POSITION PAPER

Exchange of strains between Culture Collections

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Revised by: ECCO Board

Introduction

Microbial Culture Collections (CCs) supply strains for many purposes including research, academia and industrial applications. Users rely on the authenticity and the reproducible properties of these strains to support their work in i) taxonomy; ii) teaching iii) as reference strains to perform assays following quality standards (e.g. ISO norms); and iv) as representative research strains to confirm previous findings and to make progress on discoveries published in the scientific literature, amongst other examples. Therefore, the microorganisms provided by collections must be authentic and well-preserved, and any associated information must be valid and sufficient to facilitate confirmation of their identity. Meanwhile, the huge, estimated number of microorganisms yet to be discovered requires global strategies to improve both the technologies for identification, purification, isolation and maintenance of the biological material, as well as increasing the capacity of relevant facilities to hold the diversity of strains. Not one single collection can carry out this task alone (Smith, 2012).

To ensure the sustained availability of the curated microbial resources, CCs must have sufficient resources, specialist staff, and appropriate physical and digital infrastructure available. The long-term financial security of a public collection depends on the provision of a stable platform which may be a balance between public/governmental and/or institutional support, service fees, and other leveraged income. Globally, there are many publicly accessible biological culture collections, however, very few are fully supported by Government (Smith, 2012). Each culture collection is unique in terms of type and biodiversity of organisms under curation, speciality, number of strain holdings, physical and digital technology employed for curation, services offered to the community, and legal framework.

The European Culture Collections' Organization (ECCO, 2022) is a network of European repositories, who work jointly to overcome collective challenges such us those expressed above. ECCO was created in 1981 with the aim to promote collaboration and exchange of ideas and information about all aspects of culture collection activity, to better curate the microorganisms under their guardianship. Currently, ECCO comprises 90 members, spanning 24 European countries, maintaining over 930,000 biological resources encompassing yeast, fungi, bacteria, archaea, bacteriophages, animal and plant viruses, algae, protozoa, plasmids, recombinant DNA constructs, animal and human cell lines. Since its inauguration, ECCO members have participated in several projects and initiatives, all of them designed to meet the stakeholders' needs regarding the acquisition and intended use of microbial material. Projects such as MINE (EU-FP2-BRIDGE-BIOT0280, Publications Office of the European Union, 1998), CABRI (EU-ERBBIO4-CT96-0231, CABRI, 2023), MOSAICC (EU-FP4-BIOTECH 2-BIO4-CT97-2206, BELSPO, n.d., BCCM: MOSAICC), MOSAICS (EU-FP6-2002-FOOD-1-506436, Publications office of the European Union, 2013), EBRCN (EU-FP5-LIFE QUALITY-QLRI-CT-2000-00221, EBRCN, 2024) and EMbaRC (EU-FP7-INFRASTRUCTURES-2008-1.1.2.9-228310, EMbaRC, n.d.) focused on the improvement, coordination and validation of collection procedures to supply high quality microbial material and associated data to European and International researchers, in accordance with the applicable legal framework and recommended best practices. Besides these projects, ECCO promoted the use of model documents for Material Deposit Agreements (MDA) and Material Transfer Agreements (MTA) (ECCO, ECCO MTA and MDA, 2022; Verkley et. al, 2020) to facilitate compliance with the Convention on Biological Diversity (CBD, Secretariat of the Convention on Biological Diversity, 2011a) and harmonization across the collections. A recent example of an endeavour where 30 partner collections (most of them ECCO members) participate is the Microbial Resource Research Infrastructure - European Research Infrastructure Consortium (MIRRI-ERIC, n.d.), the pan-European distributed Research Infrastructure for the preservation, systematic investigation, provision and valorisation of microbial resources and biodiversity, which was launched in June 2022 (European Commission, 2022).

In the context of this intensive collaboration, it is a common practice to exchange strains between ECCO member collections. And although ECCO has been successful in its mission to support and stimulate such collaborations, it has never developed any form of policy or guidance specific for exchange. Recently, some collections have expressed some concerns about this practice, as it may have implications in their financial sustainability. This position paper discusses the impact, advantages, and pitfalls related to the exchange of strains among ECCO collections and proposes new terms for cooperation.

Rationale

Collections incorporate strains into their public catalogues mainly from two sources: their own research projects or from external users.

In both cases the main reasons for deposit are the following:

- a) Type strains (i.e. the strain used for the description of a new taxon) of bacteria and archaea must be deposited in at least two different public collections from two different countries to have a valid publication of the name. For other groups of microorganisms (filamentous fungi, microalgae, etc.), this is a recommended practice, but it is not a requirement.
- b) Some peer-reviewed journals recommend depositing the strains and microbiomes cited in papers (or at least the most representative ones when the number is high).
- c) Strains that are used as a reference in quality standards (e.g. ISO norms). The World Data Centre for Microorganisms (WDCM) maintains a catalogue of unique identifiers for strains recommended for use in quality assurance (<u>World Data Centre for Microorganisms</u>, n.d.). The strains in this catalogue should I be available in at least two culture collections.
- d) Strains from scientific orphan collections transferred to public collections.
- e) To preserve the biodiversity of a given country.
- f) To extend the collection offer of new/unique resources for scientific and commercial purposes.

In most cases, scientists deposit their strains in one to two culture collections, and sometimes up to three. Some duplication may be desired to safeguard reference organisms (e.g. to avoid complete loss after a catastrophic event) and mitigate the risks associated with maintaining cell lines or delicate strains (e.g. contamination, fastidious organisms which are difficult to preserve).

Other sources of new accessions come from the exchange of strains between culture collections. European collections have a non-written agreement to share strains on a one-to-one basis since (or even before) the creation of ECCO. This practice is also frequent with other non-European collections, and in some cases, the bilateral collaborations have been formalized in writing. The shared material has been used by the receiving collection for research projects, to fill in gaps in the strains they offer (e.g. taxonomy, WDCM strains) or to be supplied to their users, usually following multiple user requests. Mostly, the receiving collection incorporates the new strain into its public catalogue, following their corresponding quality standards. However, there have been significant changes in the contextual framework (e.g. changes in transport fees, sustainability challenges for the collections, new policies and regulations) since collections began cooperating in the 80's, advising to consider new terms of collaboration. To analyse this matter, the European Culture Collections' Organisation organised a working group (WG) with member volunteers to discuss the

terms of strain exchange between collections, looking at common benefits and respecting good practices in the sustainable use of microbial materials for research and biotechnological applications.

Arguments, advantages and pitfalls

Main aspects influenced by the exchange of strains between collections:

1. Strain availability for the users

Reference organisms should be as widely accessible as possible with a short delivery time and at low expense (i.e. shipping and custom charges), to suit user demands.

Ideally, microbial collection's research users would like to have a centralised catalogue of strains where they can find all specimens they need and receive them in the shortest time possible. Considering the diversity of strains already available, and the ones yet to be discovered, there is no single collection with the capacity to preserve and deliver all of them. Some attempts to achieve this are being made through the distributed infrastructure MIRRI-ERIC, but unfortunately not all ECCO collections participate in this consortium.

Within the EU borders the movement of goods is not subject to customs clearance fees and shipment is usually affordable and relatively quick (1-2 working days). From this perspective, users can obtain strains from different EU collections in a reasonable time and at a reasonable price (depending on each collection fee policy), which would not justify the need to maintain the same strain in several EU collections. However, there are some exceptions to consider, such as the transport of Category A biological materials (infectious substances in a form that, when exposure to it occurs, can cause permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals), which can be very expensive even between EU countries, or transport between ECCO collections and their depositors or customers in countries outside the EU borders.

A different situation could be the users working at reference laboratories that need reference strains for quality control purposes (e.g. WDCM strains). Strains used for quality assurance are usually in high demand and, in some countries, users requesting them are not competent in English. Due to the high turnover of these strains, and the language barriers, it could make sense to have them broadly available in collections from different countries.

2. Traceability and genetic integrity

Collections apply procedures to guarantee as much as possible the genetic integrity of the preserved microbial materials. However, equivalent strains from different collections may have some level of genetic drift, induced through different practices for maintaining and sub-culturing living organisms. Considering this, it would be important to provide the user with information about the history of transfers of the strains, as it was available in previous versions of <u>StrainInfo</u> (DSMZ, 2024), when hosted by BCCM/LMG. Other data repositories (e.g. <u>LPSN</u>, DSMZ, n.d.; <u>BacDive</u>, DSMZ, n.d.; MIRRI catalogue, MIRRI-ERIC, <u>MIRRI Strains Catalogue</u>, n.d.) also show the equivalent strains in different collections but they lack the integrated history of transfers among them. Promoting the use of the original specimens would minimize the risks associated with the genetic divergence of strains sharing the same origin.

3. Economic sustainability of the collections

ECCO member collections are very heterogeneous in terms of size, type of resources, mission, and funding models. For some collections, their operations are mostly (or solely) funded on revenue generated through the supply of strains and services. In other cases, the funders of collections (governments, public institutions, private corporations, etc.) exercise a close control of the collection's operations and demand diligent use of public funds and, in some cases, to reach economic self-sustainability. Therefore, collections may need to verify how the free exchange of

strains can influence its long-term sustainability and act accordingly (e.g. market surveillance, competitive analysis).

With the aim of gathering information about the presumptive impact of the provision of type strains on the collections, a questionnaire was sent to all ECCO collections (Annex 1). A summary of the results of the survey is shown in Annex 2 which reflects the wide range of responses among participants (44% of the ECCO collections). Considering this, the financial impact on specific collections might be very different. To obtain more detailed information about the financial significance of this activity on the total budget of collections, a wider study including economic aspects would be needed.

4. Environmental impact

To preserve the microbial resources following the best practice guidelines for microbial domain Biological Resource Centres (mBRCs) requires significant resourcing, particularly human, consumables, chemicals, and energy. At the same time, the United Nations (through the Sustainable Development Goals, SDGs) and the European Union, among others, are strategizing towards sustainable use of the planet's resources. To adhere to the European Green Deal and the 2020 Circular Economy Action Plan, the European Commission proposes guidelines and recommendations to reduce the environmental footprint of European organizations (EC, 2021). Therefore, as custodians of biological resources and biodiversity, ECCO collections ought to champion and be proactive in their support, collaboration and compliance with these policies and be mindful of the environmental and societal impact of their activities. In this context, collections may need to consider if authenticating, preserving, and maintaining a particular strain already available in other repositories has a justified added value to the stakeholders.

5. Legal instruments regulating the transfer of microbial resources

The CBD entered into force on 29th December 1993, which recognizes the sovereign rights of countries over the genetic resources under their jurisdiction. Besides the conservation of biological diversity and the sustainable use of its components, the CBD looks for the fair and equitable sharing of the benefits arising out of the utilization of genetic resources (Access and Benefit Sharing, ABS), providing a mechanism to establish the conditions of use of such resources. To ensure compliance with this latter objective, the Parties of the CBD implemented the <u>Nagoya Protocol</u> (Secretariat of the Convention on Biological Diversity, 2011), in place since 12th October 2014.

Likewise, the use of genetic resources beyond national jurisdiction or governed by other instruments may also be regulated (e.g. the Agreement under the United Nations Convention on the Law of the Sea on the Conservation and Sustainable Use of Marine Biological Diversity of Areas beyond National Jurisdiction; the International Treaty on Plant Genetic Resources for Food and Agriculture).

Adding more layers of complexity, use of biological material may be subject to further legislation and rights from third parties (e.g. biosecurity and biosafety measures, Intellectual Property Rights).

To cope with all the above-mentioned issues, it is advised to always transfer biological material and associated data together with a Material Transfer Agreement (MTA), specifying the rights and obligations of the parties involved in the transfer. To facilitate the development of MTAs suiting the needs of the collections and their users, ECCO proposes the use of a model template (Verkley, 2020) gathering the main clauses that should be considered when transferring microbial strains. Indeed, the exchange of strains between culture collections is acknowledged in the ECCO model MTA as a legitimate exchange, provided the supplying and the recipient collections have MTA conditions equivalent and compatible. Besides, the document can and should be adapted to meet the requirements of the collections' own context (e.g. type of institution, national laws). In this sense, the MTA could be adapted and include additional clauses for the benefit of the supplying collection, if they believe that the legitimate exchange could impact their business.

Considerations for collections wanting to do exchanges

The WG discussed the following proposals to evaluate those of the greatest benefit and interest to the collections:

- Exchange of strains on a one-to-one basis for research purposes is generally agreed by all WG participants.
- In cases where the receiving collection wants to incorporate the strain into their public catalogue some concerns could be raised as discussed above. In these cases, it is generally agreed that non-type material is an important asset for the collection, and it is well justified that collections may not agree to share these resources. In contrast, it may be considered preferable that reference strains used for quality control standards are exchanged and made available in all countries, as they are in high demand. In any case, collections have the freedom to decide whether or not they would like to share a particular resource, for the reasons explored in this paper or due to other constraints.
- In cases where a collection agrees to transfer a strain, the WG discussed some measures to reward the supplying collection:
 - To acknowledge the collection where the strain was originally deposited in scientific publications.
 - To establish collaboration agreements between collections by which the collection receiving a request for a strain would recommend the user to obtain the isolate from the collection(s) cited in the original publication or where the strain was originally deposited
 - Include *ad-hoc* clauses in the MTA for legitimate exchanges (e.g. prohibit commercial use, share benefits derived from the provision of the strain).

Conclusions

The operating framework of the collections has evolved since ECCO was established in 1981. Therefore, collections must understand that there might be some limits in their collaborating activities, which must not affect the friendly environment of cooperation between the members of the organization.

Besides the agreements and proposals made in this paper, it is worth considering that some of ECCO's member collections participate in MIRRI-ERIC, a legally constituted Research Infrastructure in which partner collections must adhere to the "MIRRI-ERIC Partner Charter and associated policies", a set of principles defining the criteria to participate in the Consortium. One of the policies deals with the targeted accession of microbial material and may include recommendations about the exchange of strains between collections. Discussions within this group could complement the ideas discussed in this report.

This document has been developed with the aim of analysing the current context relating to the exchange of strains among ECCO collections and can be used as a reference when collections share material.

Disclaimer

"The opinions expressed in this position paper do not necessarily reflect the opinions of all ECCO members."

References

- D. Smith, 2012. Chapter 4 Culture Collections. Advances in Applied Microbiology. Volume 79, 2012, Pages 73-118
- 2. ECCO, 2022. European Culture Collections' Organisation website. Accessed 26 July 2024, https://www.eccosite.org/
- Publication Office of the European Union, 1998. Development of Microbial Information Network in Europe to a centralized European culture collections data base system website. Accessed 26 July 2024, <u>https://cordis.europa.eu/project/id/BIOT0280/</u>
- 4. CABRI, 2023. Common Access to Biological Resources and Information website. Accessed 26 July 2024, <u>http://www.cabri.org/</u>
- 5. BELSPO, n.d. *MOSAICC*, Belgian Coordinated Collections of Microorganisms website. Accessed 26 July 2024, <u>https://bccm.belspo.be/mosaicc</u>
- Publication Office of the European Union, 2013. Development of a system for appropriate management of access and transfer of microbial resources - micro-organisms sustainable use and access regulation integrated conveyance system. Accessed 26 July 2024, <u>https://cordis.europa.eu/project/id/506436</u>
- 7. EBRCN, 2024. European Biological Resource Centres Network website. Accessed 26 July 2024, <u>https://ebrcn.org/</u>
- 8. EMbaRC, n.d. European Consortium of Microbial Resources Centres website. Accessed 26 July 2024, <u>http://www.embarc.eu/project.html</u>
- 9. ECCO, ECCO MTA and MDA, 2022. ECCO MTA and MDA website. Accessed 26 July 2024, https://www.eccosite.org/ecco-mta-and-mda/
- Verkley, G. et. al., 2020. New ECCO model documents for Material Deposit and Transfer Agreements in compliance with the Nagoya Protocol. FEMS Microbiology Letters, 2020 Mar 1;367(5):fnaa044. doi: 10.1093/femsle/fnaa044
- 11. Secretariat of the Convention on Biological Diversity, 2011a. Convention on Biological Diversity. Accessed 26 July 2024, <u>https://www.cbd.int/doc/legal/cbd-en.pdf</u>
- 12. MIRRI-ERIC, n.d. Microbial Resource Research Infrastructure European Research Infrastructure Consortium website. Accessed 26 July 2024, <u>https://www.mirri.org/</u>
- 13. European Commission, 2022. Commission Implementing Decision (EU) 2022/1204 of 16 June 2022 setting up MIRRI-ERIC
- 14. National Microbiology Data Center, n.d. WDCM Reference Strain Catalogue. Accessed 26 July 2024, <u>https://refs.wdcm.org/</u>
- 15. DSMZ, 2024. StrainInfo webpage. Accessed 26 July 2024, https://straininfo.dsmz.de/
- 16. DSMZ, n.d. LPSN webpage. Accessed 26 July 2024, https://lpsn.dsmz.de/
- 17. DSMZ, n.d. BacDive webpage. Accessed 26 July 2024, https://bacdive.dsmz.de/
- 18. MIRRI, MIRRI Strains Catalog, n.d. MIRRI Strains Catalog website. Accessed 26 July 2024, https://catalog.mirri.org/
- 19. European Commission, 2021. Commission Recommendation of 16.12.2021 on the use of the Environmental Footprint methods to measure and communicate the life cycle environmental performance of products and organisations.
- 20. Secretariat of the Convention on Biological Diversity, 2011b. Nagoya Protocol. Accessed 26 July 2024, <u>https://www.cbd.int/abs/doc/protocol/nagoya-protocol-en.pdf</u>

ANNEX 1

Questionnaire about the Type strain holdings of ECCO Collections (numbers or estimates based upon the most recent assessment)

Name of Culture Collection:					
Member of MIRRI (yes / no):					
Name of person providing information					
Position in Culture Collection:					
Country, Region/City					
I) Total number of microbial strain holdings:					
Of these, how many bacteria:					
how many yeast / fungi:					
how many algae:					
how many viruses / phages:					
how many other:					
2) Total number of Type strains:					
 P) Total number of Type strains:					
 4) Total number of Type strain requests per year: 					
) Estimate of % of Type strains per total number of requests:					
6) Estimate of % of total sales from Type strains:					

Date of assessment: _____ Today's date: _____

ANNEX 2

Report from the Questionnaire about the Type strain holdings of ECCO Collections

1)	Number of Collections responding:	39 (of 90 ECCO CCs) = 43% of ECCO CCs.	
	e CCs indicated that the questionnaire is not rele questionnaire pertains only to CCs holding bacter		
2)	Number of MIRRI Collections responding:	13	
3)	Total number of microbial strain holdings:	Range = 300 – 93 686;	Total = 480 387
4)	Number of bacterial strain holdings: Numbers are from CCs that hold bacterial strains	Range = 10 – 37 278	Total = 229 764
5)	Number of yeast / fungi strain holdings: Numbers are from CCs that hold yeast / fungi strains	Range = 5 – 93 686	Total = 235 733
6)	Number of algae: Numbers are from CCs that hold algae strains	Range = 1 – 2 749	Total = 9 325
7)	Number of viruses / phages: Numbers are from CCs that hold viruses / phages	Range = 1 – 2 027	Total = 3 741
8)	Total number of Type strains:	Range = 3 – 15 246	Total = 58 328
9)	Total number of strain requests per year:	Range = 0 – 41 686	Total = 63 524
10)	Total number of Type strain requests per year:	Range = 0 – 17 680	Total = 24 186
11)	Type strains (%) per total number of requests:	Range = 0.0% - 100%	Total = 38%
12)	Estimate of % of total sales from Type strains:	Range = 0.0% - 100%	