

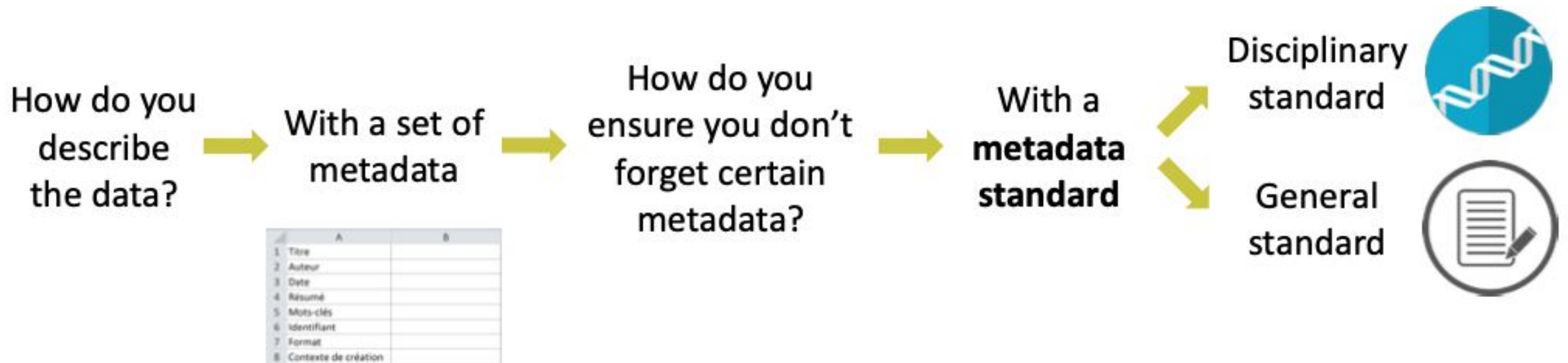


# Life science standards and ENA submission

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# Metadata & standards in life sciences

# Metadata standards help describing data



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*

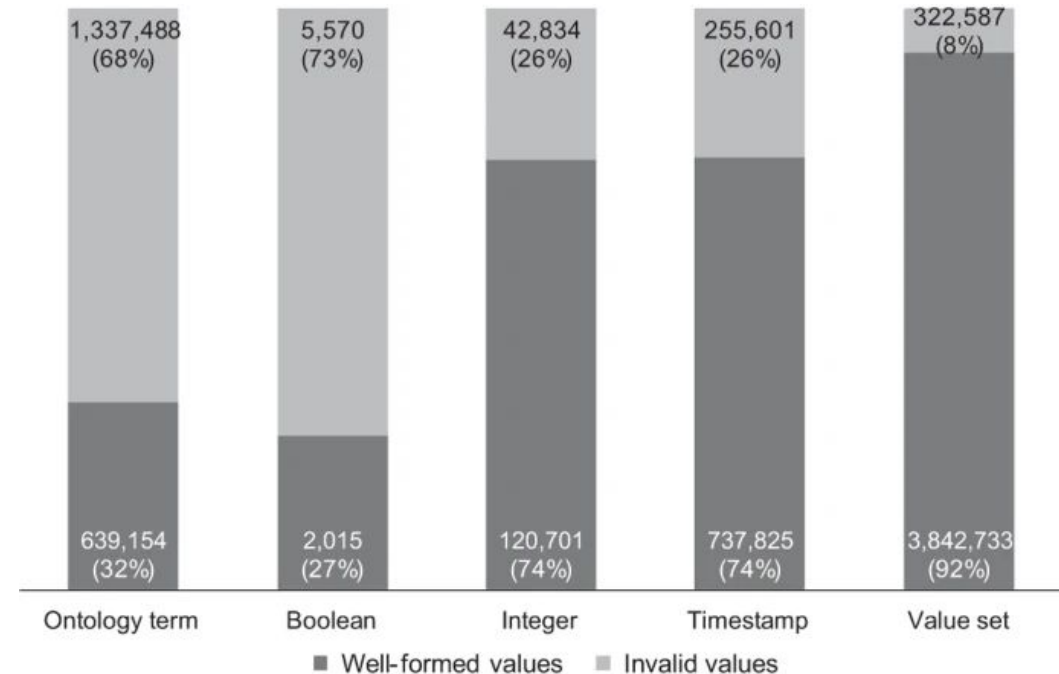
<https://scrumblr.ethibox.fr/standard>

# Metadata exhibit questionable quality in biology

Submission in public resources is often a complex task

Submission procedures are heterogeneous

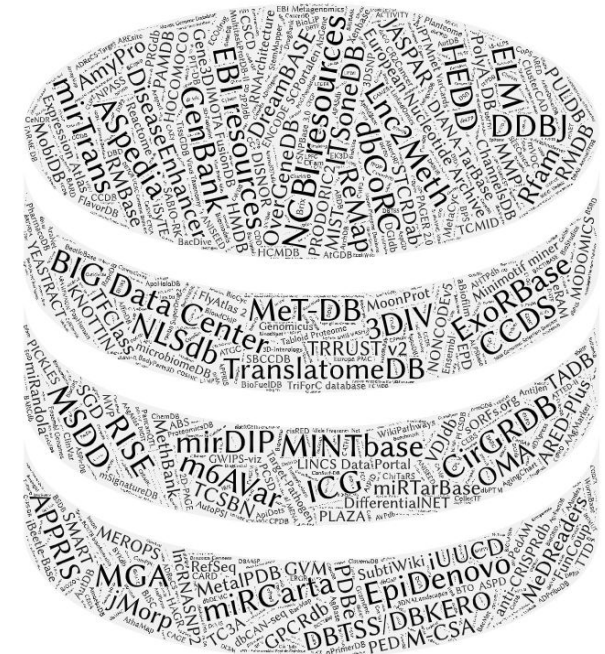
**Metadata are often incomplete, inconsistent, redundant or not enough informative**



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



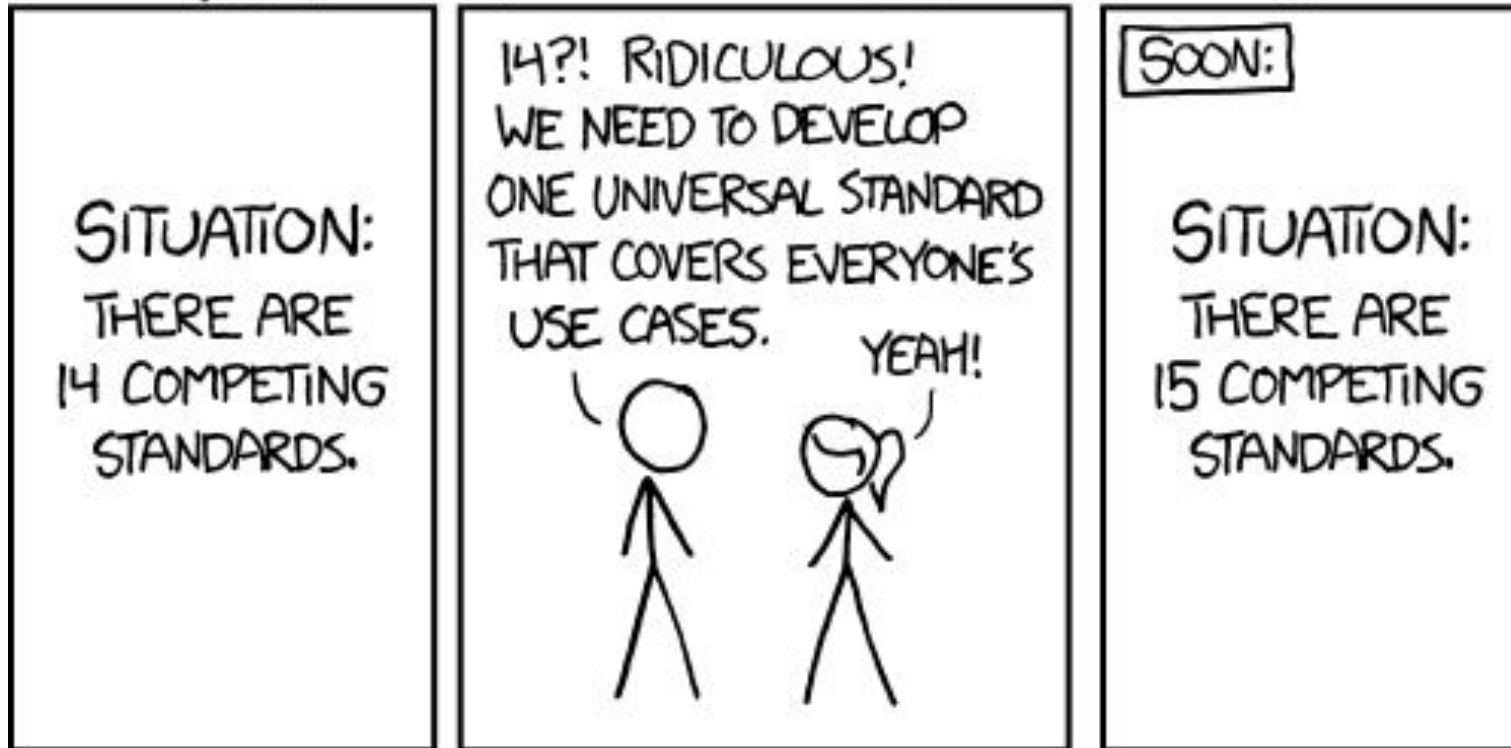
1641 databases in NAR Database 2021

[Rigden et al, 2021](#)



# Standard adoption and perenity

HOW STANDARDS PROLIFERATE:  
(SEE: A/C CHARGERS, CHARACTER ENCODINGS, INSTANT MESSAGING, ETC)



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

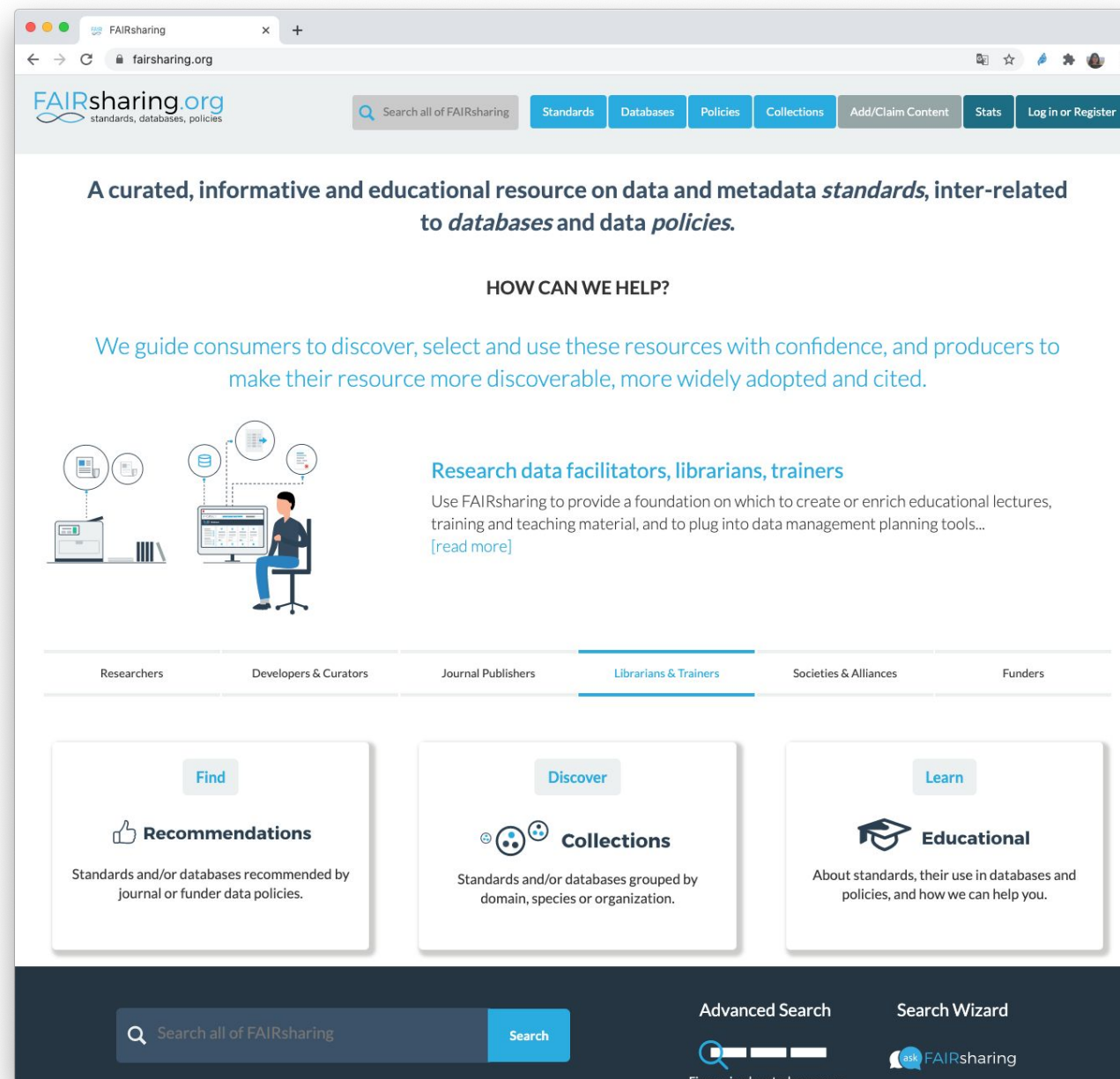
# How do I find the standard I need?

# 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>



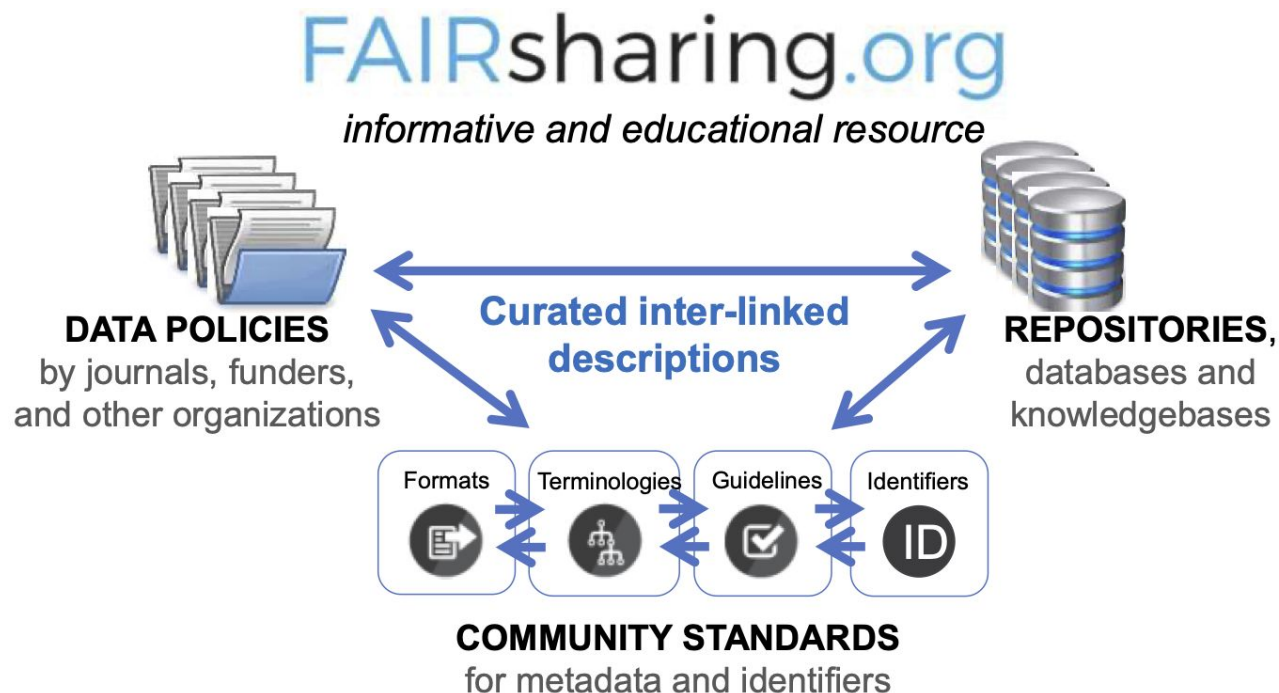
<https://fairsharing.org>

# The FAIRsharing portal

Citable *DOI* for all records

Accessible via *API* or *web interface*

*Curation*







**RECORD STATUS**

- R** Ready for use, implementation, or recommendation
- Dev** In development
- U** Status uncertain
- D** Deprecated as subsumed or superseded

All records are manually **curated in-house**, verified and claimed by the community behind each resource

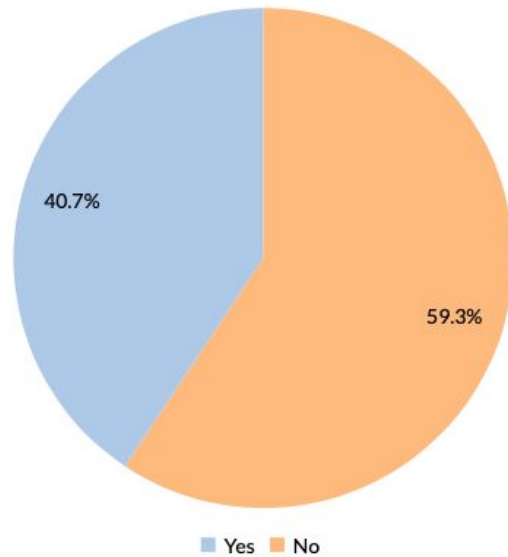
# The FAIRsharing portal: record status

-  **Ready for use, implementation, or recommendation**
-  **In development**
-  **Status uncertain**
-  **Deprecated as subsumed or superseded**

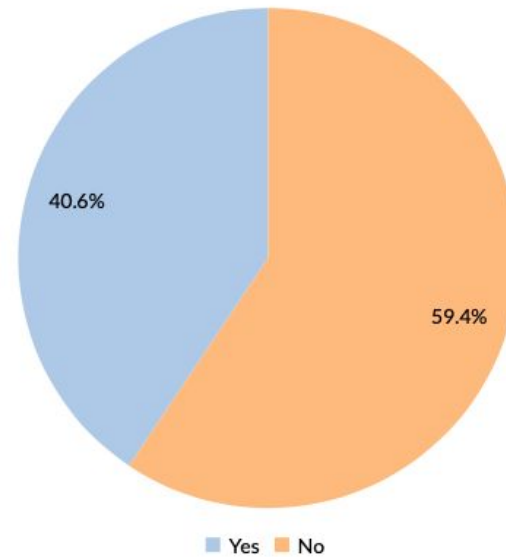
Please don't use "Uncertain" or "Deprecated" standards

# Standard maintenance is a key point

Standard records that have maintainers



Standards that have a publication



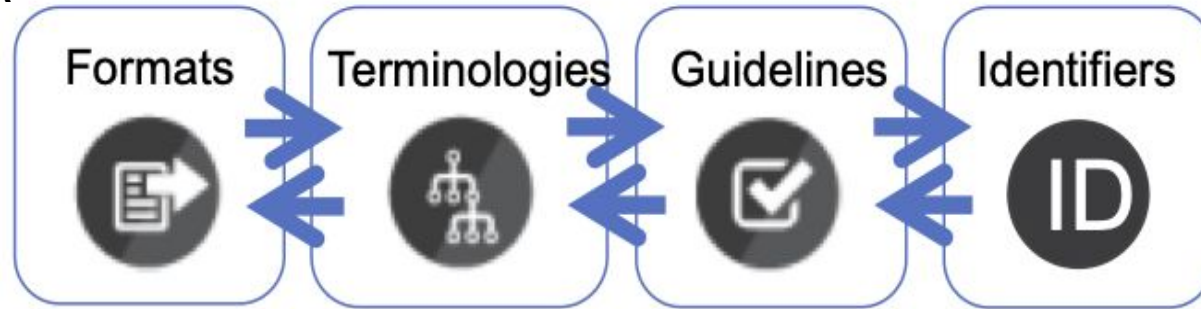
59.3 % of standards have no maintainer

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



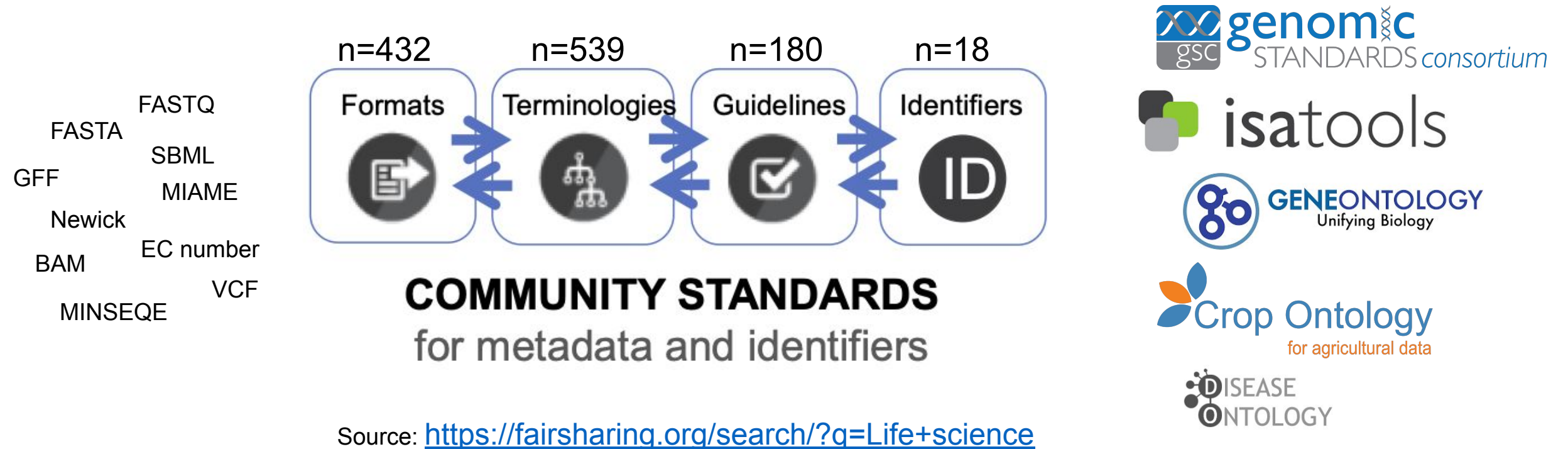
**Minimum information reporting requirements, checklists...**  
e.g. MIAME guidelines

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

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



# The landscape of standards in life sciences





# 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/>

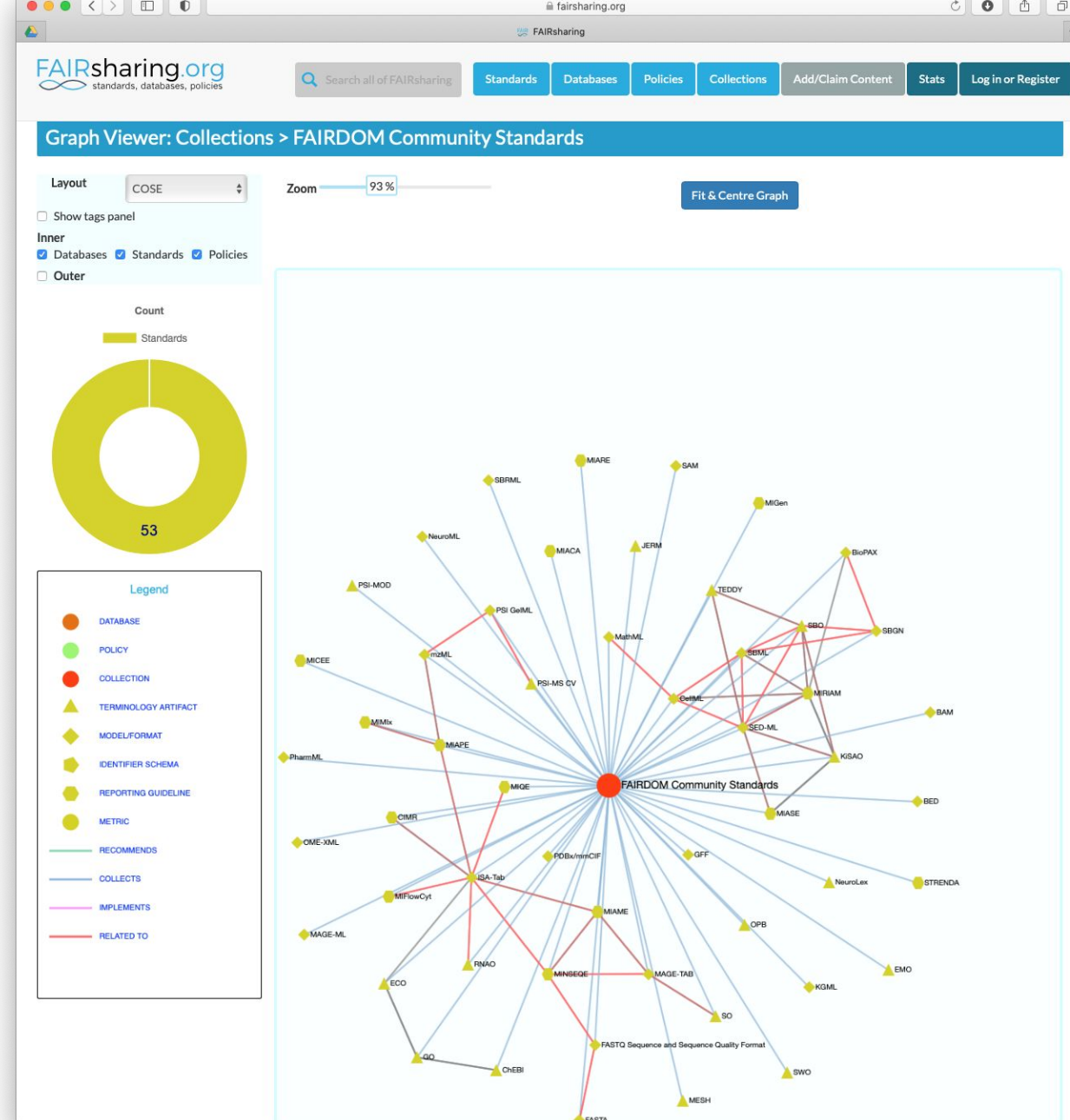
The screenshot displays the FAIRsharing.org interface for a collection titled "COVID-19 Resources". The page features a navigation bar with tabs for Standards, Databases, Policies, Collections, Add/Claim Content, Stats, and Log In or Register. Below the navigation, there are subject filters (Biomedical Science, Clinical Studies, Epidemiology, Global Health, Health Science, Preclinical Studies, Public Health, Virology) and user-defined tags (Respiratory Disease). A "View as Graph" button is visible, along with a "Show edit history" button and a "Compare with collection/recommendation (Beta)" dropdown menu. The main content area shows "General collection/recommendation statistics" for "COVID-19 Resources (bsg-c000070)" with a "Show Stats" button. Below this, there is a table of records with columns: Registry Name, Abbreviation, Type, Subject, Domain, Taxonomy, Related Database, Related Standard, Related Policy, and In Collection? The table shows records for "American Type Culture Collection Database", "Australian New Zealand Clinical Trials Registry", and "BMRI-ERIC Directory".

# 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

FAIRsharing.org  
standards, databases, policies

Search all of FAIRsharing

Standards Databases Policies Collections Add/Claim Content Stats Log in or Register

Graph Viewer: Collections > COVID-19 Resources

Layout COSE Zoom 93% Fit & Centre Graph

Show tags panel

Inner  
 Databases  Standards  Policies

Outer

Count

- Policies 4
- Standards 5
- Databases 70

Legend

- DATABASE
- POLICY
- COLLECTION
- ▲ TERMINOLOGY ARTIFACT
- ◆ MODEL/FORMAT
- ◆ IDENTIFIER SCHEMA
- REPORTING GUIDELINE
- METRIC
- RECOMMENDS
- COLLECTS
- IMPLEMENTS
- RELATED TO

Registry Name	Abbreviation	Type	Subject	Domain	Taxonomy	Related Database	Related Standard	Related Policy	In Collection?
American Type Culture Collection database	ATCC	Database	Microbiology	Microbiology	Microbiology	None	None	Springer Nature	Yes
Australian New Zealand Clinical Trials Registry	ANZCTR	Database	Clinical Trials	Clinical Trials	Clinical Trials	ClinicalTrials.gov	None	None	Yes
EBMIR-ERIC Directory	EBMIR-ERIC Directory	Database	EBMIR-ERIC	EBMIR-ERIC	EBMIR-ERIC	ERIC-Caseat	None	None	Yes

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

FAIRsharing.org  
standards, databases, policies

Search all of FAIRsharing

Standards Databases Policies Collections Add/Claim Content Stats Log in or Register

Graph Viewer: Collections > COVID-19 Resources

Layout COSE Zoom 93% Fit & Centre Graph

Show tags panel

Inner  
 Databases  Standards  Policies

Outer

Count

- Policies 4
- Standards 5
- Databases 70

Legend

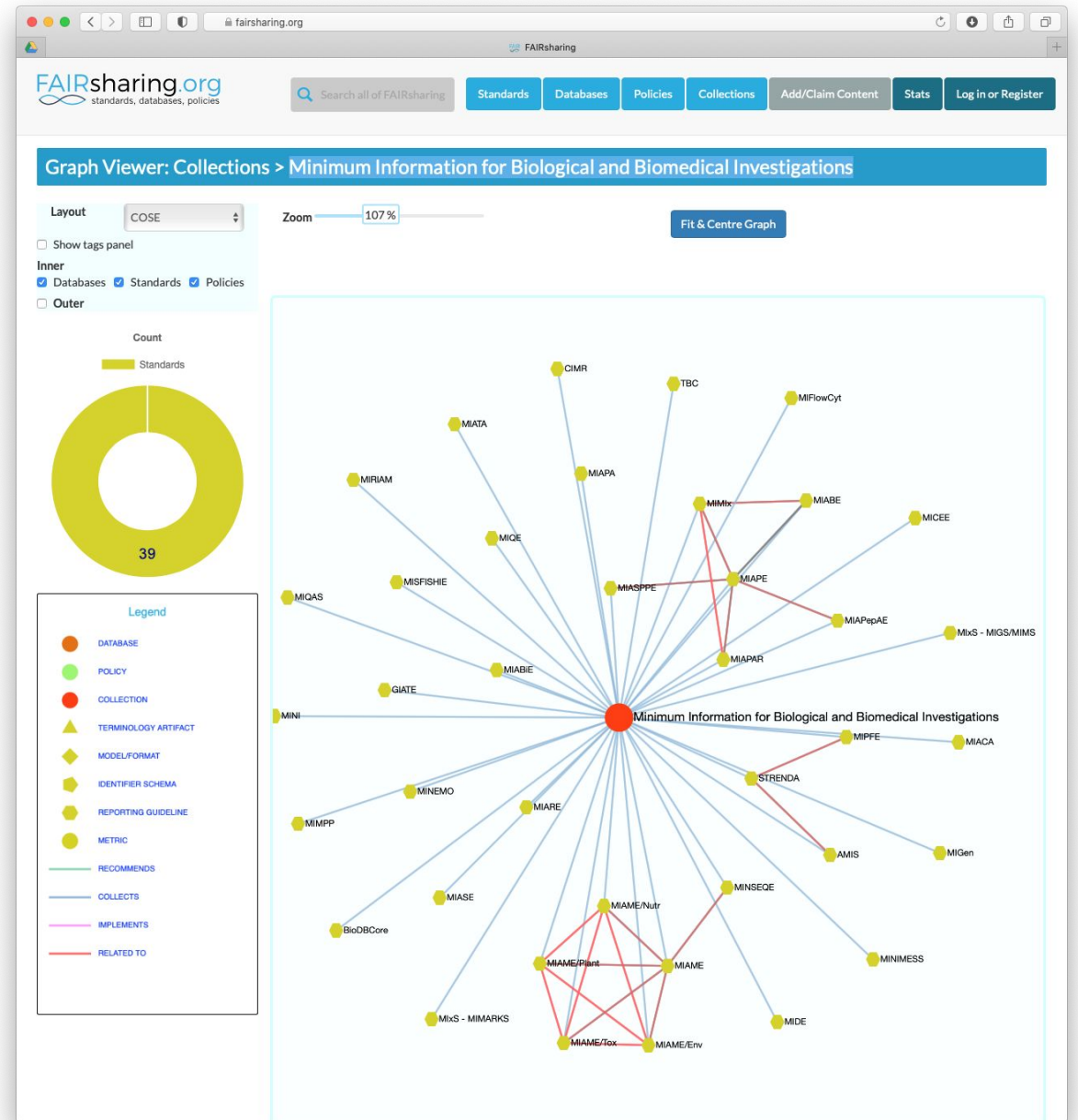
- DATABASE
- POLICY
- COLLECTION
- ▲ TERMINOLOGY ARTIFACT
- ◆ MODEL/FORMAT
- ◆ IDENTIFIER SCHEMA
- REPORTING GUIDELINE
- METRIC
- RECOMMENDS
- COLLECTS
- IMPLEMENTS
- RELATED TO

<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

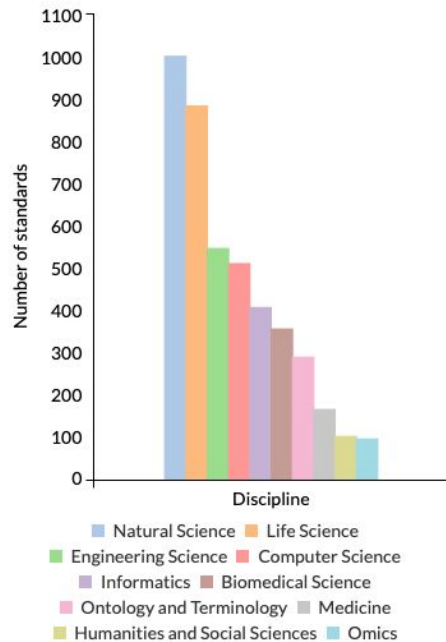
<https://fairsharing.org/collection/MIBBI>



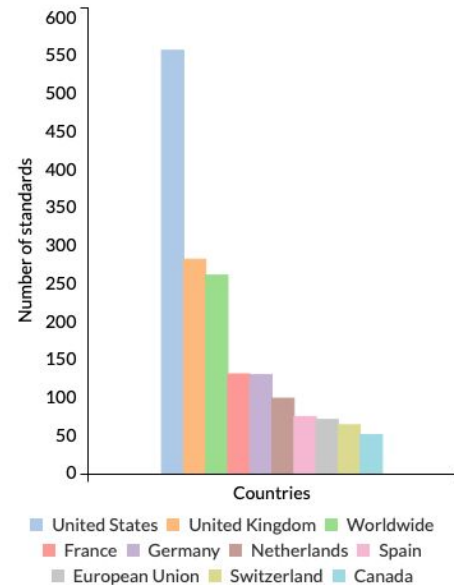


# Summary statistics about standards

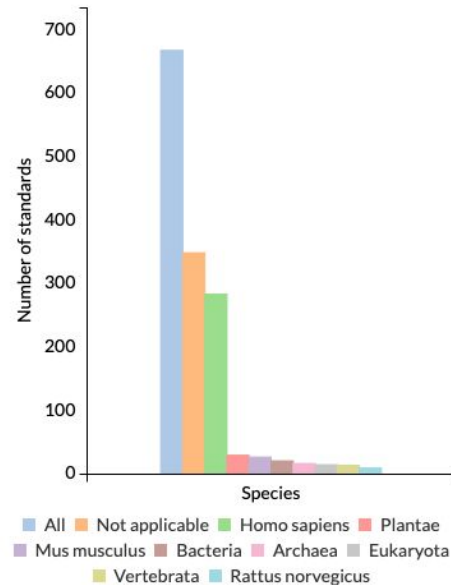
Top 10 disciplines covered by standards



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>

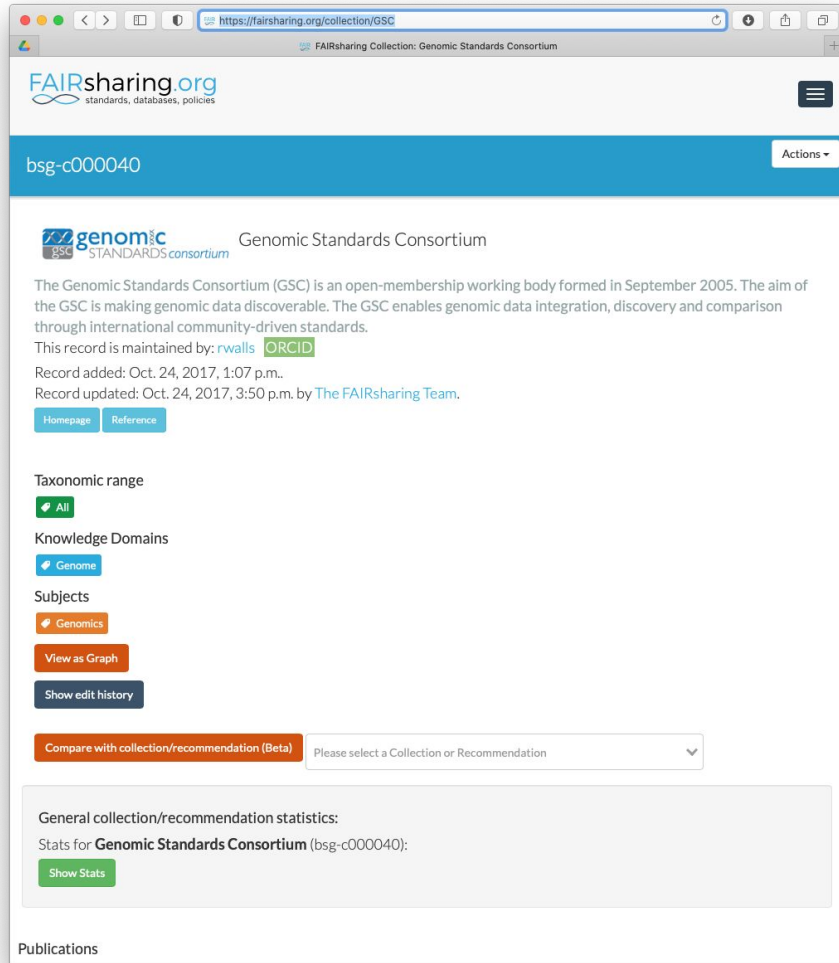
# Practice

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:

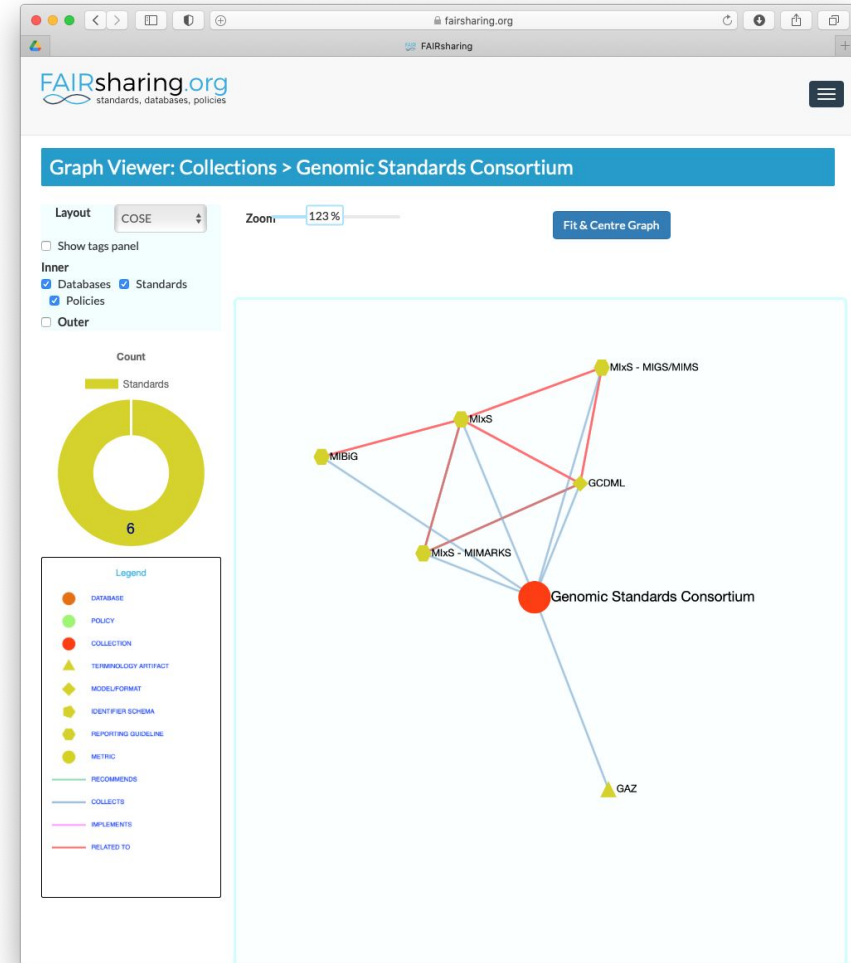
1. How many records (*i.e.* standards) are associated to the *GSC* ?
2. What type of standard is *Minimum Information about any (x) Sequence (MiXS)* ?
3. What is the record status of the *GAZ* record ?

# The Genomic Standards Consortium (GSC)



The screenshot shows the FAIRsharing.org interface for the collection 'bsg-c000040'. The header includes the FAIRsharing.org logo and a menu icon. Below the header, the collection ID 'bsg-c000040' is displayed. The main content area features the 'genomc STANDARDS consortium' logo and a description of the GSC as an open-membership working body formed in September 2005. It lists the aim of making genomic data discoverable and provides contact information for 'rwalls' with an ORCID link. A 'Taxonomic range' section shows 'All' selected. 'Knowledge Domains' includes 'Genome'. 'Subjects' includes 'Genomics'. A 'View as Graph' button is visible. At the bottom, there is a 'Compare with collection/recommendation (Beta)' section and a 'General collection/recommendation statistics' section with a 'Show Stats' button.

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



The screenshot shows the 'Graph Viewer: Collections > Genomic Standards Consortium' interface. It features a 'Layout' dropdown set to 'COSE', a 'Zoom' slider at 123%, and a 'Fit & Centre Graph' button. On the left, there are checkboxes for 'Show tags panel', 'Inner' (with 'Databases' and 'Standards' checked), and 'Outer'. A donut chart shows a count of 6 for 'Standards'. A legend on the left lists various entities: DATABASE (red circle), POLICY (green circle), COLLECTION (red circle), TERMINOLOGY ARTIFACT (yellow triangle), MODELFORMAT (yellow diamond), IDENTIFIER SCHEMA (yellow square), REPORTING GUIDELINE (yellow circle), METRIC (yellow circle), RECOMMENDS (green line), COLLECTS (blue line), IMPLEMENTS (purple line), and RELATED TO (red line). The graph shows a central red circle labeled 'Genomic Standards Consortium' connected to several other nodes: 'MIBIG', 'MixS', 'MixS - MIMARKS', 'MixS - MIGS/MIMS', 'GCDML', and 'GAZ'.

<https://fairsharing.org/graph/#/collection/bsg-c000040>

# The Genomic Standards Consortium (GSC)

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

Specification projects	MIGS		MIMS	MIMARKS	New checklists				
Checklists	EU	BA	PL	VI	ORG	metagenomes	survey	specimen	e.g., pan-genomes
Shared descriptors	collection date, environmental package, environment (biome), environment (feature), environment (material), geographic location (country and/or sea, region), geographic location (latitude and longitude), investigation type, project name, sequencing method, submitted to INSDC								
Checklist-specific descriptors	assembly, estimated size, finishing strategy, isolation and growth condition, number of replicons, ploidy, propagation, reference for biomaterial			target gene					
Applicable environmental packages (measurements and observations)	Air Host-associated Human-associated Human-oral Human-gut Human-skin Human-vaginal			Microbial mat/biofilm Miscellaneous natural or artificial environment Plant-associated Sediment Soil Wastewater/sludge Water					

[Yilmaz et al, 2011](#)

Source: <https://gensc.org>



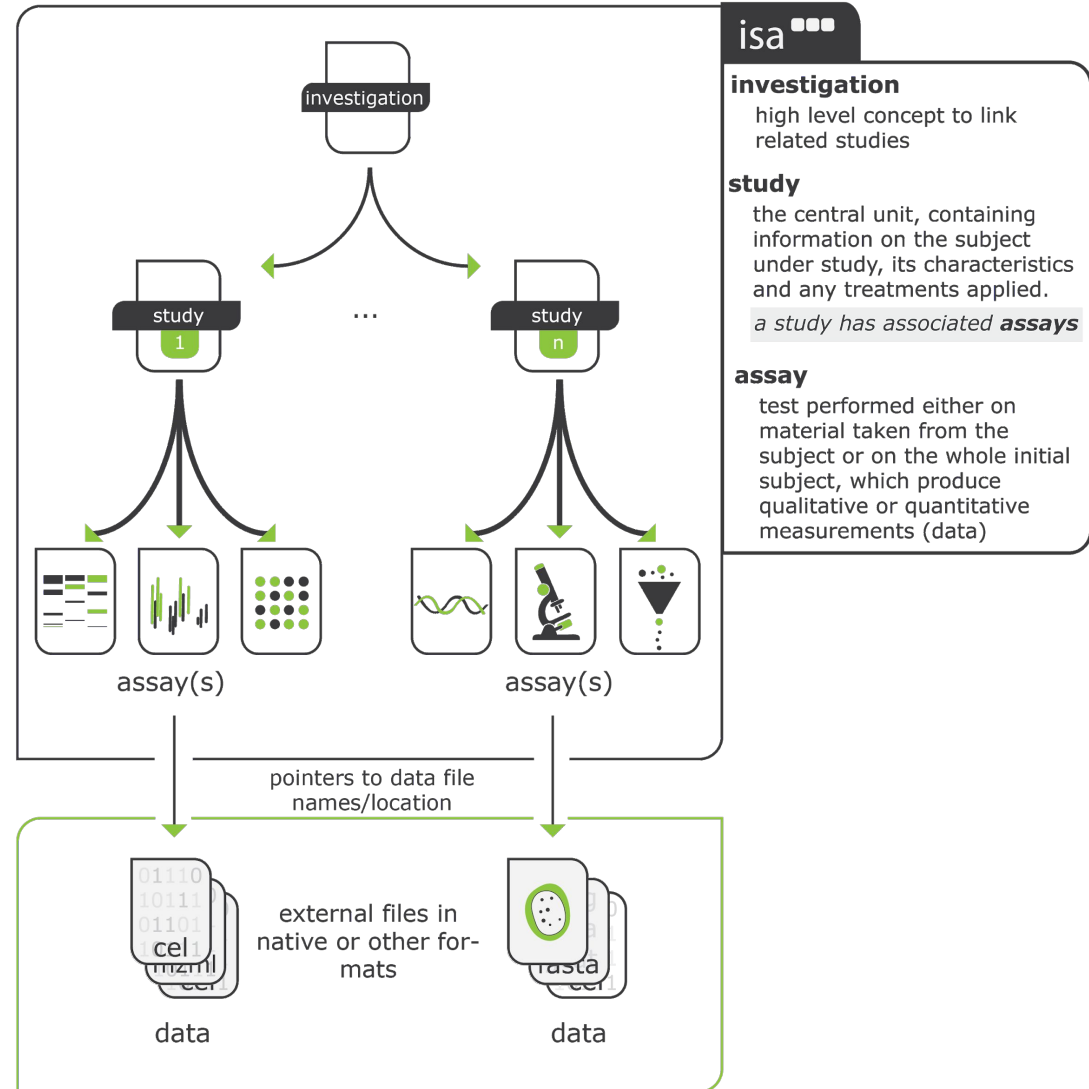
# The ISA model

## 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

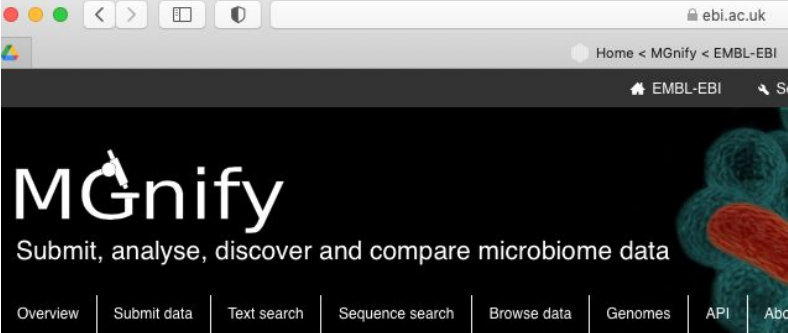


EMBL-EBI



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

- Open Science and reproducibility of experiments
- 3<sup>rd</sup> party access
- Archival
- Publication
- Analyses, example: [MGinfy](https://mgify.ebi.ac.uk/)

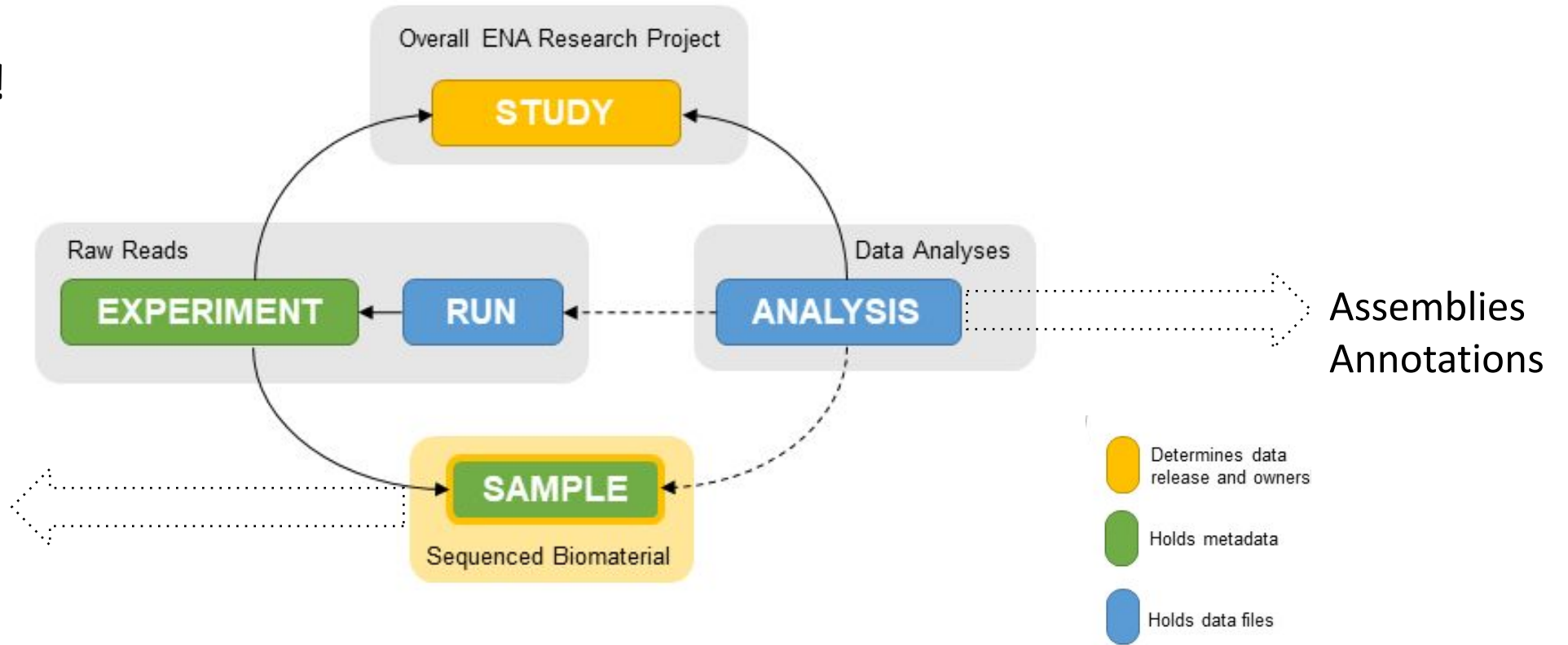


The screenshot shows the MGinfy website interface. At the top, there is a navigation bar with the MGinfy logo and the tagline "Submit, analyse, discover and compare microbiome data". Below the navigation bar, there are several search and filter options: "Text search", "Sequence search", "Browse data", "Genomes", "API", and "About". The main content area is titled "Getting started" and features a "Search by" section with two search methods: "Name, biome, or keyword" (with a "Text search" button) and "Sequence similarity" (with a "Sequence search" button). Below this, there is a section "Or by data type" with a list of data types and their counts: amplicon (350874), assemblies (30079), metabarcoding (2050), metagenomes (32855), and metatranscriptomes (2204). To the right of this list, there are two more data points: "4088 studies" and "281377 samples" (with a lock icon), and "431639 analyses". Below the data type section, there is a section "Or by selected biomes" with five icons representing different biomes: Human (141077), Digestive system (102702), Aquatic (44755), Marine (32218), and Digestive system (32024). On the right side of the page, there is a "Latest" section with a "View more" link and a "EMG p Salivar" link.

# 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)** recommendations
- 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

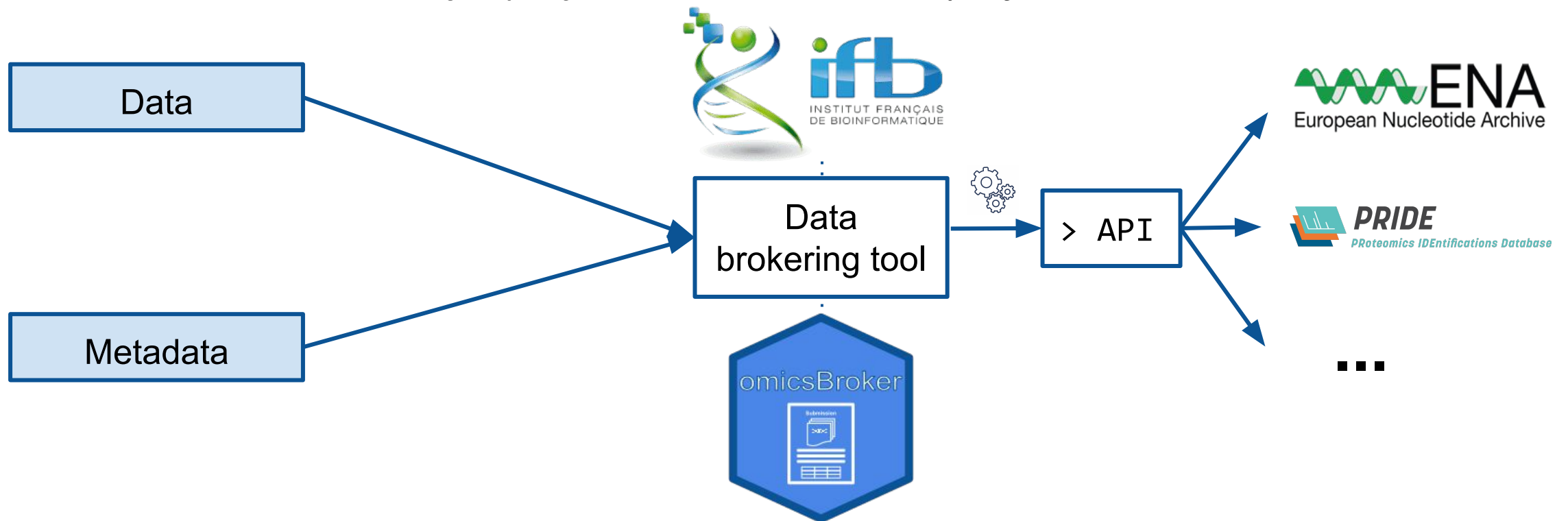
**Main idea:** offer a national service of **data brokering at IFB** to simplify and rationalize data exchange between international resources and the french Elixir node IFB.

**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](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	<a href="https://fairsharing.org">https://fairsharing.org</a>
Investigation, Study, Assay (ISA) resource: A standard model and a set of tools to capture experimental data in life sciences	ISAtools	<a href="https://isa-tools.org">https://isa-tools.org</a>
Genomics Standard Consortium (GSC): An international consortium developing standards and checklists in genomics	GSC	<a href="https://gensc.org">https://gensc.org</a>
European National Archive Checklists	ENA Checklists	<a href="https://www.ebi.ac.uk/ena/browser/checklists">https://www.ebi.ac.uk/ena/browser/checklists</a>
European National Archive submission documentation	ENA submission guide	<a href="https://ena-docs.readthedocs.io/en/latest/submit/general-guide.html">https://ena-docs.readthedocs.io/en/latest/submit/general-guide.html</a>
A prototype to test submission of samples and DNaseq or RNAseq reads to ENA	omicsBroker	<a href="https://github.com/IFB-ElixirFr/omicsBroker">https://github.com/IFB-ElixirFr/omicsBroker</a>

# Thanks



Paulette Lieby



Jean-François Dufayard



Frédéric de Lamotte

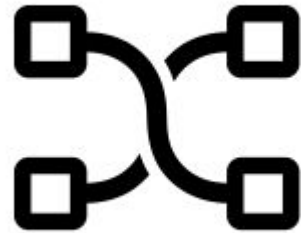
# Supplementary slides

# Standard for data and metadata



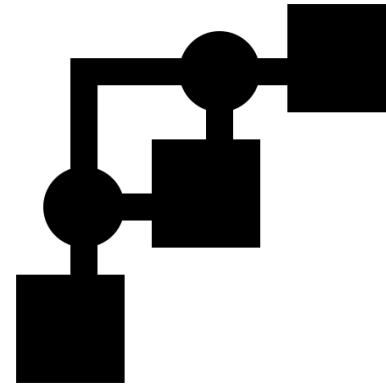
**Guidelines or checklists**

*Ex: the GSC checklist*



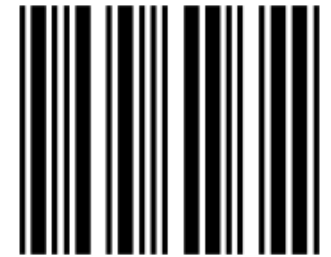
**Models or schemas**

*Ex: ISA model*



**Terminology artefacts,  
ontology**

*Ex: The Gene Ontology*

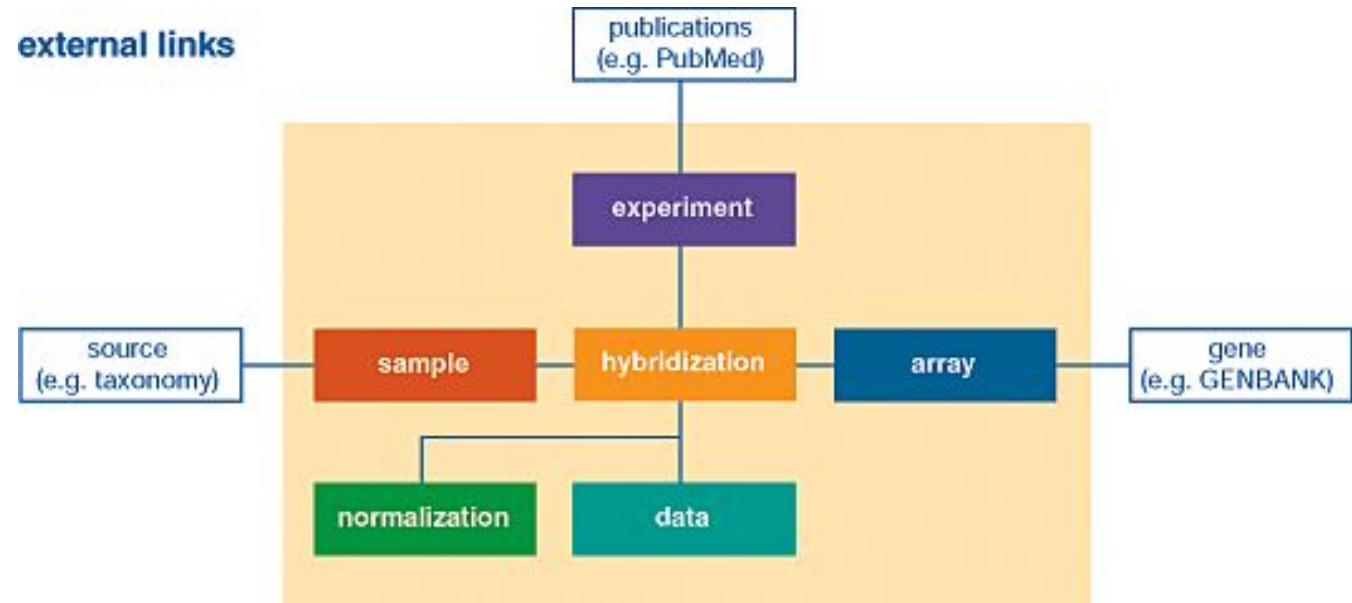


**Identifier schemata**

<https://fairsharing.org>

# The Minimum information standard initiative

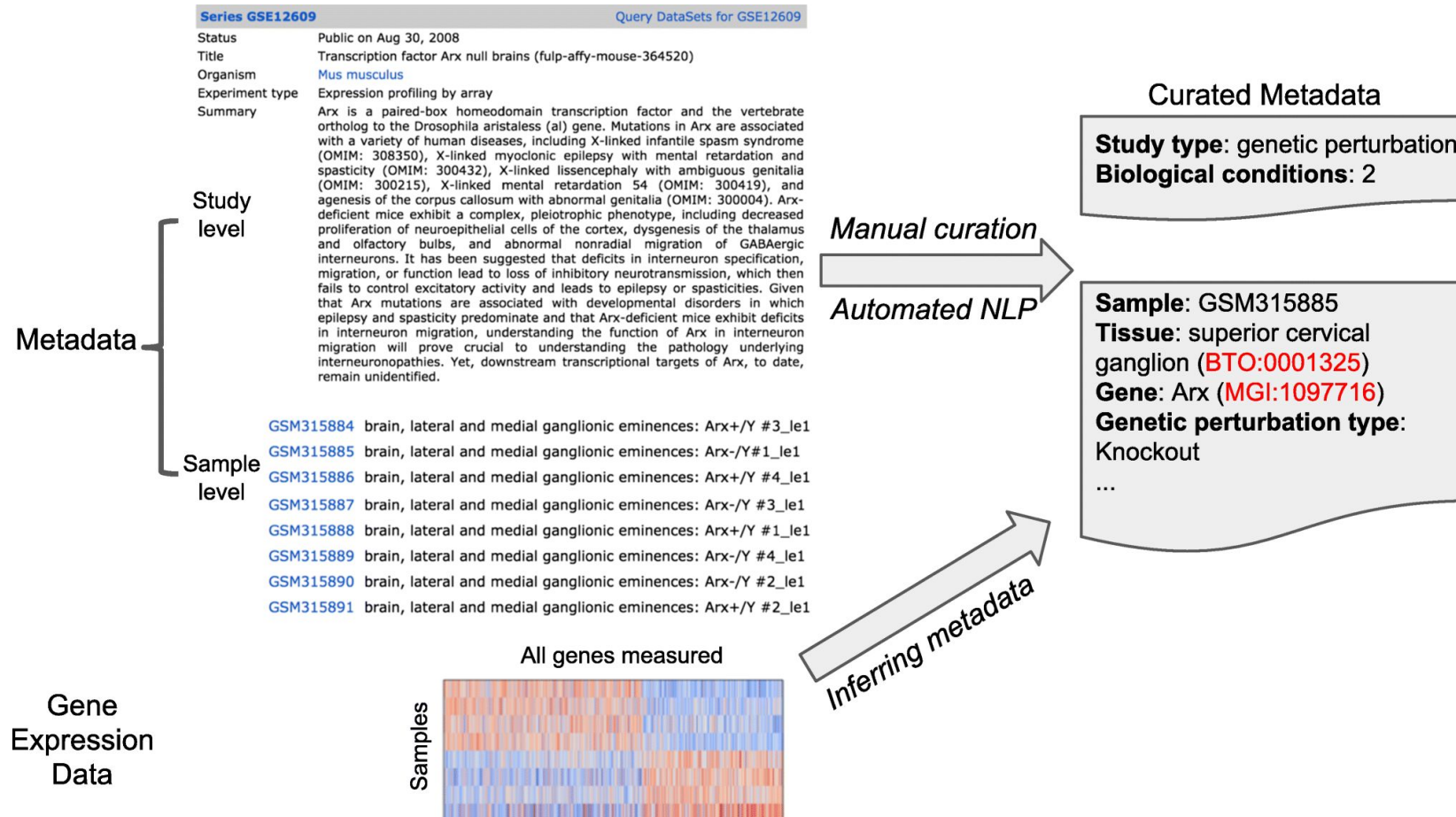
- A set of **guidelines** for **reporting data** derived by relevant methods in biosciences.
- Example : the **Minimum Information About a Microarray Experiment (MIAME)**



A schematic representation of six components of a microarray experiment.

[https://en.wikipedia.org/wiki/Minimum\\_information\\_standard\\_10.1038/ng1201-365](https://en.wikipedia.org/wiki/Minimum_information_standard_10.1038/ng1201-365)

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



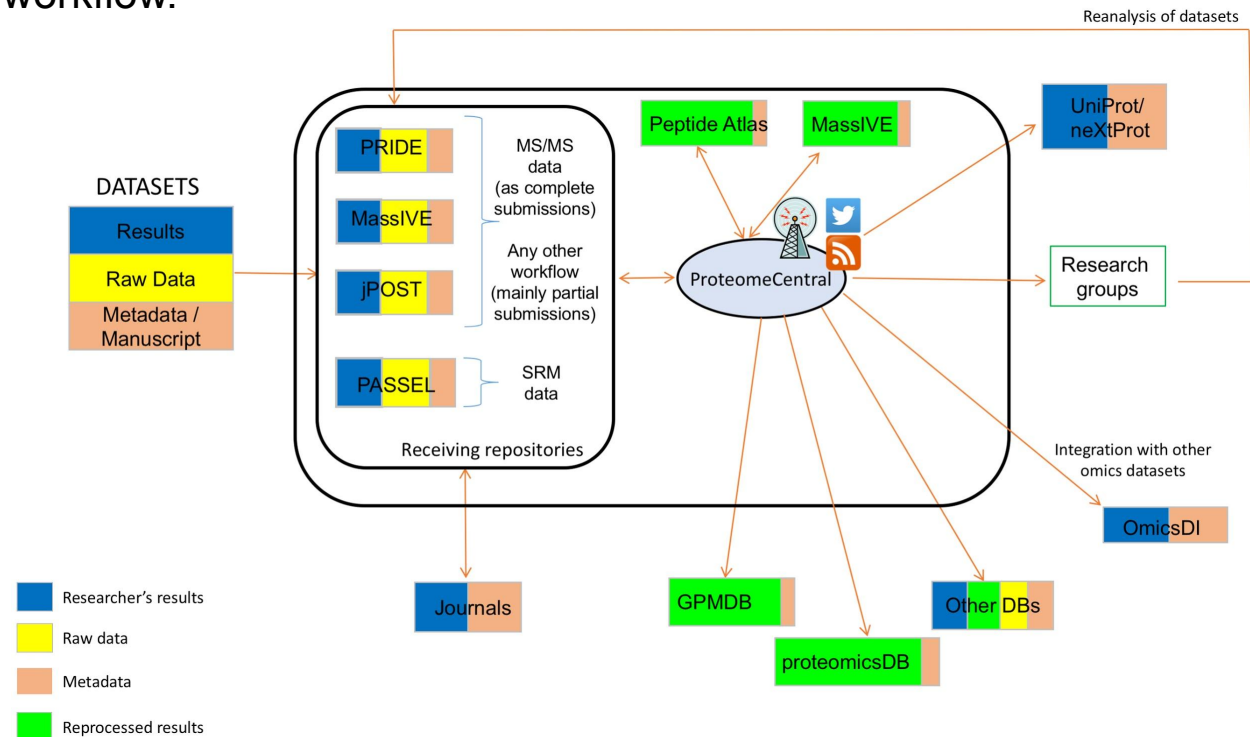
<https://www.ncbi.nlm.nih.gov/geo/s12551-018-0490-8/figures/2>



# 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

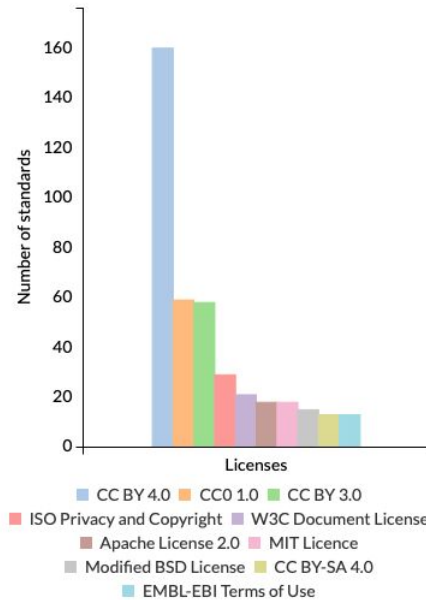
**Figure 1.** Schematic representation of the ProteomeXchange data workflow.



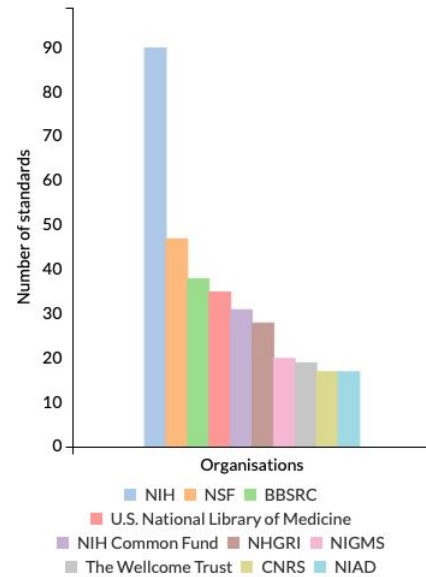
Source: **The ProteomeXchange consortium in 2017: supporting the cultural change in proteomics public data deposition** *Nucleic Acids Res*, Volume 45, Issue D1, January 2017, Pages D1100–D1106, <https://doi.org/10.1093/nar/gkw936>

# Summary statistics about standards

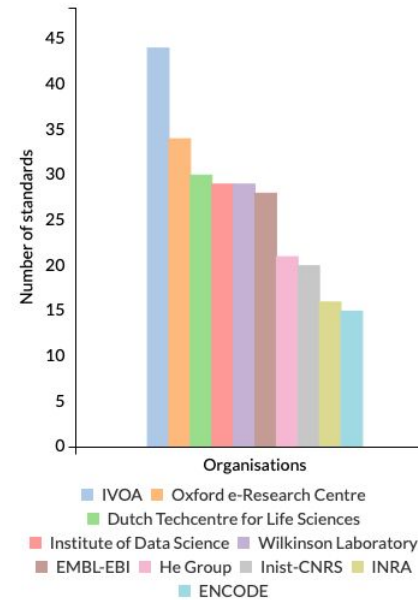
Top 10 licenses for standards



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*

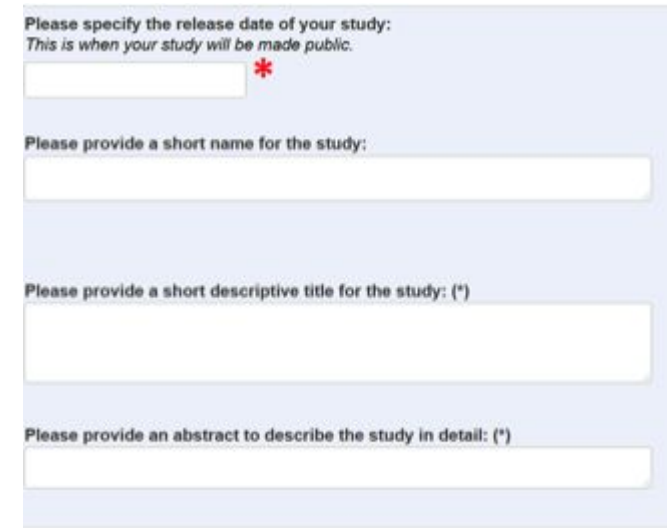
Using either *test* or *production service*:

<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>



Please specify the release date of your study:  
This is when your study will be made public.

\*

Please provide a short name for the study:

Please provide a short descriptive title for the study: (\*)

Please provide 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/accessions.html>