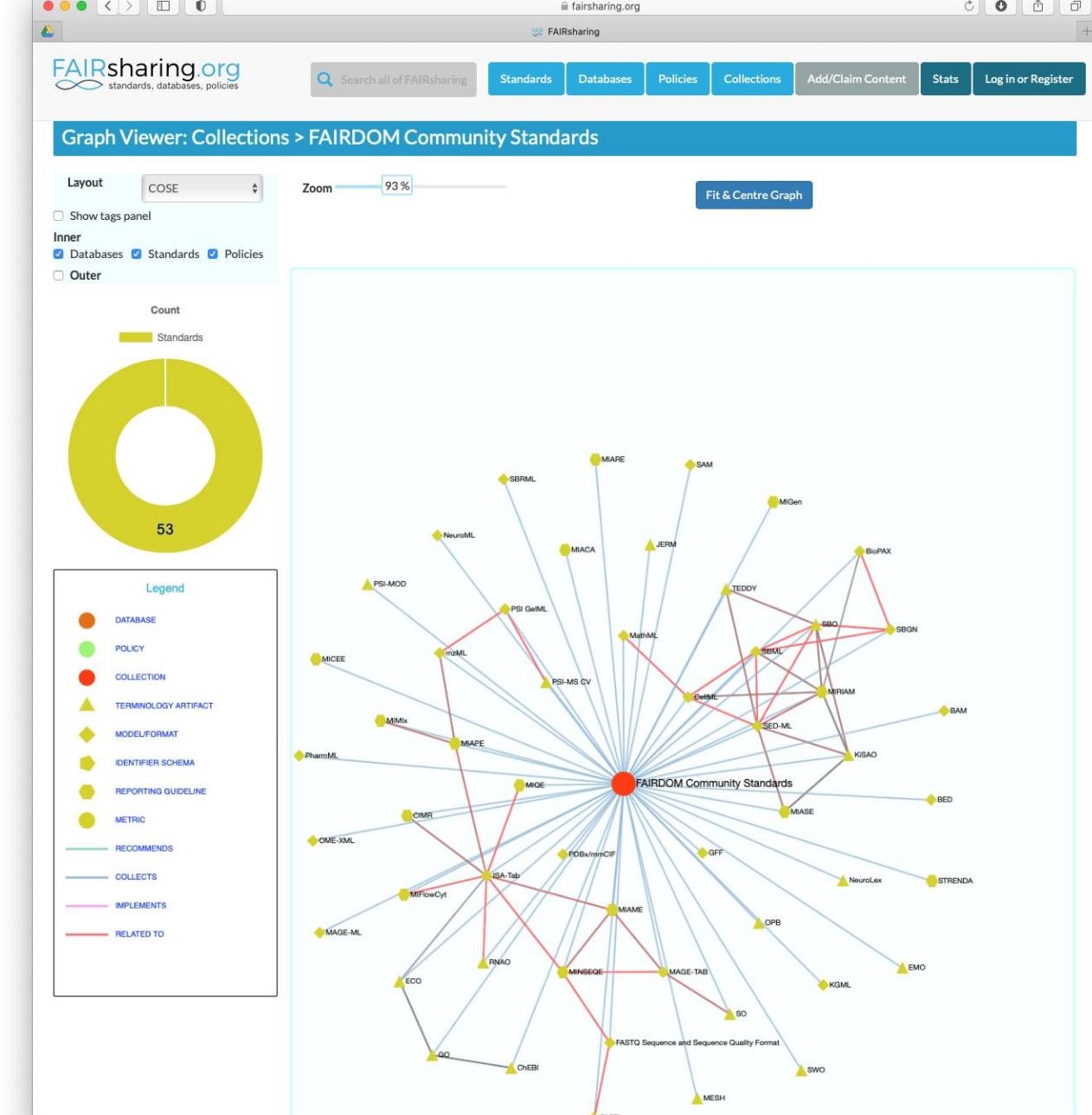
The screenshot shows the FAIRsharing.org interface for a collection named "COVID-19 Resources". The top navigation bar includes links for Standards, Databases, Policies, Collections, Add/Claim Content, Stats, and Log In or Register. Below the navigation is a search bar and a menu bar with categories like Biomedical Science, Clinical Studies, Epidemiology, Global Health, Health Science, Preclinical Studies, Public Health, and Virology. A sidebar on the left contains sections for Subjects (e.g., Biomedical Science, Clinical Studies, Epidemiology, Global Health, Health Science, Preclinical Studies, Public Health, Virology), User-defined Tags (Respiratory Disease), and a "View as Graph" button. The main content area displays general collection statistics for "COVID-19 Resources" (bsg-c000070) and a table of records. The table has columns for Registry, Name, Abbreviation, Type, Subject, Domain, Taxonomy, Related Database, Related Standard, Related Policy, and In Collection/Policy. The table shows 50 records out of 80, with various resource types like Database, Standard, and Policy. A "View as Grid" button is also present in the table header. On the right side of the table, there are two vertical lists of related resources: "Related Resources" and "Plus 8 more...". At the bottom of the page, there are links for "COVID-19 Resource" and "ISA-Covid-19 WG".

Collections in Life Sciences

63 collections related
to Life Science
standards in
FAIRsharing

Example 1: the *FAIRdom community Standards collection* (System biology)

<https://fairsharing.org/collection/FAIRDOM>

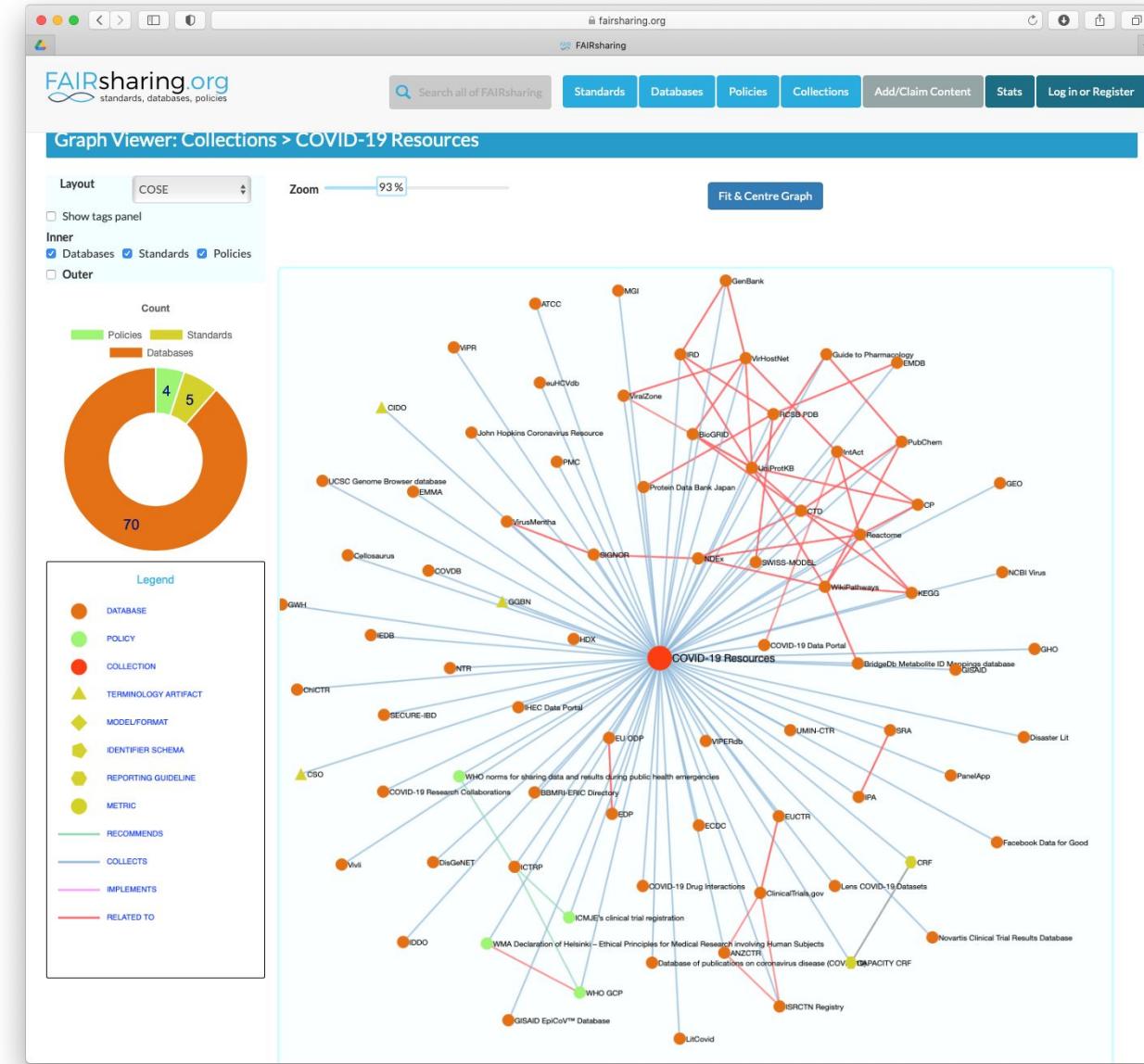


Some collections are recent

Example 2: The Covid-19 collection

This screenshot shows the FAIRsharing.org collection page for COVID-19 Resources. The top navigation bar includes links for Standards, Databases, Policies, Collections, Add/Claim Content, Stats, and Log in or Register. The main content area displays general collection statistics and a detailed list of records. The list includes columns for Registry, Name, Abbreviation, Type, Subject, Domain, Taxonomy, Related Database, Related Policy, and In Collection(s). A legend on the right provides a key for various record types.

<https://fairsharing.org/collection/COVID19Resources>

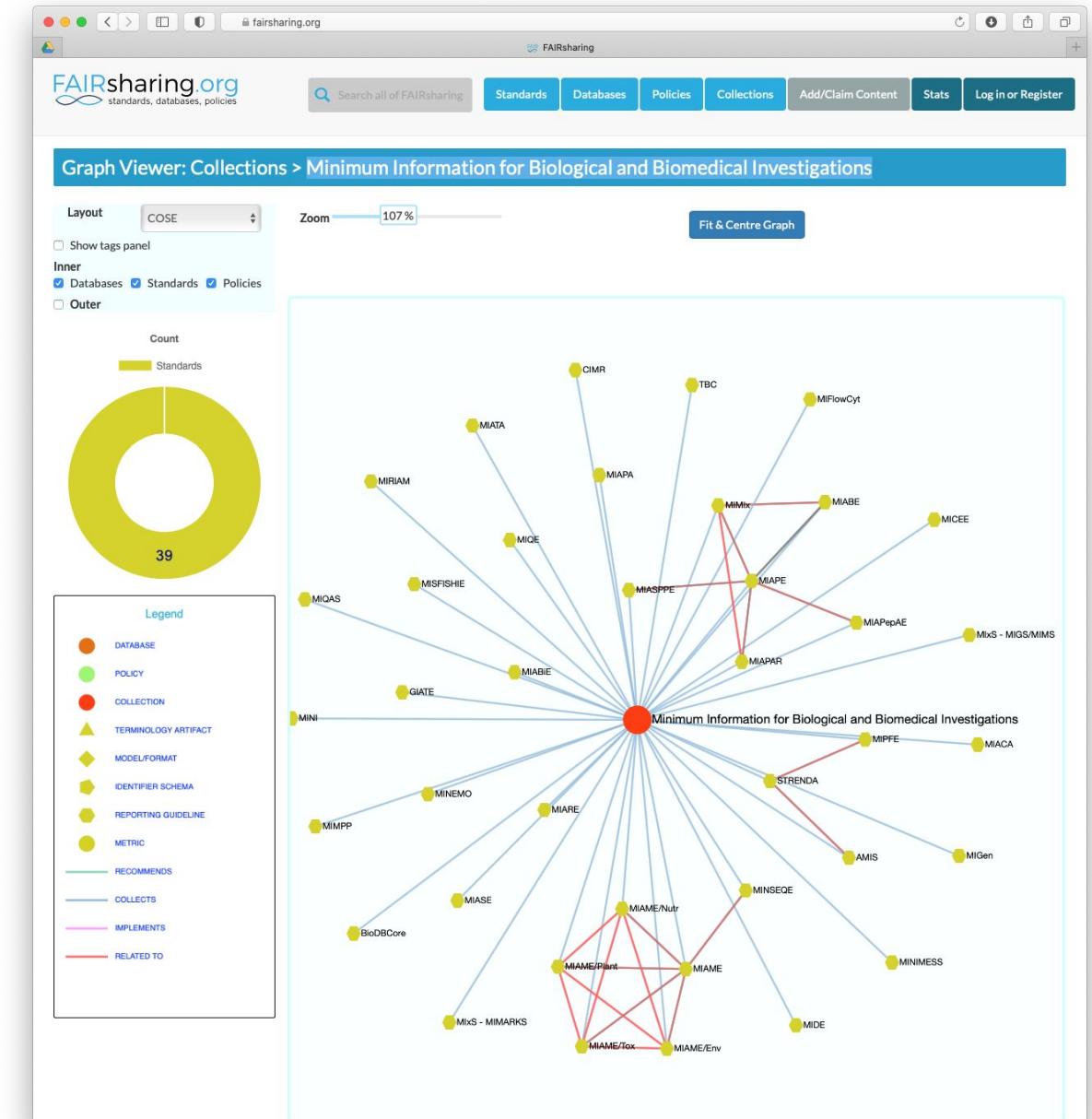


<https://fairsharing.org/graph/#/collection/bsg-c000070>

What about the minimum required metadata in biology?

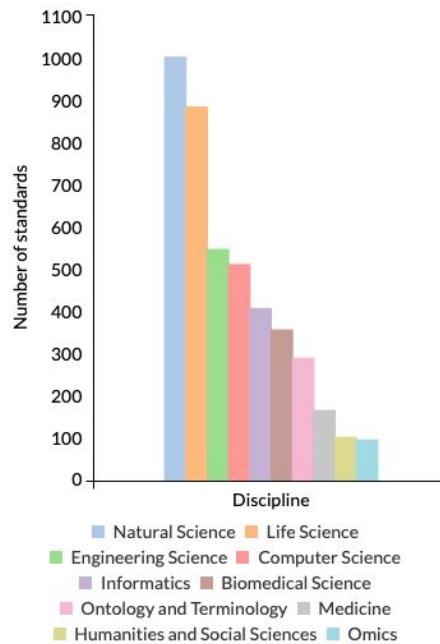
Example 3: the *Minimum Information for Biological and Biomedical Investigations* collection

<https://fairsharing.org/collection/MIBBI>

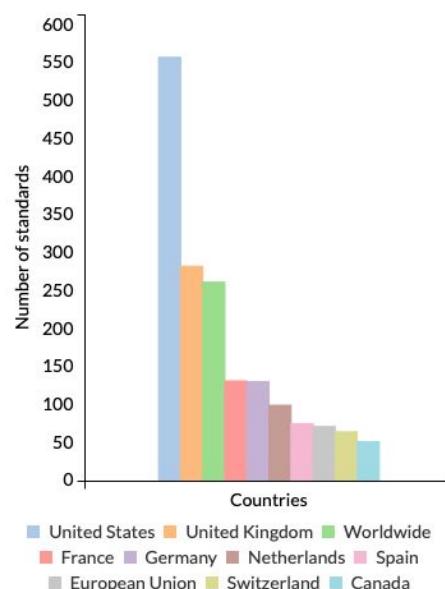


Summary statistics about standards

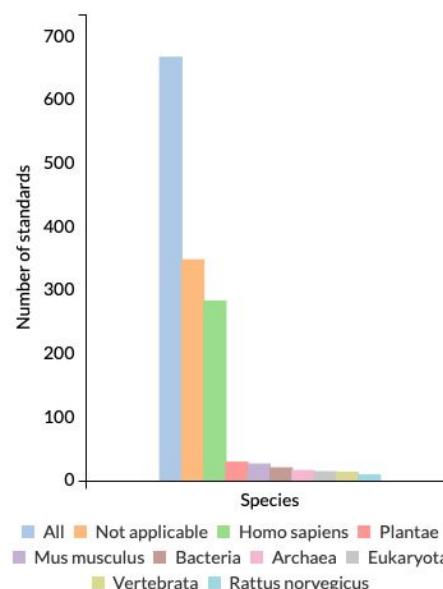
Top 10 disciplines covered by standards



Top 10 standard producing countries



Top 10 species covered by standards



Life Science is one of the best covered discipline

US and UK are the main standards producers

Human species is the best covered species

<https://fairsharing.org/summary-statistics/?collection=standards>

Practice

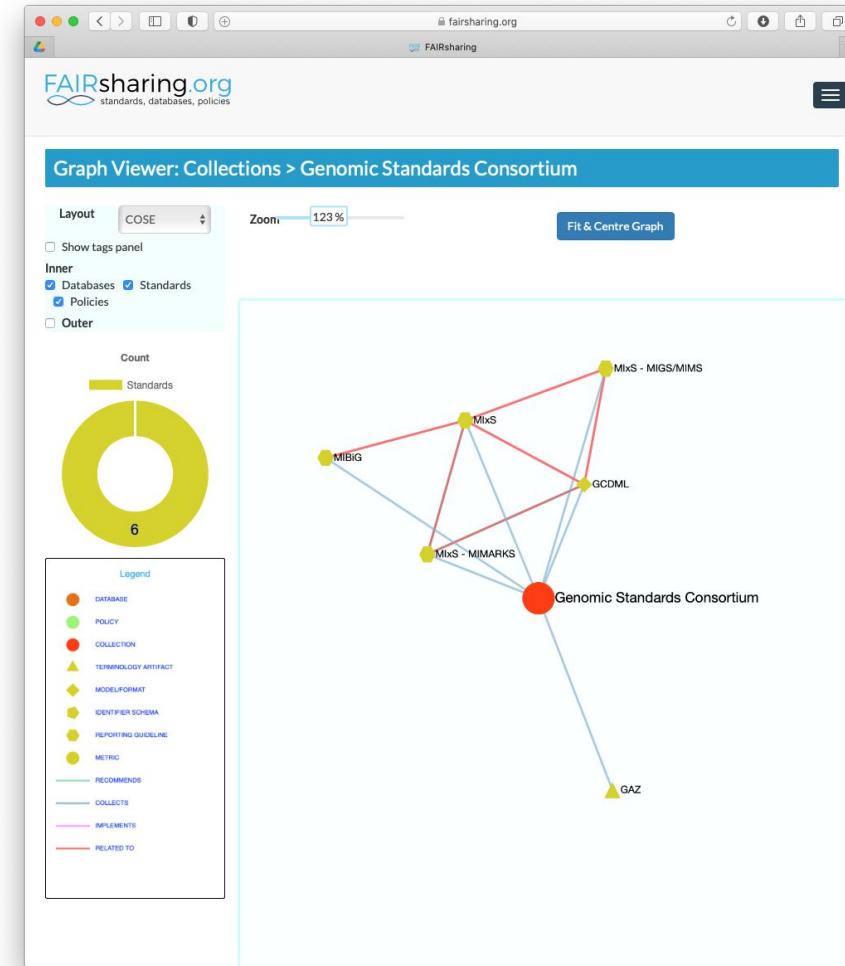
Find the *Genomic Standards Consortium (GSC)* used by both ENA and SRA databases in the **FAIRsharing collections**

Use both the record summary and the Graph visualization to interpret and answer the questions in zoom:

1. How many records (*i.e.* standards) are associated to the *GSC* ?
2. What type of standard is *Minimum Information about any (x) Sequence (MiXS)* ?
3. What is the record status of the *GAZ* record ?

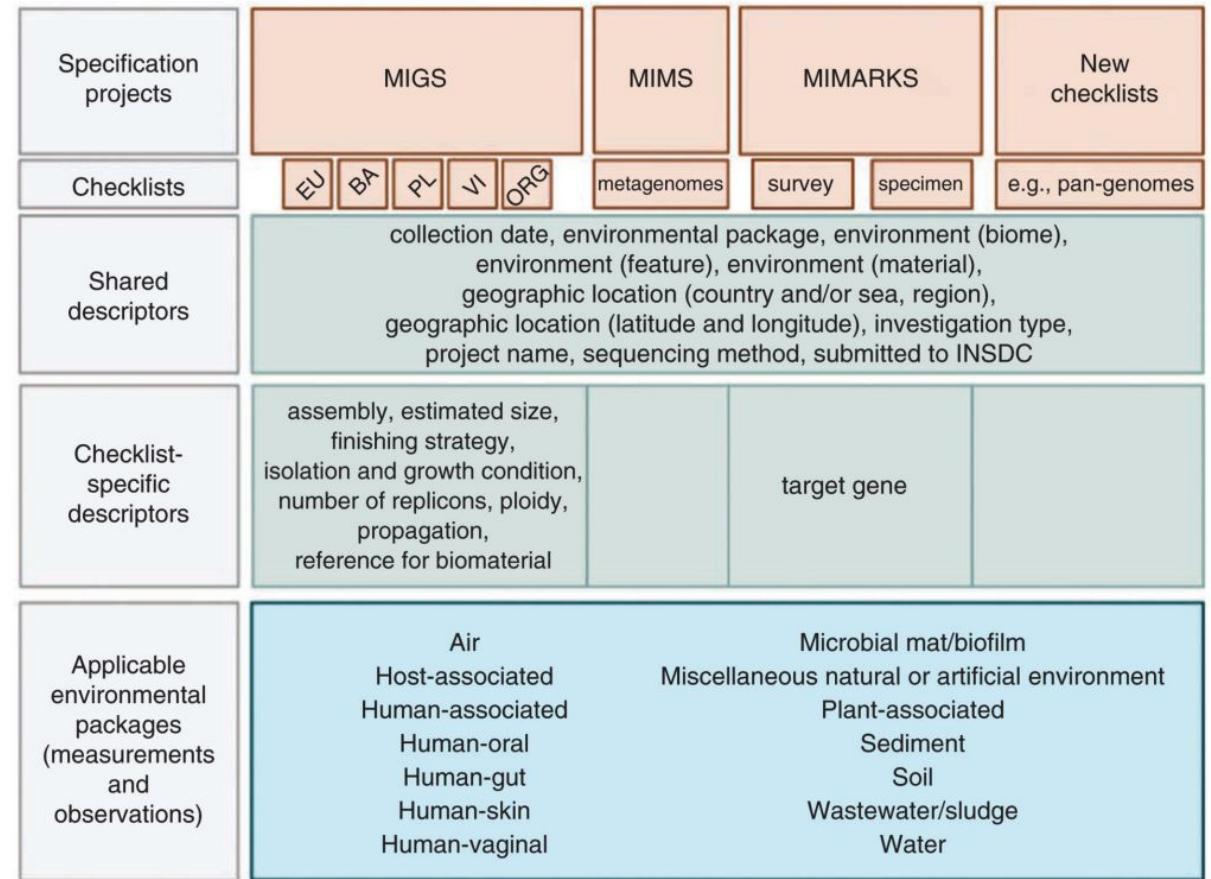
The Genomic Standards Consortium (GSC)

https://fairsharing.org/collection/GSC



The Genomic Standards Consortium (GSC)

- An international community-driven standard in **Genomics** producer of the **MIxS: Minimum Information Standards about any(X) Sequence**
- MIxS includes **technology-specific checklists** (MIGS, MIMS, MIMARKS,...) and also allows **annotation of sample data** using environmental packages



[Yilmaz et al, 2011](#)

Source: <https://gensc.org>

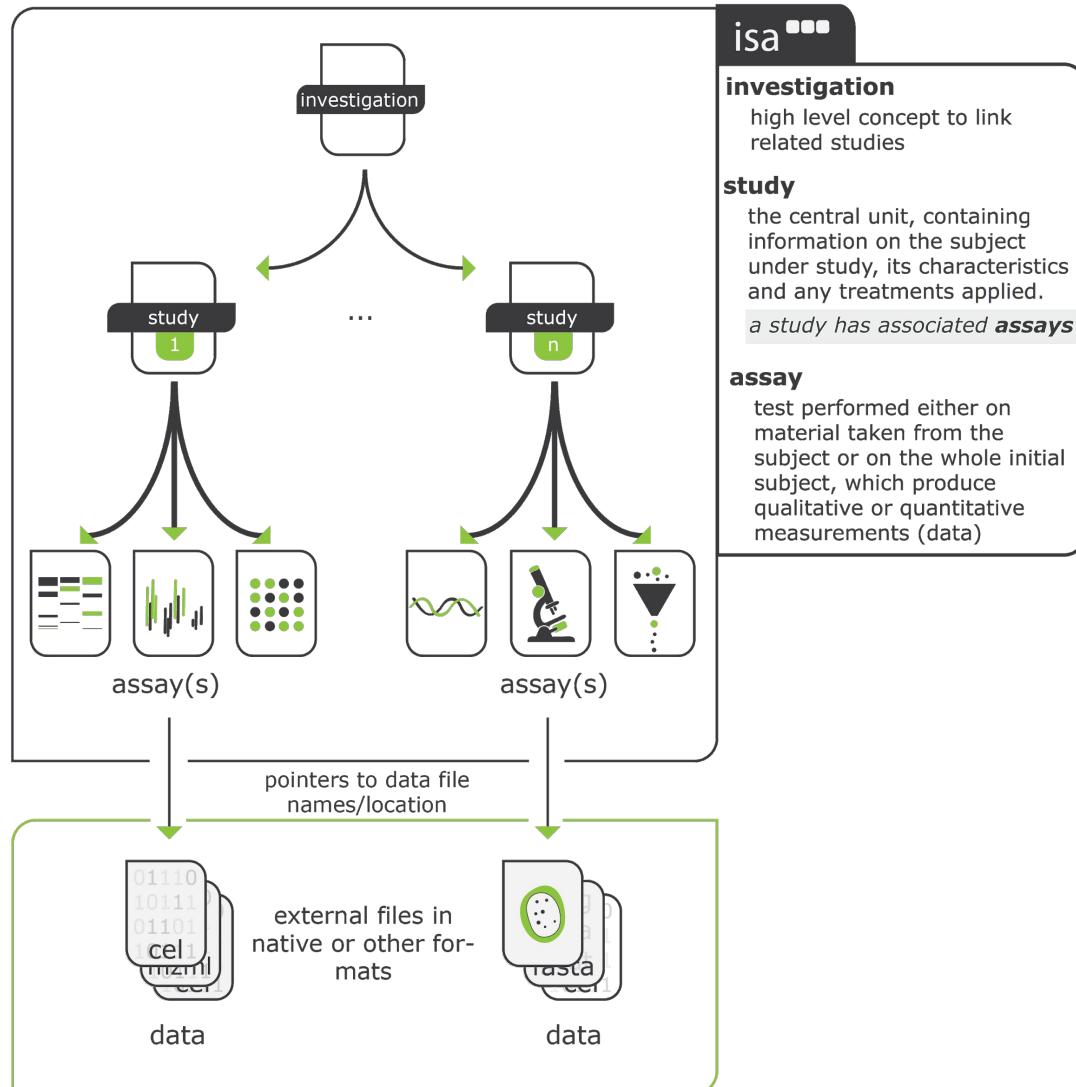
The ISA model

A standard for Life ScienceData

A model to capture experimental metadata through 3 core entities:

- **Investigation:** the project context
- **Study:** an experimentation in one location
- **Assay:** a specific measurement that targets a trait with a method and a scale

ISA software suite: supporting standards-compliant experimental annotation and enabling curation at the community level. Rocca-Serra P et al. **Bioinformatics** 2010.
<https://doi.org/10.1093/bioinformatics/btq415>



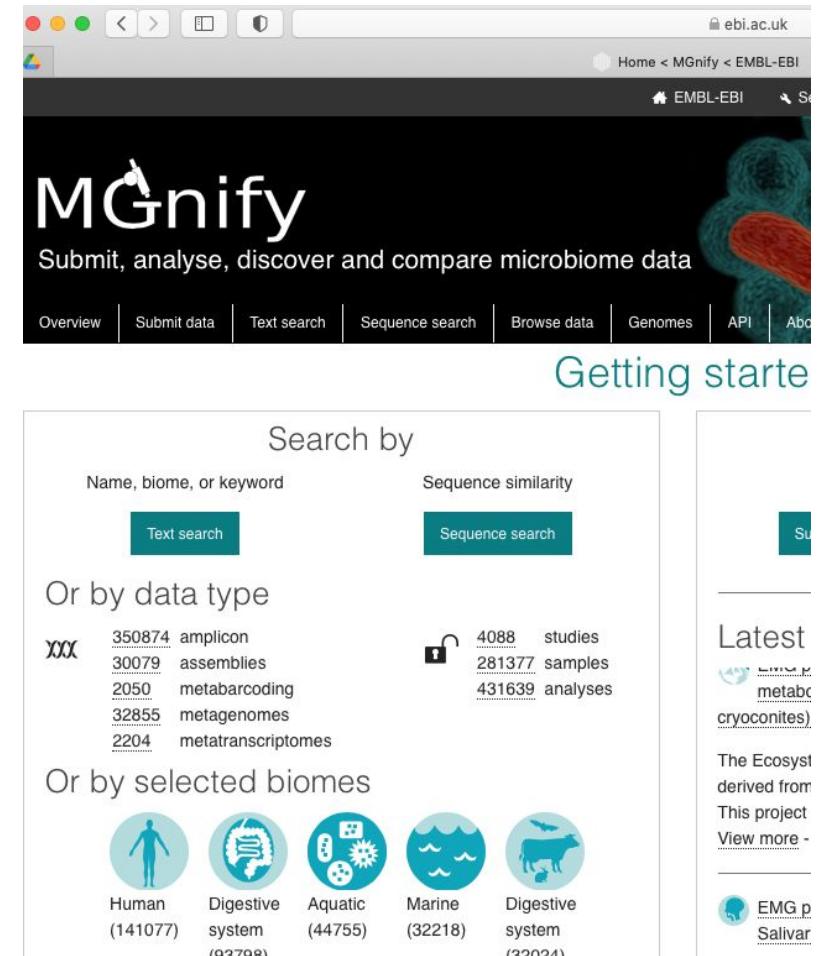
Sources: <https://isa-tools.org> and :
<https://isa-specs.readthedocs.io/en/latest/isamodel.html>

European Nucleotide Archive (ENA) submission



Why do I need to submit my data and metadata to ENA ?

- Open Science and reproducibility of experiments
- 3rd party access
- Archival
- Publication
- Analyses, example: [MGinify](#)

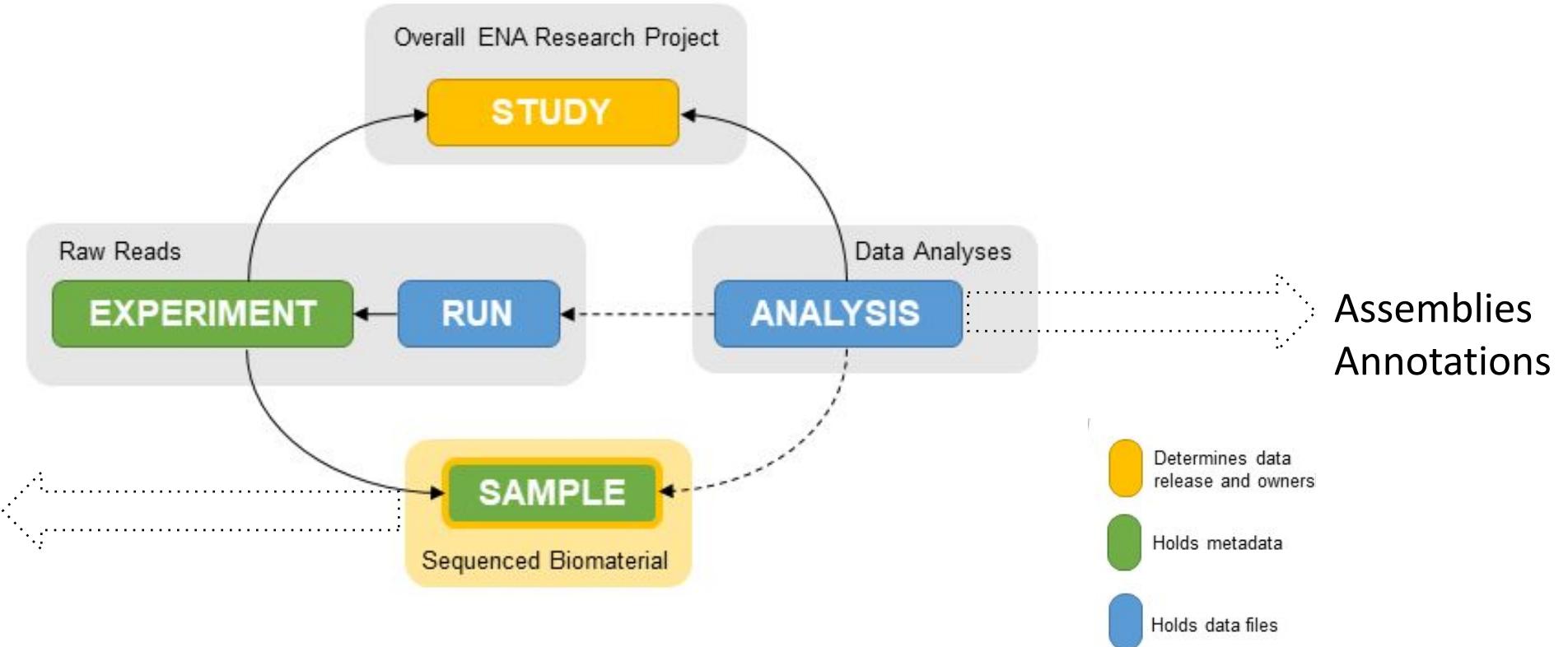


The screenshot shows the MGinify homepage. At the top, there's a navigation bar with links for Overview, Submit data, Text search, Sequence search, Browse data, Genomes, API, and About. Below the navigation is a main search area with two tabs: 'Text search' (selected) and 'Sequence search'. To the right of the tabs, there are sections for 'Sequence similarity' and 'Sequence search'. Below these are sections for 'Or by data type' and 'Or by selected biomes'. The 'Or by data type' section lists various microbiome types with their counts: 350874 amplicon, 30079 assemblies, 2050 metabarcoding, 32855 metagenomes, 2204 metatranscriptomes, 4088 studies, 281377 samples, and 431639 analyses. The 'Or by selected biomes' section shows icons for Human (141077), Digestive system (1927981), Aquatic (44755), Marine (32218), and Digestive system (1390941). On the right side of the page, there are sections for 'Latest' (listing entries like 'Lysogenic conversion in Escherichia coli K12 MG1655'), 'The Ecosystem' (derived from ENA), and 'View more -'. At the bottom, there are links for 'EMG p' and 'Salivar'.

The ENA metadata model

ISA compliant !

All **samples** submitted to ENA must conform to a **Checklist**



Source: <https://ena-docs.readthedocs.io/en/latest/submit/general-guide/metadata.html>

THE ENA Checklists

- A **checklist** defines the **minimum and optional metadata** expected to describe biological samples
- ENA are based on the **Genomic Standards Consortium (GSC)** recommandations
- The **most suitable checklist** depends on the type of the sample:
<https://www.ebi.ac.uk/ena/browser/checklists>
- All ENA checklist are defined by an **access number** like ERCxxx (Ena R Checklist xxx)
 - example: GSC MIxS plant associated
<https://www.ebi.ac.uk/ena/browser/view/ERC000020>

Data brokering at IFB

Why developing data brokering at IFB?

Observations:

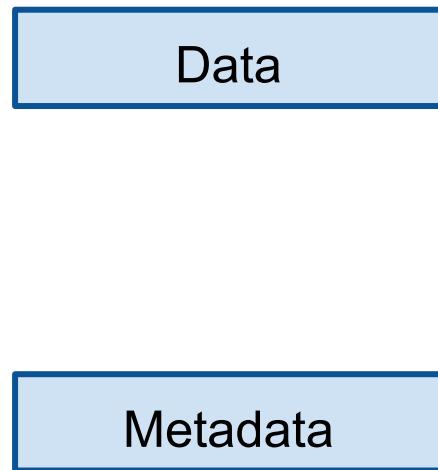
- Submissions are often complex and difficult to perform by individual teams
- Metadata are often poorly understood resulting in incomplete, redundant and inconsistent submissions
- ENA asks that IFB becomes the French national broker

Main idea: offer a national service of **data brokering at IFB** to simplify and rationalize data exchange between international resources and the french Elixir node IFB.

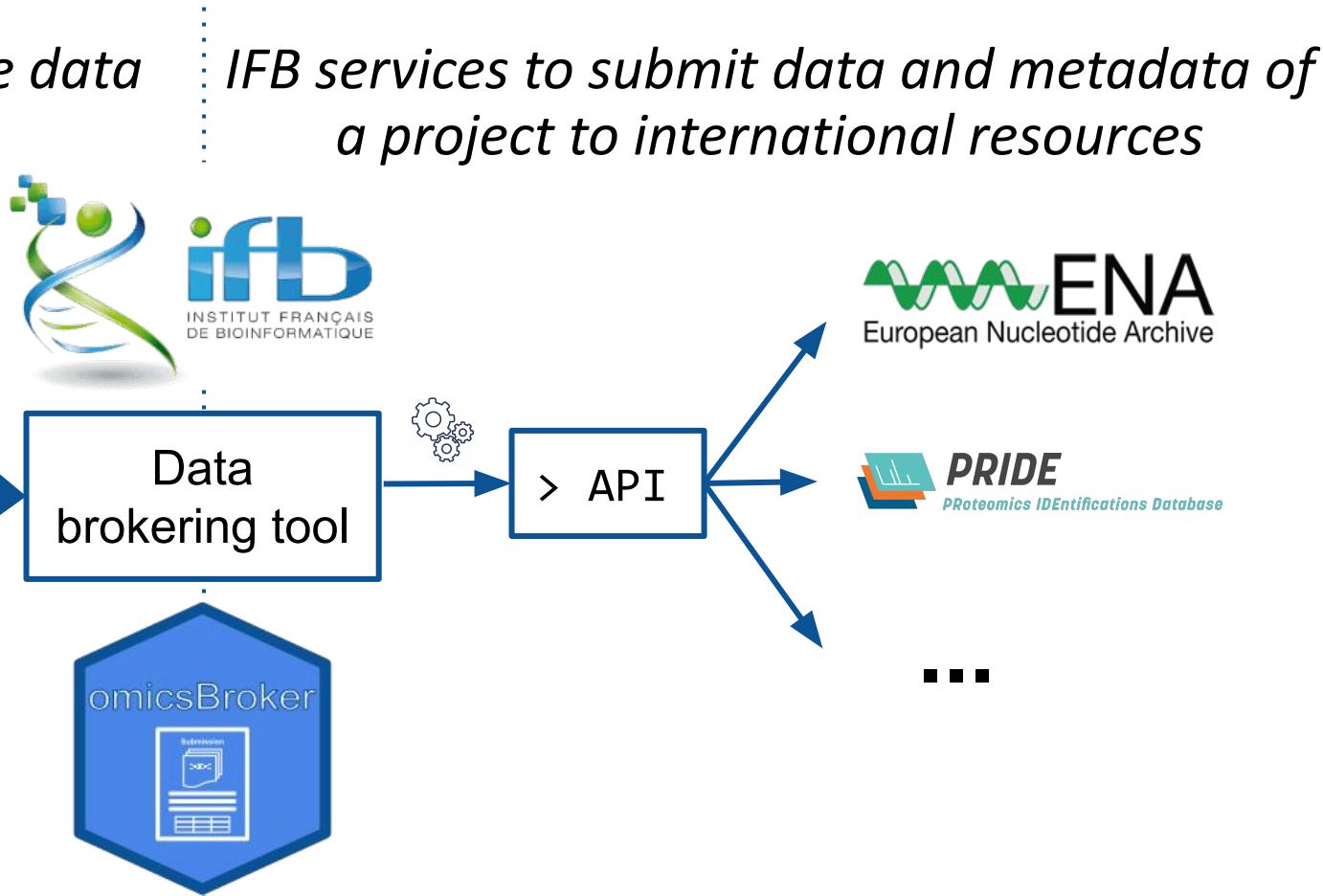
Brokering include 3 types of activities: tools development, training and support to users

Data Brokering service developed by IFB

IFB services to manage and centralize data and metadata of a project



IFB services to submit data and metadata of a project to international resources





The omicsBroker tool

- **omicsBroker** is a tool to easily annotate and submit **omics data** to **international repositories**
- For now, only available as a **PROTOTYPE**
 - based on **R Shiny** technology
 - allowing to test submission of genomic and transcriptomic samples and reads to **ENA test instance**
- The final tool will be developed using Django technology and will **manage data and metadata from different sources** to make submission to international resources easier

<https://github.com/IFB-ElixirFr/omicsBroker>

Practice

Use omicsBroker prototype (<http://134.158.247.47:443> or <http://134.158.247.47:443/app/omicsBroker>) to test submission of samples to ENA

Use information of the corresponding DMP to associate relevant metadata to data <https://dmp.opidor.fr>

3 groups

- bacterial genome ([IFB_Training_salivarius](#))
- SARS-CoV2 genome ([IFB Training : Sars-CoV-2](#))
- plant transcriptome ([IFB_Training_plant](#))

https://ifb-elixirfr.github.io/IFB-FAIR-data-training/sequences/module3_sequence3_tp.html

To conclude: sources & useful links

Description	Name	URL
A curated, informative and educational resource on data and metadata standards, inter-related to databases and data policies.	FAIRsharing portal	https://fairsharing.org
Investigation, Study, Assay (ISA) ressource: A standard model and a set of tools to capture experimental data in life sciences	ISAtools	https://isa-tools.org
Genomics Standard Consortium (GSC): An international consortium developing standards and checklists in genomics	GSC	https://gensc.org
European National Archive Checklists	ENA Checklists	https://www.ebi.ac.uk/ena/browser/checklists
European National Archive submission documentation	ENA submission guide	https://ena-docs.readthedocs.io/en/latest/submit/general-guide.html
A prototype to test submission of samples and DNAseq or RNAseq reads to ENA	omicsBroker	https://github.com/IFB-ElixirFr/omicsBroker

Thanks



Paulette Lieby



Jean-François Dufayard



Frédéric de Lamotte

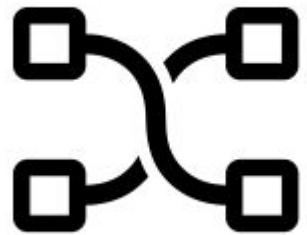
Supplementary slides

Standard for data and metadata



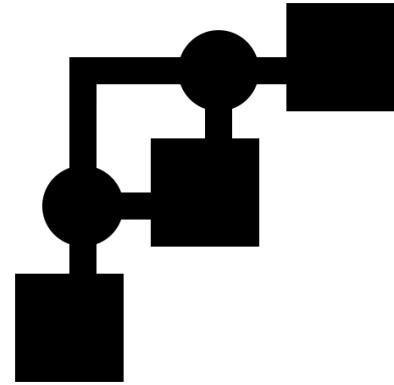
Guidelines or checklists

Ex: the GSC checklist



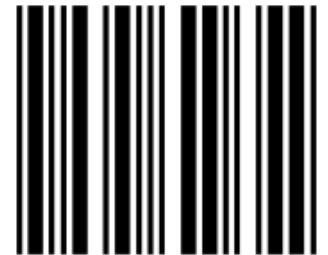
Models or schemas

Ex: ISA model



Terminology artefacts,
ontology

Ex: The Gene Ontology

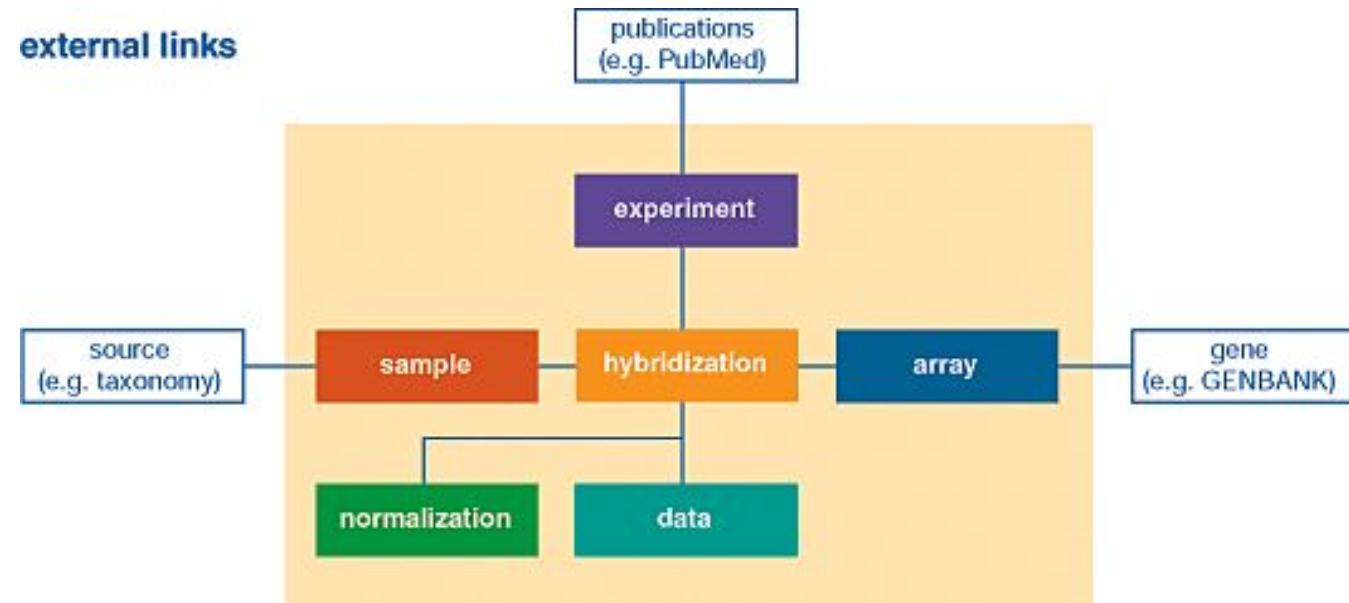


Identifier schemata

<https://fairsharing.org>

The Minimum information standard initiative

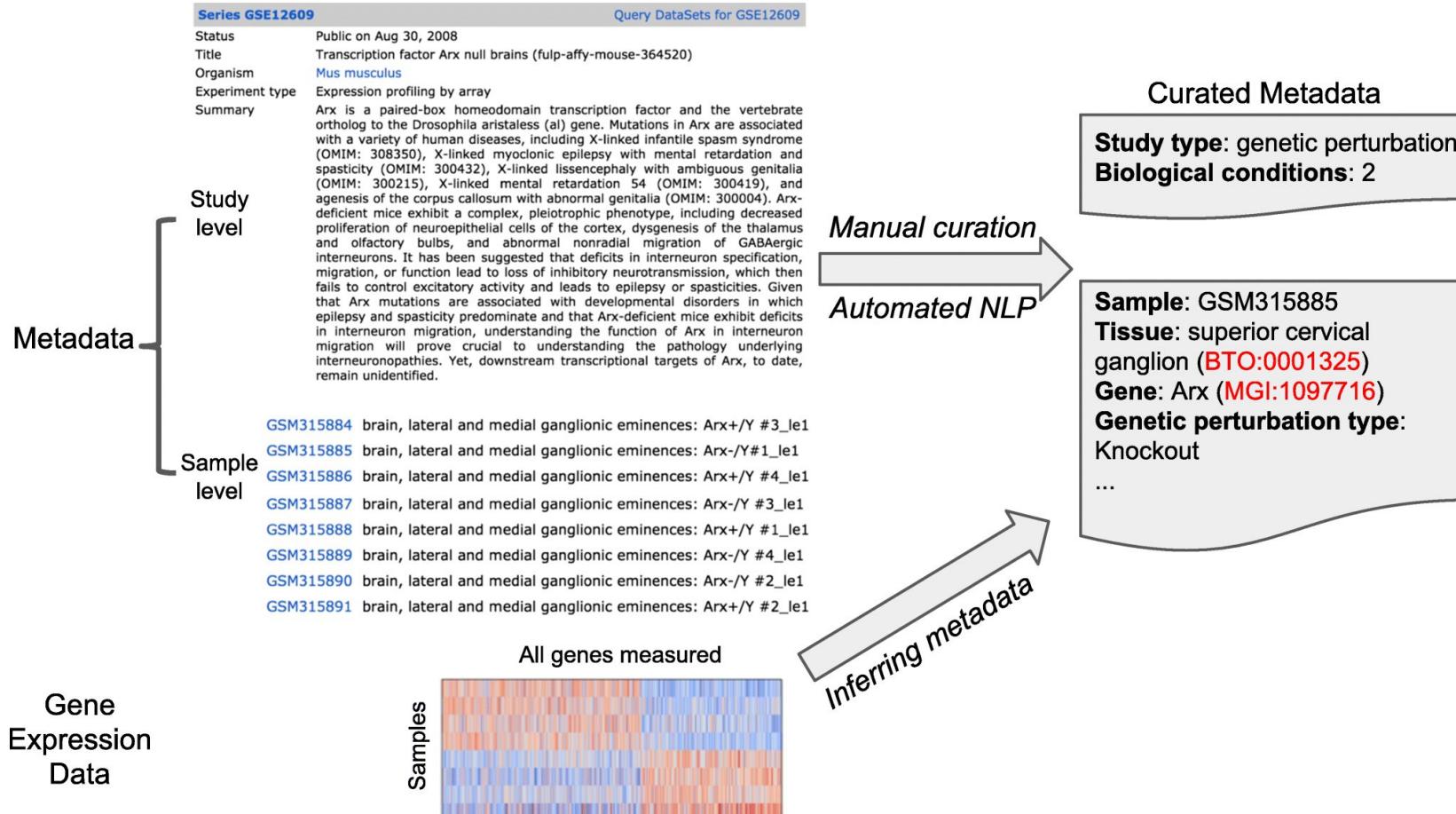
- A set of **guidelines** for **reporting data** derived by relevant methods in biosciences.
- Example : the **Minimum Information About a Microarray Experiment (MIAME)**



A schematic representation of six components of a microarray experiment.

https://en.wikipedia.org/wiki/Minimum_information_standard
[10.1038/ng1201-365](https://doi.org/10.1038/ng1201-365)

Example 2: GEO (Gene Expression Omnibus) data & metadata

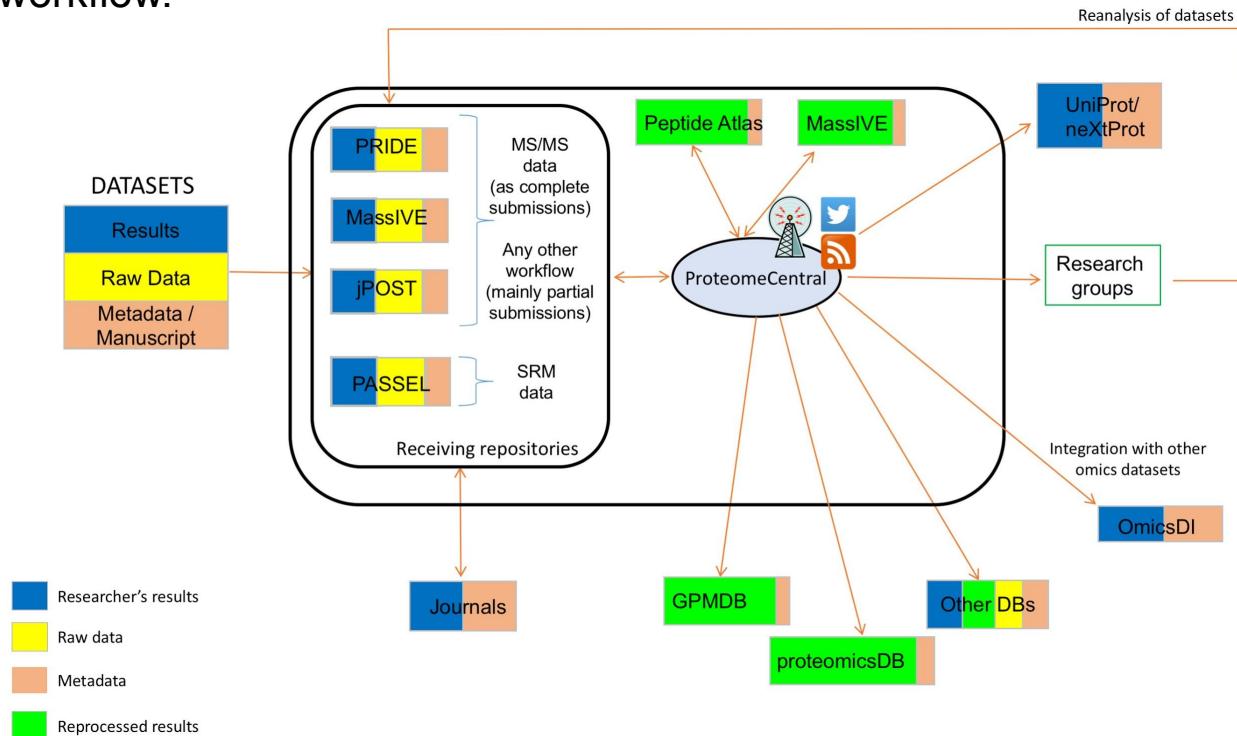


07/s12551-018-0490-8/figures/2

Example 3: The ProteomeXChange initiative

- An international consortium devoted to mass spectrometry (MS)-based proteomics data
- Overall objective: provide a common framework and infrastructure for the **cooperation of proteomics resources by defining and implementing consistent, harmonized, user-friendly data deposition and exchange procedures** among the members

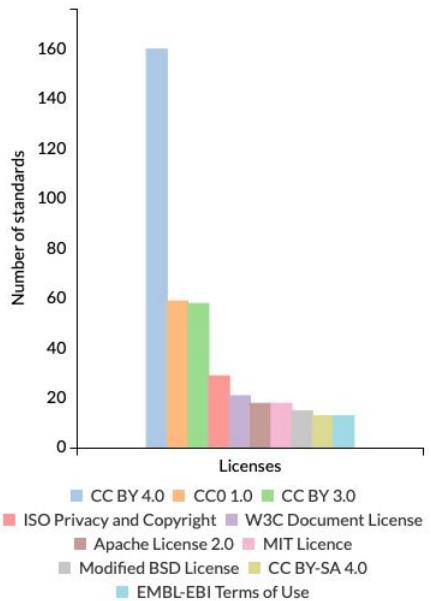
Figure 1. Schematic representation of the ProteomeXchange data workflow.



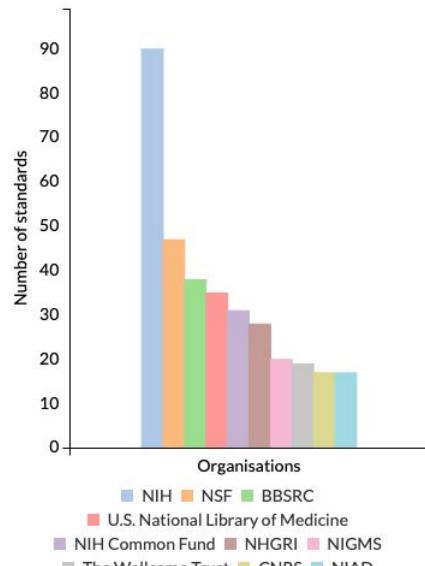
Source: The ProteomeXchange consortium in 2017: supporting the cultural change in proteomics public data deposition
Nucleic Acids Res, Volume 45, Issue D1, January 2017, Pages D1100–D1106, <https://doi.org/10.1093/nar/gkw936>

Summary statistics about standards

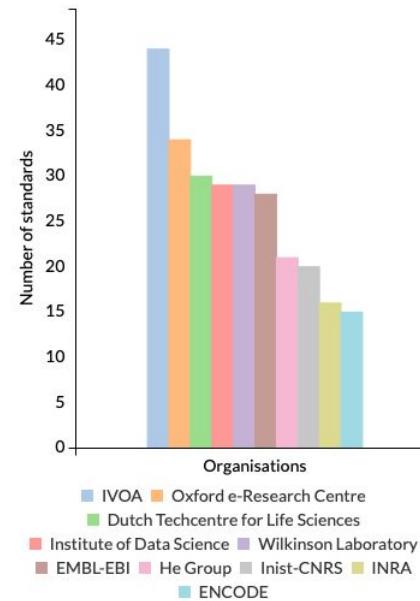
Top 10 licenses for standards



Top 10 funders of standards



Top 10 organisations (excluding funder) of standards



The CC by 4.0 licence is the most adopted

US and UK National institutes are the most important funders

Worldwide Research Organisations produce standards

<https://fairsharing.org/summary-statistics/?collection=standards>

ENA proposes 3 types of submission

- Be careful: it is not possible to submit all objects using the 3 submission types
- IFB is currently being developing **brokering services to simplify submission to ENA**

	Interactive	Webin-CLI	Programmatic
Study	Y	N	Y
Sample	Y	N	Y
Read data	Y	Y	Y
Genome Assembly	N	Y	N
Transcriptome Assembly	N	Y	N
Template Sequence	Y	Y	Y
Other Analyses	N	N	Y

An ENA submission step by step

1. Register a **submission account**

<https://www.ebi.ac.uk/ena/submit/sra/#home>

2. Register a **Study** (~a Project)

either *Interactively* or *Programmatically*

Using either test or production service:

<https://wwwdev.ebi.ac.uk/ena/submit/sra> or

<https://www.ebi.ac.uk/ena/submit/sra>

3. Choose a **Checklist**

<https://www.ebi.ac.uk/ena/browser/checklists>

The screenshot shows a web form for registering a study. It includes fields for specifying the release date (marked with a red asterisk), providing a short name for the study, giving a descriptive title, and writing an abstract to describe the study in detail.

An ENA submission step by step

4. Register **samples** using the chosen Checklist and taxonomy
either *Interactively* or *Programmatically*

Using either test or production service

5. Register **experiments** and submit **raw data files** using the **run object**
either *Interactively* or *Programmatically* or *with the Webin-CLI application*

the run object includes the raw data filename and checksum code

6. Optionally describe **analyses** (assemblies, annotations,... not discussed in this training session)

Formats for an ENA submission

Metadata

- **Tabular** (Spreadsheets) files for the interactive mode
- **XML** files for the programmatic mode

```
<PROJECT_SET>
  <PROJECT alias="cheddar_cheese">
    <TITLE>Characterisation of Microb
    <DESCRIPTION>This study aimed to
    <SUBMISSION_PROJECT>
      <SEQUENCING_PROJECT/>
    </SUBMISSION_PROJECT>
  </PROJECT>
</PROJECT_SET>
```

Data

- **Raw files:** standards formats like bam, cram, fastq, see
<https://ena-docs.readthedocs.io/en/latest/submit/fileprep/reads.html>
- **Analysis files**
 - Assemblies: fasta file + manifest file + AGP file
 - Annotations: standards formats like bed or gff, see
<https://ena-docs.readthedocs.io/en/latest/submit/analyses.html>

An ENA submission produce accession numbers

ENA project citation:

“the data for this study have been deposited in the European Nucleotide Archive (ENA) at EMBL-EBI under accession number PRJEBxxxx (<https://www.ebi.ac.uk/ena/browser/view/PRJEBxxxx>).”

Accession Type	Accession Format	Example
Projects *	PRJ(E D N)[A-Z][0-9]+	PRJEB12345
Studies *	(E D S)RP[0-9]{6,}	ERP123456
BioSamples	SAM(E D N)[A-Z]?[0-9]+	SAMEA123456
Samples *	(E D S)RS[0-9]{6,}	ERS123456
Experiments*	(E D S)RX[0-9]{6,}	ERX123456
Runs *	(E D S)RR[0-9]{6,}	ERR123456
Analyses*	(E D S)RZ[0-9]{6,}	ERZ123456
Assemblies	GCA_[0-9]{9}.[0-9]+	GCA_123456789.1
Assembled/Annotated Sequences (including contig, scaffold and chromosome sequences generated from an assembly submission)	[A-Z]{1}[0-9]{5}.[0-9]+ [A-Z]{2}[0-9]{6}.[0-9]+ [A-Z]{2}[0-9]{8} [A-Z]{4}[0-9]{2}S?[0-9]{6,8} [A-Z]{6}[0-9]{2}S?[0-9]{7,9}	A12345.1 AB123456.1 AB12345678 ABCD01123456 ABCDEF011234567
Protein Coding Sequences	[A-Z]{3}[0-9]{5}.[0-9]+ [A-Z]{3}[0-9]{7}.[0-9]+	ABC12345.1 ABC1234567.1

* ‘E’ for ENA, ‘D’ for DDBJ, or ‘S’ for NCBI

<https://ena-docs.readthedocs.io/en/latest/submit/general-guide/acccessions.html>