Towards a common standard for data and specimen provenance in life sciences

DOI:
10.1002/lrh2.10365

Document Version
Submitted manuscript

Published in:
Learning Health Systems

Towards a common standard for data and specimen provenance in life sciences

Rudolf Wittner[*1,2], Petr Holub[1,2], Cecilia Mascia[3], Francesca Frexia[3], Heimo Müller[4], Markus Plass[4], Clare Allocca[5], Fay Betsou[6], Tony Burdett[7], Ibon Cancio[8], Adriane Chapman[9], Martin Chapman[10], Mélanie Courtot[31], Vasa Curcin[10], Johann Eder[11], Mark Elliot[12], Katrina Exter[13], Carole Goble[14], Martin Golebiewski[15], Bron Kisler[16], Andreas Kremer[17], Simone Leo[3], Sheng Lin-Gibson[18], Anna Marsano[19], Marco Mattavelli[20], Josh Moore[21,32], Hiroki Nakae[22], Isabelle Perseil[23], Ayat Salman[24,25], James Sluka[26], Stian Soiland-Reyes[14,27], Caterina Strambio-De-Castillia[28], Michael Sussman[29], Jason R. Swedlow[21], Kurt Zatloukal[4], Jörg Geiger[30]

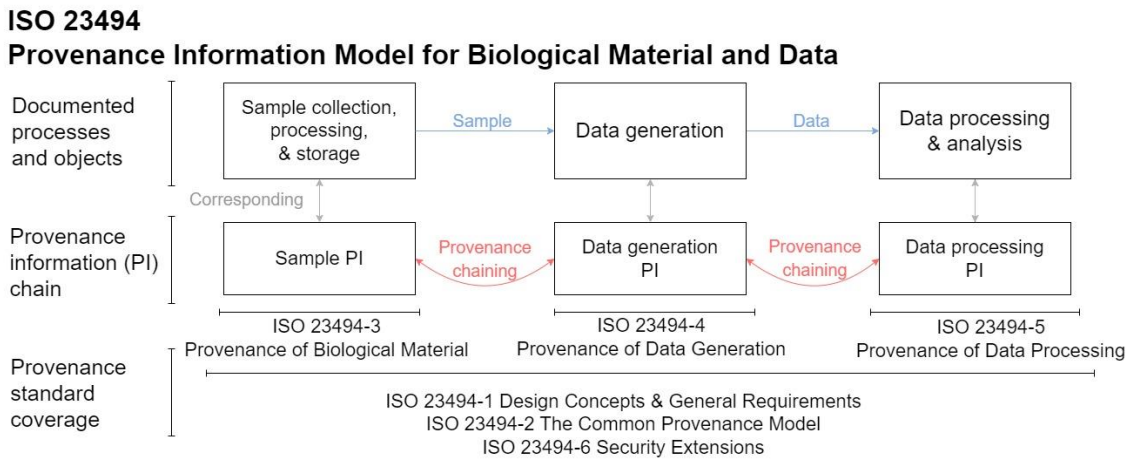
**Corresponding author: RNDr. Rudolf Wittner, <wittner@ics.muni.cz>*

[1]*BBMRI-ERIC, Graz, AT*
[2]*Institute of Computer Science & Faculty of Informatics, Masaryk University, Brno, CZ*
[3]*CRS4 – Center for Advanced Studies, Research and Development in Sardinia, IT*
[4]*Medical University Graz, AT*
[5]*National Institute of Standards and Technology, Gaithersburg, MD, USA*
[6]*Biological Resource Center of Institut Pasteur (CRBIP), FR*
[7]*EMBL's European Bioinformatics Institute (EMBL-EBI), UK*
[8]*Plentzia Marine Station (PiE-UPV/EHU), University of the Basque Country, EMBRC-Spain*
[9]*University of Southampton, UK*
[10]*King's College London, UK*
[11]*University of Klagenfurt, AT*
[12]*Department of Social Statistics, School of Social Sciences, University of Manchester, UK*
[13]*Flanders Marine Institute (VLIZ), EMBRC-Belgium*
[14]*Department of Computer Science, University of Manchester, UK*
[15]*Heidelberg Institute for Theoretical Studies (HITS gGmbH), Heidelberg, DE*
[16]*Independent consultant*
[17]*ITTM S.A., LU*
[18]*Biosystems and Biomaterials Division, NIST, USA*
[19]*Department of Biomedicine, University of Basel, CH*
[20]*SCI-STI-MM, École Politechnique Fédérale de Lausanne, Lausanne, CH*
[21]*Centre for Gene Regulation and Expression and Division of Computational Biology, School of Life Sciences, University of Dundee, Dundee, UK*
[22]*Japan bio-Measurement and Analysis Consortium, JPN*
[23]*INSERM - Institut National de la Sante et de la Recherche Medicale, FR*
[24]*Standards Council of Canada*
[25]*Canadian Primary Care Sentinel Surveillance Network (CPCSSN) Department of Family Medicine, Queen's University, CA*
[26]*Biocomplexity Institute, Indiana University, USA*
[27]*Informatics Institute, University of Amsterdam, NL*
[28]*Program in Molecular Medicine, University of Massachusetts Chan Medical School, USA*
[29]*US Department of Agriculture, USA*
[30]*Interdisciplinary Bank of Biomaterials and Data Würzburg (ibdw),Würzburg, DE*
[31]*Ontario Institute for Cancer Research, CA*
[32]*German BioImaging – Gesellschaft für Mikroskopie und Bildanalyse e.V., Konstanz, DE*

Abstract

Open and practical exchange, dissemination, and reuse of specimen and data has become a fundamental requirement for life sciences research. The quality of the data obtained and thus the findings and knowledge derived is thus significantly influenced by the quality of the samples, the experimental methods and the data analysis. Therefore, a comprehensive and precise documentation of the pre-analytical conditions, the analytical procedures and the data processing is essential to be able to assess the validity of the research results. With the increasing importance of the exchange, reuse and sharing of data and samples, procedures are required that enable cross-organizational documentation, traceability, and non-repudiation. At present, this information on the provenance of samples and data is mostly either sparse, incomplete, or incoherent. Since there is no uniform framework, this information is usually only provided within the organization and not interoperably. At the same time, collection and sharing of biological and environmental specimens increasingly requires definition and documentation of benefit sharing and compliance to regulatory requirements rather than consideration of the pure scientific needs. In this publication, we present an ongoing standardization effort to provide trustworthy machine-actionable documentation of the data lineage and specimens. We would like to invite experts from biotechnology and biomedical fields to further contribute to the standard.

Graphical abstract



Keywords

Provenance information; Standardization; Biotechnology; International Organization for Standardization;

1 Introduction

The profound crisis of scientific reproducibility has its roots in the enhanced availability of large volumes of data that are produced at ever increasing velocity, which in turn often leads to the dissolution of the control mechanisms that traditionally ensured the quality of data and processes [1-7]. At the same time the origin and history of specimens used to generate research data often remains inexplicit. While considerable effort has been put in the development of standards for specimen quality, the actual documentation has been left to the discretion of the provider of the specimen and data. As a result, the situation is exacerbated by the lack of consistent and comprehensive documentation of specimens and data, which could support the identification of suspected, or proven use of, fabricated data or specimen of unclear origin. Hence, **the urgent need for the trustworthy documentation of the data lineage and specimens is evident**, especially when considering the serious impact of irreproducible or even flawed scientific results on health, economics, and political decisions [8-12].

It is generally accepted that the reliability of data generated in downstream analytical procedures [13-15] is significantly impacted by the properties and quality attributes of specimens which are precursors of the data. Experts from multiple life sciences domains have called for the improvement and standardization of the documentation of research and scientific service processes [16-22]. This has led in turn to the progressive development and implementation of data management and other functional tools, such as discovery services, access pipelines, and standardized data models, enabling the sharing of data and specimens [23-28]. In practice, however, there remains a gap between the needs and the reality of the requirements specified in accepted standards, including technical, operational and legal specifications needed to ensure the trustworthiness and traceability of data and specimens. In an effort to remedy these deficiencies in the provenance captured and reported, **we are endeavoring to develop an *international standard on provenance information system for the life sciences* accepted by both academia and industry**. Provenance information can be used to assess the quality and reliability, and hence the reusability of the object, i.e. the data, the metadata, the biological materials, or the specimens.

1.1 Objectives for a provenance standard

One of the main characteristics of present-day research in life-sciences is that the research objects, such as datasets or specimens, are exchanged between organizations. Therefore each of the organizations involved can only provide documentation for a part of the object's life cycle. Consequently, an uninterrupted chain of provenance information documenting the whole life cycle can only be formed from individual parts of provenance distributed across different sources. To enable meaningful integration and harmonized processing of the distributed provenance parts, the semantic interoperability between standalone distributed provenance parts must be ensured. In addition, the processing of the resulting chain of distributed provenance must be designed to: a) deal with missing provenance components in the chain, so the chain is not interrupted or corrupted when an intermediary organization has not generated appropriate provenance information, or if the organization ceased to exist; b) handle sensitive or confidential information contained in provenance information, keeping it opaque and disclosed only by authorization; c) handle several versions of the same provenance information, for instance, when an error in provenance is found and is fixed; d) enable verification of the integrity and authenticity of provenance components, even for opaque provenance components, to ensure trustworthiness of provenance.

The distributed provenance chain must be suited to answer essential queries independent of the research domain, such as *"What are the precursors of a given dataset?"*, or *"Which processes precede a given dataset creation?"*. The underlying query resolution mechanism must be able to navigate through the chain, regardless of the actual site where the corresponding part of the distributed provenance is stored, which processes or objects are documented, or what the actual source of the provenance is.

The provenance standard must therefore include a general concept, providing a basis for common aspects shared between various domains which are part of the life-cycle of a documented research object. In particular, these common aspects include: a) traversing distributed provenance chains; b) implementing domain-independent properties for the provenance, such as confidentiality, authenticity, integrity, non-repudiation, and validity; c) locating a specific part of provenance in the distributed provenance. In addition, support for any domain-specific aspect, such as quality related queries, must be provided and aligned with the common foundation without disrupting the general properties of the chain.

2 Results and Discussion

The novelty of the proposed standard is that it is the first provenance information standard for the biomedical domain that aims to address the aforementioned requirements. In addition, the standard covers both, physical and digital objects and links them to a common provenance chain, while ensuring the common properties of resulting provenance parts. It supports fully distributed provenance information management, and aims to handle a wide range of complex real-world scenarios. As part of the standard development, we have proposed the Common Provenance Model (CPM) [29], which forms the conceptual foundation of the standard. The CPM is the only provenance model that provides a baseline for distributed provenance chains, as they were described above.

The need for an effort to address the issues in provenance was proposed to the International Standards Organization (ISO) Technical Committee 276 "Biotechnology" (ISO/TC 276) in 2017 and approved as a preliminary work item. In 2020, ISO/TC 276 approved a new work item proposal to develop an international standard for biological material and data provenance which is registered as committee draft, ISO/DTS 23494-1 *Biotechnology – Provenance information model for biological material and data – Part 1: Design concepts and general requirements*. To the best of our knowledge, this standard is the first provenance information standard for the biotechnology domain, addressing the need for consistent documentation of the life-cycle of related research objects from acquisition of a specimen to analytical procedures and downstream data processing and analysis. This standard is conceptualized according to the FAIR principles [30], which provide high-level methodological recommendations, including guidance on provenance[1]. As the FAIR principles themselves do not provide detailed instructions for the implementation of provenance standards and documentation, the ISO 23494 series is intended for provenance of data and biological samples and will be built on the World Wide Web Consortium's (W3C) PROV model [31], a generic provenance information standard that defines a general model, corresponding serializations[2] and other supporting specifications to enable the interoperable exchange of provenance information between data environments. W3C PROV serves as a framework that is adaptable and extensible to fit the needs of diverse domains. The W3C PROV standard has already been adopted in life science research areas [32], e.g., for computational workflows [33], pharmacologic pipelines [34], neuroscience [35, 36], microscopy experiments [37], medical sciences [38] and health implementation care[3] in HL7 FHIR [39]. Unfortunately, **these implementations occurred without coordination and the resulting solutions are often incompatible, incomplete, expressed at different levels of granularity, and do not use a consistent approach for creating a continuous chain of provenance from the "source" to the resulting data**. Instead of redefining the W3C PROV concepts, we have identified gaps that need to be filled in order to develop a distributed, fully technically and semantically interoperable provenance information standard that covers uninterrupted documentation of the whole life cycle of a dataset back to its "source". The "source" can include a complex, multi-institutional environment and can be

[1] Principle R1.2: (Meta)data are associated with detailed provenance.
[2] As defined in ISO 21597-1:2020: encoding of an ontology or dataset into a format that can be stored, typically in a file.
[3] https://www.hl7.org/fhir/provenance.html

both the source specimen and data, but also a link to a specific biological entity, or environmental specimen collected at a given time and location (*connectivity* requirement [40]).

The main goals of the provenance information standard are

i. to support improved traceability and reproducibility of life-sciences research, to provide a voluntary provenance framework enabling concordance of governments, businesses, academia and the international community;
ii. to enable decision-making about the fitness-for-purpose of particular data and specimens, by collecting and linking provenance information from the whole life-cycle of the object (from specimen collection and processing, through data generation and analysis) as depicted in Figure 1;
iii. to achieve harmonization of documentation of specimens that is compliant with international conventions, recognized ethical practices and legal requirements such as the Nagoya Protocol [41] and the Declaration of Taipei [42];

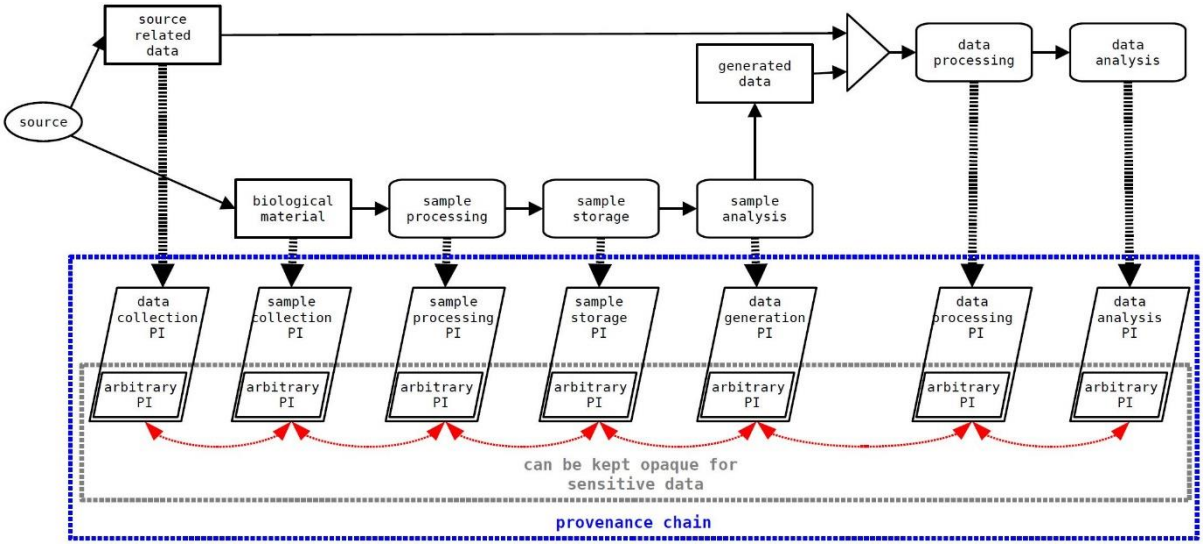


Figure 1: An overview of provenance chain. A sample obtained from a donor (or other source) is created and an initial set of provenance information (PI) is generated. As that sample moves through time and space, is processed and/or analyzed, additional provenance data is appended to the provenance chain for each new item. The chain can be extended as a complete unit of later stages of provenance or use unique identifiers to refer to early stages of provenance data. Figure cited from [29].

The standard will enhance the trustworthiness of provenance information by including requirements and guidelines on its integrity, authenticity, and non-repudiation [43], to prevent the production and/or use of unreliable, flawed or fabricated data (the potential harms of which have become evident also during the COVID-19 pandemic [2, 10], as well as accidental or malicious modification of data. Since provenance information may also include sensitive or personal data (related, e.g., to the health condition of an individual), the standard aims to enable sensitive information to be concealed and disclosed only under strictly controlled conditions, while preserving its core properties of integrity, authenticity, and non-repudiation. Additional advanced application scenarios include tracking of provenance information to: (i) track research error propagation, (ii) identify people affected by incidental research findings, (iii) check compliance with applicable regulations, or (iv) support production of reference material by maintaining full documentation of provenance (complementing work of ISO/TC 334 [44]). For research concerned with highly regulated fields in life

sciences, such as development of medical products or drugs, the standardized provenance model will also contribute to a level of accountability and auditability of research organisations.

The proposed standard is designed to cover the majority of the organizations involved in life-sciences research, both academic and industrial, government labs and research centers. Included organizations are university and industrial research
laboratories, hospitals, biobanks and biorepositories, culture collections, research centres, and private companies (e.g., pharmaceutical companies or lab reagent suppliers). The broader audience includes not only research data producers, but also those publishing, cataloguing, archiving, or reusing research data [45]. The standard can also be adopted by manufacturers and vendors of laboratory instruments – e.g., automation devices, microscopes, sequencers, spectrometers – to enable automated standard-compliant generation of provenance information. Automated generation of provenance information will minimize human errors and the burden put on workers, both in terms of effort and training. Provenance information generated automatically by devices should be interoperable to enable automated integration and quality control as well as validity checks demonstrating standard-compliant provenance. The standard is intended to cover a wide range of research and applications in life sciences and for that reason a modular structure has been used to enable extensibility to evolving requirements, processes, or technologies.

The current draft proposal ISO/DTS 23494-1 is the first part of a planned series of six parts, with the intent that each will become a distinct ISO standard:

1. *Design concepts and general requirements* defines the overall structure of the standard and provides general requirements on provenance information management, thus enabling interconnections between the various components of provenance information in distributed environments. It also specifies requirements applicable to entities responsible for generating the provenance information.
2. *The Common Provenance Model* builds on the W3C PROV model, defining representations of elements common to all stages of research, such as interlinking of distributed components of provenance information, the identification of physical and digital objects, provenance information patterns for common scenarios, such as missing provenance components in the chain, the compound processes, versioning of provenance information or documentation of accountabilities. The model will also define mechanisms to embed or reference entire records of provenance information.
3. *Provenance of Biological Material* defines requirements and scope of the provenance information documenting biological material or specimen acquisition, handling and processing and builds on the Common Provenance Model. This includes, but is not limited to, data on collection and collection procedure, transport conditions, and documentation of the legal and ethical basis (e.g. consent, terms of access and benefit sharing) of the collection. It will also provide mechanisms to reference Standard Operating Procedures (SOPs) and compliance with or deviations from them. Referencing the widely accepted de-facto reporting standard for biological specimen quality SPREC [46] will also be enabled. Actual techniques or practices for handling biological material are not specified in the standard, in favor of technical specifications enabling consistent interoperable and machine-actionable documentation of handling biological material. With the provenance information provided, however, the standard facilitates the verification of compliance with other pre-analytical ISO standards covering biobanking, analytical and processing methods, generation of reference material and related fields (ISO 20387:2018, ISO 20184 series, ISO 20166 series, and ISO 20186 series).

4. *Provenance of Data Generation* defines the provenance of data generated from the analysis or observation of biological material, e.g., sequencing, microscopy, spectrometry, etc. Provenance information specific for diverse analytical or observational data generation methods will be embedded in a way meeting the requirements of particular domain, but as well compliant with the provenance model standard allowing seamless integration in a complete provenance chain. This will be supported by the definition of standardized links from provenance to domain-specific information documenting the applied data generation method. As the syntax and semantics of the domain-specific information may be in scope of another standard, the standardized links will provide information about the conformance of the domain-specific information to a particular standard.
5. *Provenance of Data Processing* defines provenance of computational aspects of life sciences research such as the execution of computational workflows, for which we plan to leverage existing standards such as CWLProv [33] and RO-Crate [47], which is being complemented by a specialized profile to capture the provenance of workflow runs[4].
6. *Security Extensions* define optional extensions supporting authenticity, integrity, and non-repudiation of provenance information, and hence its trustworthiness and reliability. Demonstration of these properties will also be supported for sensitive elements of provenance information.

The ISO standards development process responds to a market need and is based on globally-relevant expertise. The product is a voluntary consensus standard developed through a multi-stakeholder process. ISO/DTS 23494-1 and ISO/PWI TS 23494-2 has a proven market need and has passed through the preliminary stages of the ISO voting process – as a result, they are part of the ISO Work Programme. ISO/DTS 23494-1 *Provenance information model for biological material and data – Part 1: Design concepts and general requirements* is currently at the committee draft stage. Part 2 of this series, *Biotechnology — Provenance information model for biological material and data — Part 2: Common provenance model*, has been accepted by ISO/TC 276/WG 5 as preliminary work item ISO/PWI TS 23494-2. Part 3 of the series, *Biotechnology — Provenance information model for biological material and data — Part 3: Provenance of biological material*, will be proposed to become a Preliminary Work Item in 2023. The future documents in this series are in planning stages, but not yet submitted to ISO/TC 276/WG 5. The standards development process builds on existing standards for collection and processing of specimens, analytical techniques and data generation and analysis, as well as use-cases from the biomedical domain. BBMRI-ERIC, which is also active in developing international standards for biobanking, has drafted use-cases for biological material provenance. Collaborations and ISO liaisons with professional societies like the European, Middle Eastern and African Society for Biobanking (ESBB) and the International Society for Biological and Environmental Repositories (ISBER) have also contributed to the development of specimen provenance use cases. In addition, use cases on data generation and processing can come from subject matter experts and the scientific community including the European EOSC-Life project[5], Open Microscopy Environment, OME[6], genetic data compression (ISO/IEC JTC1/SC 29/WG 08 MPEG-G) [48], clinical trials and decision support systems and other life sciences domains such as biodiversity, marine biology, and systems biology.

[4] https://www.researchobject.org/workflow-run-crate/
[5] https://www.eosc-life.eu/
[6] https://www.openmicroscopy.org/

2.1 Industrial vs. community-based standards

Alternatives to ISO standards process[7] exist – some community-based efforts have developed widely adopted specifications that have become *de facto* global standards[8]. The success of these examples lies, at least in part, in the pairing of a specification with an accessible implementation that validates the utility of the specification and allows a broad community to explore integration into applications that extend far beyond the initial target [52]. We believe that community-led and ISO-based approaches for developing and delivering standards can complement each other and that a combination of parallel efforts for developing a provenance chain standard might ultimately be the most productive approach. As the provenance information model development is grounded in the EOSC-Life project, collaboration with these communities is already established. Industrial collaboration is established by grounding the standardization effort in the ISO, where industry experts drive all aspects of a standard development process through their involvement in the ISO Technical Committees. **The presented ISO standard development is thus considered as a standardized instance of a publicly available provenance model** [29] developed in parallel under auspices of EOSC-Life project [53].

Another challenge is the continuous dissemination and periodic revision of the standard once published. Though ISO standards are not "open access", they can be purchased for a moderate fee[9] or accessed through institutional libraries, and, barring any patent restrictions, can be freely implemented, for instance, in Open Source software. ISO standards can also include Open Source reference implementations as specific normative or informative parts of the standards. ISO standards can be implemented independently or based on such source code, in compliance with the reasonable and non-discriminatory (RAND) licensing terms imposed by the ISO requirements. Such licensing terms, like for instance the one applied to all ISO/IEC/SC29 (MPEG) standards that are free from any charge for scientific and non-profit research purposes, may or may not include licensing fees.

2.2 Open issues

The Common Provenance Model can be seen as a current state of the art provenance model for distributed provenance, which is the most advanced provenance model that aims to provide a foundation for distributed provenance chains [29]. The development of the CPM was piloted using a distributed research pipeline covering biological material acquisition and storage, samples processing, data generation and data processing. The prototype implementation of provenance generation was provided for the computational steps of the research pipeline.

However, the model should be rigorously validated in different domains, including multiple scientific communities and industry, in order to verify its applicability in diverse domains in life sciences. The model is currently being applied in the BY-COVID project[10], which aims to develop a platform to integrate sources related to viral infections (clinical data, biological material, research results). As part of this activity, the model will be integrated with RO-Crate [47] and applied to various use cases, including machine learning computational workflows and federated analysis.

We would like to invite experts from biotechnology and biomedical fields to further contribute to the standard, in particular to the provenance of biological specimens, the data-generation and data-processing modules. Help is needed to develop applications of the general modules and the development of specific use cases, as well as direct contributions to the text of the standard itself.

---

[7] https://www.iso.org/developing-standards.html

[8] E.g., for on-line cryptography (RSA public keys [49]), scientific workflows (Common Workflow Language [50]) and bioimaging data formats (OME-TIFF [51]).

[9] In some cases ISO standards can be obtained without any fee, e.g. https://www.iso.org/covid19

[10] https://by-covid.org/

Contributions are possible through a liaison organization, a national ISO body or by engaging with EOSC-Life project events and calls.

Acknowledgments

This work has been co-funded by EOSC-Life supported by EU Horizon 2020, grant agreement no. 824087; EJP-RD supported by EU Horizon 2020, grant agreement no. 825575; BioExcel-2 supported by EU Horizon 2020, grant agreement no. 823830; the DIFRA and the SVDC Projects, funded by the Sardinian Regional Authority. VC and MCh supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' National Health Service NHS) Foundation Trust and King's College London. TB, MCo acknowledge funding from EMBL-EBI Core Funds and the FAIRplus project (H2020 No 802750). MCo supported by Wellcome Trust GA4GH award number 201535/Z/16/Z and the CINECA project (H2020 No 825775). AC was supported by EPSRC (EP/S028366/1). JS was supported by the US National institute of Health (U24 EB028887, R01 GM122424, and OT2OD026671), the US National Science Foundation (NSF 2054061) and the US EPA (RD840027). ME was supported by the Alan Turing Institute (ProvAnon). KZ was supported by the Austrian ministry (BMBWF-10.470/0010-V/3c/2018, BBMRI.at). CS was supported by NIH grant #U01CA200059 and by grant #2019-198155 (5022) awarded by the Chan Zuckerberg Initiative DAF, an advised fund of Silicon Valley Community Foundation, as part of their Imaging Scientist Program. The opinions in this paper are those of the authors and do not necessarily reflect the opinions of the funders.

Representation of communities

The co-authors team represents wide coverage of life-sciences communities. PH, RW, CM, FF, HM, MP, JG come from human biobanking and biomolecular resources communities, BBMRI-ERIC Research Infrastructure, and are directly involved as experts in the ISO standardization process. KZ and JE come from cancer research, biobanking and medical informatics and are long-term contributors to data quality standardization efforts. TB, MCo is a director of Ontario Institute for Cancer Research. IC and KE come from marine biology and EMBRC Research Infrastructure. CG and SSR have worked with bioinformatics, CWL and RO-Crate. JRS and JM come from bio-imaging communities and EUBioImaging Research Infrastructure. VC, and MCh come from health informatics. HN participates in provenance standardization process as an expert from Japan, MS and JS as experts from the U.S.A, and AK as an expert from Luxembourg. ME contributes to privacy protection and provenance aspects. FB is a biobanking expert and director of the microbiological resource center CRBIP, Institut Pasteur. AS is a biobanking expert and ESBB councillor. SL-G and CA are from NIST and convenor and secretary of ISO/TC 276/WG 3 "Analytical Methods". AM belongs to the tissue engineering and biomedical research community. MM is a standard expert in the digital media, genomic sequencing and annotation data fields, and convenor of ISO/IEC SC29/WG 8 "MPEG Genomic Coding". AC contributes to capture and handling of provenance within large organizations. CS is a Cell Biologists actively engaged in the development of quality control and reproducibility specifications and tools for light microscopy as member of the Data Coordination and Integration Center of the NIH-funded 4D Nucleome initiative, Chair of the Quality Control and Data Management WG of BioImaging North America, and Co-Chair of the WG on Metadata (WG7) of the QUality Assessment and REProducibility for Instruments and Images in Light-Microscopy (QUAREP-LiMI) initiative. SLe is a member of the RO-Crate community and co-chair of a working group for the development of an RO-Crate profile for capturing the provenance of scientific workflow executions.

Conflict of interest

The authors report that they have no conflicts of interest.

References

1. Begley CG and Ioannidis JP. Reproducibility in Science. Circulation Research 2015;116:116–26. https://doi.org/10.1161/CIRCRESAHA.114.303819
2. Servick K and Enserink M. The pandemic's first major research scandal erupts. Science 2020;368:1041–2. https://doi.org/10.1126/science.368.6495.1041
3. Lagoze C. Big Data, data integrity, and the fracturing of the control zone. Big Data & Society 2014;1:2053951714558281. https://doi.org/10.1177/2053951714558281
4. Mobley A, Linder SK, Braeuer R, et al. A Survey on Data Reproducibility in Cancer Research Provides Insights into Our Limited Ability to Translate Findings from the Laboratory to the Clinic. PLOS ONE 2013;8:1–4. https://doi.org/10.1371/journal. pone.0063221
5. Morrison SJ. Time to do something about reproducibility. eLife 2014;3:1–4. https://doi.org/10.7554/eLife.03981
6. Byrne JA, Grima N, Capes-Davis A, et al. The Possibility of Systematic Research Fraud Targeting Under-Studied Human Genes: Causes, Consequences, and Potential Solutions. Biomarker Insights 2019;14. https://doi.org/10.1177/1177271919829162
7. Prinz F, Schlange T, and Asadullah K. Believe it or not: how much can we rely on published data on potential drug targets? Nature Reviews Drug Discovery 2011;10. Number: 9 Publisher: Nature Publishing Group:712–2. https://doi.org/10.1038/nrd3439-c1
8. Freedman LP, Cockburn IM, and Simcoe TS. The Economics of Reproducibility in Preclinical Research. PLOS Biology 2015;13:1–9. https://doi.org/10.1371/journal.pbio.1002165
9. Nickerson D, Atalag K, Bono B de, et al. The Human Physiome: how standards, software and innovative service infrastructures are providing the building blocks to make it achievable. Interface Focus 2016;6. 00001:20150103. https://doi.org/10.1098/rsfs.2015.0103
10. Mahase E. Covid-19: 146 researchers raise concerns over chloroquine study that halted WHO trial. BMJ 2020;369. https://doi.org/10.1136/bmj.m2197
11. Chaplin S. Research misconduct: how bad is it and what can be done? Future Prescriber 2012;13:5–76. https://doi.org/10.1002/fps.88
12. Committee on Responsible Science, Committee on Science, Engineering, Medicine, and Public Policy, Policy and Global Affairs, et al. Fostering Integrity in Research. Pages: 21896. Washington, D.C.: National Academies Press, 2017. https://doi.org/10.17226/21896
13. Simeon-Dubach D and Perren A. Better provenance for biobank samples. Nature 2011;475:454–5. https://doi.org/10.1038/475454d
14. Holub P, Kohlmayer F, Prasser F, et al. Enhancing Reuse of Data and Biological Material in Medical Research: From FAIR to FAIR-Health. Biopreservation and Biobanking 2018;16:97–105. https://doi.org/10.1089/bio.2017.0110
15. Müller H, Reihs R, Zatloukal K, et al. State-of-the-Art and Future Challenges in the Integration of Biobank Catalogues:13. https://doi.org/10.1007/978-3-319-16226-3_11.
16. Ioannidis JP, Greenland S, Hlatky MA, et al. Increasing value and reducing waste in research design, conduct, and analysis. The Lancet 2014;383:166–75. https://doi.org/10.1016/S0140-6736(13)62227-8
17. Freedman LP and Inglese J. The Increasing Urgency for Standards in Basic Biologic Research. Cancer Research 2014;74:4024–9. https://doi.org/10.1158/0008-5472.CAN-14-0925
18. Begley CG and Ellis LM. Drug development: Raise standards for preclinical cancer research. Nature 2012;483:531–3. https://doi.org/10.1038/483531a arXiv: 9907372v1
19. Landis SC, Amara SG, Asadullah K, et al. A call for transparent reporting to optimize the predictive value of preclinical research. Nature 2012;490. nature11556[PII]:187–91. https://doi.org/10.1038/nature11556
20. Consortium of European Taxonomic Facilities (CETAF) Code of Conduct and Best Practice for Access and Benefit-Sharing. https://ec.europa.eu/environment/nature/biodiversity/international/abs/pdf/CETAF%20Best%20Practice%20-

%20Annex%20to%20Commission%20Decision%20C(2019)%203380%20final.pdf (visited on 12/30/2022).
21. Benson EE, Harding K, and Mackenzie-dodds J. A new quality management perspective for biodiversity conservation and research: Investigating Biospecimen Reporting for Improved Study Quality (BRISQ) and the Standard PRE-analytical Code (SPREC) using Natural History Museum and culture collections as case studies. Systematics and Biodiversity 2016;14:525–47. https://doi.org/10.1080/14772000.2016.1201167
22. A-E. K and Tillin H. The EMBRC guide to ABS compliance. Recommendations to marine biological resources collections' and users' institutions. A handbook produced by the European Marine Biological Resource Centre. European Marine Biological Resource Centre. 2020. url: https://bluebiobank.eu/docs/EMBRCGuideABS.pdf
23. Villanueva AG, Cook-Deegan R, Koenig BA, et al. Characterizing the Biomedical Data-Sharing Landscape. The Journal of Law, Medicine & Ethics: A Journal of the American Society of Law, Medicine & Ethics 2019;47:21–30. https://doi.org/10.1177/1073110519840481
24. Hulsen T. Sharing Is Caring-Data Sharing Initiatives in Healthcare. International Journal of Environmental Research and Public Health 2020;17:E3046. https://doi.org/10.3390/ijerph17093046
25. Banzi R, Canham S, Kuchinke W, et al. Evaluation of repositories for sharing individual-participant data from clinical studies. Trials 2019;20:169. https://doi.org/10.1186/s13063-019-3253-3
26. Toh S. Analytic and Data Sharing Options in Real-World Multidatabase Studies of Comparative Effectiveness and Safety of Medical Products. Clinical Pharmacology and Therapeutics 2020;107:834–42. https://doi.org/10.1002/cpt.1754
27. Grossman RL. Data Lakes, Clouds, and Commons: A Review of Platforms for Analyzing and Sharing Genomic Data. Trends in genetics: TIG 2019;35:223–34. https://doi.org/10.1016/j.tig.2018.12.006
28. Wilson SL, Way GP, Bittremieux W, et al. Sharing biological data: why, when, and how. FEBS Letters 2021;595:847–63. https://doi.org/10.1002/1873-3468.14067
29. Wittner R, Mascia C, Gallo M, et al. Lightweight Distributed Provenance Model for Complex Real–world Environments. Scientific Data 2022;9:503. https://doi.org/10.1038/s41597-022-01537-6
30. Wilkinson MD, Dumontier M, Aalbersberg IJ, et al. .e FAIR Guiding Principles for scientific data management and stewardship. Scientific Data 2016;3:160018. https://doi.org/10.1038/sdata.2016.18
31. Groth P and Moreau L. PROV-Overview: An Overview of the PROV Family of Documents. 2013. url: https://www.w3.org/TR/2013/NOTE-prov-overview-20130430/
32. Huynh TD, Groth P, and Zednik S. PROV Implementation Report. 2013. url: http://www.w3.org/TR/2013/NOTE-prov-implementations-20130430/
33. Khan FZ, Soiland-Reyes S, Sinnott RO, et al. Sharing interoperable workflow provenance: A review of best practices and their practical application in CWLProv. GigaScience 2019;8. giz095. https://doi.org/10.1093/gigascience/giz095
34. Mammoliti A, Smirnov P, Safikhani Z, et al. Creating reproducible pharmacogenomic analysis pipelines. Scientific Data 2019;6:166. https://doi.org/10.1038/s41597-019-0174-7
35. McClatchey R, Shamdasani J, Branson A, et al. Traceability and Provenance in Big Data Medical Systems. In: 2015 IEEE 28th International Symposium on Computer-Based Medical Systems. 2015:226–31. https://doi.org/10.1109/CBMS.2015.10
36. Giesler A, Czekala M, Hagemeier B, et al. UniProv: A Flexible Provenance Tracking System for UNICORE. In: High-Performance Scientific Computing. Ed. by Di Napoli E, Hermanns MA, Iliev H, et al. Cham: Springer International Publishing, 2017:233–42. https://doi.org/10.1007/978-3-319-53862-4_20
37. Samuel S. Integrative Data Management for Reproducibility of Microscopy Experiments. In: The Semantic Web. Ed. by Blomqvist E, Maynard D, Gangemi A, et al. Cham: Springer International Publishing, 2017:246–55. https://doi.org/10.1007/978-3-319-58451-5_19

38. Curcin V, Fairweather E, Danger R, et al. Templates as a method for implementing data provenance in decision support systems. Journal of Biomedical Informatics 2017;65:1–21. https://doi.org/10.1016/j.jbi.2016.10.022
39. HL7 and its participants. FHIR Release #4B [Standard], version 4.3.0. 2022. url: http://hl7.org/fhir/R4B/
40. Curcin V, Miles S, Danger R, et al. Implementing interoperable provenance in biomedical research. Future Generation Computer Systems 2014;34. Special Section: Distributed Solutions for Ubiquitous Computing and Ambient Intelligence:1–16. https://doi.org/10.1016/j.future.2013.12.001
41. Secretariat of the Convention on Biological Diversity. The Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity. Convention on Biological Diversity, United Nations, 2021. https://www.cbd.int/abs/ (visited on 12/30/2022).
42. WMA - The World Medical Association-WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks. https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/ (visited on 12/30/2022).
43. Fairweather E, Wittner R, Chapman M, et al. Non-repudiable provenance for clinical decision support systems. In: IPAW 2020, IPAW 2021: Provenance and Annotation of Data and Processes. Ed. by Glavic B, Braganholo V, and Koop D. Vol. 12839. Lecture Notes in Computer Science. 2021:162–82. https://doi.org/10.1007/978-3-030-80960-7_10 arXiv: 2006.11233 [cs.CR].
44. 14:00-17:00. ISO/WD Guide 85. https://www.iso.org/cms/render/live/en/sites/isoorg/contents/data/standard/07/55/75538.html (visited on 12/30/2022).
45. Cheney J, Chapman A, Davidson J, et al. Data provenance, curation and quality in metrology. In: Advanced Mathematical and Computational Tools in Metrology and Testing XII. Vol. 90. Series on Advances in Mathematics for Applied Sciences. World Scientific, 2021:167–87. https://doi.org/10.1142/9789811242380_0009 arXiv: arXiv:2102.08228v1.
46. Betsou F, Bilbao R, Case J, et al. Standard PREanalytical Code Version 3.0. Biopreservation and Biobanking 2018;16:9–12. https://doi.org/10.1089/bio.2017.0109
47. Soiland-Reyes S, Sefton P, Crosas M, et al. Packaging research artefacts with RO-Crate. Data Science 2022;5:97–138. https://doi.org/10.3233/ds-210053
48. Voges J, Hernaez M, Mattavelli M, et al. An Introduction to MPEG-G: The First Open ISO/IEC Standard for the Compression and Exchange of Genomic Sequencing Data. Proceedings of the IEEE 2021. https://doi.org/10.1109/JPROC.2021.3082027.
49. Rivest RL, Shamir A, and Adleman L. A Method for Obtaining Digital Signatures and Public-Key Cryptosystems. Commun. ACM 1978;21:120–6. https://doi.org/10.1145/359340.359342
50. Crusoe MR, Abeln S, Iosup A, et al. Methods Included: Standardizing Computational Reuse and Portability with the Common Workflow Language. Communications of the ACM 2022;65. https://doi.org/10.1145/3486897
51. Linkert M, Rueden CT, Allan C, et al. Metadata matters: access to image data in the real world. Journal of Cell Biology 2010;189:777–82. : https://doi.org/10.1083/jcb.201004104
52. Swedlow JR, Kankaanpää P, Sarkans U, et al. A global view of standards for open image data formats and repositories. Nature Methods 2021. https://doi.org/10.1038/s41592-021-01113-7
53. Wittner R, Mascia C, Frexia F, et al. EOSC-Life Common Provenance Model. EOSC-Life deliverable D6.2. 2021. https://doi.org/10.5281/zenodo.4705074