Stem Cell Reports
Perspective
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ISSCR standards for the use of human stem cells in basic research

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https://doi.org/10.1016/j.stemcr.2023.08.003

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SUMMARY

The laboratory culture of human stem cells seeks to capture a cellular state as an *in vitro* surrogate of a biological system. For the results and outputs from this research to be accurate, meaningful, and durable, standards that ensure reproducibility and reliability of the data should be applied. Although such standards have been previously proposed for repositories and distribution centers, no widely accepted best practices exist for laboratory research with human pluripotent and tissue stem cells. To fill that void, the International Society for Stem Cell Research has developed a set of recommendations, including reporting criteria, for scientists in basic research laboratories. These criteria are designed to be technically and financially feasible and, when implemented, enhance the reproducibility and rigor of stem cell research.

INTRODUCTION

There has been a dramatic expansion in the field of stem cell research since the early work with hematopoietic and teratocarcinoma stem cells over a half-century ago.

From the isolation of tissue and pluripotent stem cells to more recent advances in multi-dimensional systems that recapitulate the complexity of organs, the science continues to develop and expand. This expansion has attracted researchers from diverse backgrounds, focusing their applications of stem cell technology on very different areas, including developmental biology, cancer biology, disease modeling, drug discovery, and regenerative medicine. This cross disciplinary collaborative work has enriched the field, offered new perspectives, and served to underpin the explosion of clinical applications globally.

Continued progress in the field relies on the ability of scientists to reliably model the human system using stem cell technology. Fundamental to this process is the ability to perform rigorous and reproducible science in basic research laboratories. While the progress to date is undeniable, there remain underlying challenges that impact the ability to move forward as a cohesive community.

(1) Lack of shared understanding. While the richness of diversity in the field is undoubtedly beneficial, variance across scientific backgrounds means researchers may not always "speak the same scientific language." With the influx of new researchers, there may not always be a clear understanding of the history of the field and terminology; therefore specific definitions or contextual meaning of language and concepts may not be universal. Coming to a common understanding would reduce confusion and improve clarity in design, application, and reporting of the science.
(2) Issues in material integrity. Consistency in research requires consistency in materials. Issues that impact cell quality can impact experimental results, resulting in inconsistent data and invalid conclusions. For these reasons, it is essential to identify practical steps that each laboratory can take to help ensure the materials they are using are of good quality and not be impacted by factors that could render any data collected using them questionable.
(3) Irreproducibility. A lack of reproducibility both within and across laboratories impacts the pace of research progress and erodes confidence in scientific methods. Currently, reporting practices are not consistent, resulting in inadequate or confusing information regarding specific materials, unclear experimental design, and a potential misinterpretation of results. To address this concern, it is necessary to take steps to ensure transparency in both research materials and experimental methods. Accurate, clear, unambiguous reporting aids in the reproducibility within the laboratory and clarity within the literature, both of which are critical to good science.

To address these issues and promote rigor and reproducibility in stem cell research, the ISSCR established an international task force of scientists with expertise across pluripotent and tissue stem cells to identify best practice and to develop common standards for the use of human stem cells in basic research. The resulting recommendations are designed to be financially feasible and technically achievable for any laboratory. The recommendations focus primarily on stem cells that self-renew in culture, but when applied, these principles should promote best practice within the basic research laboratory and help to broadly promote research quality and improve clarity in reporting.

The *Standards for Human Stem Cell Use in Research* consist of a series of recommendations for scientists by scientists in the following areas.

- Basic stem cell line characterization and maintenance
- Identification, characterization, and monitoring of pluripotency
- Monitoring the genotype of cells over time
- Using *in vitro* stem cell-based models
- Reporting

In the following sections, some of the key recommendations in each of these areas are highlighted. For a full listing of recommendations and justification, please see the full *Standards for Human Stem Cell Use in Research* (ISSCR.org/standards-document).

Box 1. The process

OVERVIEW

In 2021, the ISSCR Board established a Standards Initiative to develop characterization standards for stem cells. The first phase of the project was focused on developing standards for human stem cell use in research. These recommendations, developed for scientists, students, and technicians performing basic and preclinical (laboratory) research, were aimed to be financially and technically achievable by any laboratory in the world with the goal of improving the rigor and reproducibility of stem cell research.

To develop this document, a steering committee of 11 experts in pluripotent and tissue stem cells from across the globe was assembled. This group oversaw the process and developed the scope of the recommendations, focusing on four key areas.

- Basic Cell Characterization and Maintenance
- The Characterization of the Undifferentiated State and Assessing Pluripotency
- Genomic Characterization
- Stem Cell-based Model Systems

Individual working groups, co-chaired by steering committee members, were assembled with subject matter experts to develop the specific recommendation within each section.

Process and timeline

- September 2021–June 2022: Working groups met via video conferences to develop the first draft of the standards.
- June 2022: First version of the standards document was presented at a satellite meeting of the ISSCR Annual Meeting in San Francisco, CA.
- June 2022–August 2022: Working groups revised recommendations following public feedback.
- August 2022–September 2022: The draft was sent for extensive and international peer review.
- September 2022: The full task force (the steering committee and working groups) met in person to review the comments and revise the draft.
- October–December 2022: The working groups continued revisions.
- December 2022: The ISSCR Board of Directors conditionally approved the standards.
- January 2023: The updated draft of the standards was presented in an open access webinar on ISSCR Digital.
- January–April 2023: Final revisions were made to the standards.
- April 2023: ISSCR Board of Directors approved final version of the standards.
- June 2023: The Standards for Human Stem Cell Use in Research was released.

KEY RECOMMENDATIONS

Basic cell line characterization and maintenance

The quality of science performed within the laboratory, and the quality of the results generated, is inherently linked to the quality of materials used. Ensuring that cell materials are consistent, well characterized, and genetically sound is the foundation of reproducibility within and between laboratories. How cultures are obtained, maintained, and characterized can have a significant impact on the ability to obtain reliable data and to publish meaningful results. The validity of data collected can be dramatically impacted by a decline in the quality and health of the cells due to infection with adventitious agents such as mycoplasma or by the progressive acquisition of mutations over time. Routine propagation within the laboratory also brings risk of cross-contamination and misidentification of cell lines, sometimes with disastrous consequences (Casadevall et al., 2014; Freedman et al., 2015; Horbach and Halffman, 2017; Souren et al., 2022). While concerns regarding misidentification, cross-contamination, sterility, and viral infection are not exclusive to stem cell research, they are certainly relevant, and when setting standards for quality within the laboratory for stem cell science, they cannot be ignored. A full listing of basic characterization assays recommended to ensure quality is included in Section 1 of the Standards document (ISSCR.org/standards-document); specific areas are highlighted here for emphasis.

Acquisition of materials

From the time that human stem cells or other donor-derived materials enter the laboratory, diligence must be undertaken to ensure materials were transferred with appropriate permissions and are used in alignment with donor consents (https://www.isscr.org/guidelines). Every individual must understand any restrictions for the use of materials and the reporting of data. As scientists, our responsibility to the donors that supplied the materials is paramount, and reliably adhering to their restrictions is necessary to preserve integrity in research. For this reason, materials should never be brought into the laboratory without knowledge of the rights and restrictions associated with them, generally contained within a material transfer agreement (MTA) or similar document. A copy of this transfer document (For a sample MTA or donor consent forms, please see the Guidelines for Stem Cell Research and Clinical Translation, https://www.isscr.org/guidelines) should be readily available within the laboratory, and all researchers should read and understand the conditions or restrictions associated with a given line prior to initiating any work.

Principles of cell line banking and preservation

Once materials are obtained, the first step in promoting reproducibility within the laboratory is establishing consistent, well-characterized banks that can be drawn from over time for all experimental use. These laboratory stocks, or master cell banks (MCBs), are key to experimental reproducibility within the laboratory. They help to ensure that all laboratory researchers start with the same, good quality, validated materials capable of delivering reliable data. While these banks need not be excessively large, they should contain sufficient vials to support the generation of working stocks for research use over the lifespan of the laboratory. Once characterized, it is advisable to store some portion of the MCB segregated from the primary bank, such as in a different tank, laboratory, or even offsite. These measures better protect stocks from catastrophic

failures or a natural disaster that would otherwise destroy this valuable resource.

Cell line authentication

Authentication of materials is critical in unambiguously identifying and consistently reporting materials. Misidentification or cross-contamination of materials can occur at all stages of work with cell lines, including during their derivation or isolation, culture, storage, or distribution, and its prevalence is well documented in the literature (American Type Culture Collection Standards Development Organization Workgroup ASN-0002, 2010; Freedman et al., 2015; Horbach and Halffman, 2017; Souren et al., 2022). The abundance of available stem cell lines and the emergence of accessible genetic modification technologies means that even the smallest of labs may have multiple cultures of genetically distinct yet morphologically indistinguishable lines growing in parallel, heightening the risk of undetected misidentification events. Properly authenticating the identity of cell materials at the point of entry into the laboratory, at reasonable time points throughout experimentation, and prior to publication ensures continuity of research materials throughout experimentation and enables appropriate attribution within publications. Failure to authenticate cell lines can result in erroneous conclusions, invalidate publications, and necessitate retraction. Foundationally, it is one of the easiest and most important steps that can be taken to safeguard technical and financial resources and protect research quality.

Assignment of a unique identifier

The lack of a standardized naming convention leads to confusion as common use names often change slightly between operators or laboratories, leading to ambiguity where cell lines are concerned. Additionally, over-similar names generated from different donors can lead to confusion about the provenance of data generated from those lines. Registration of cell lines can help to resolve these concerns. Cell line registration is distinct from biobanking and essential even if the lines are placed in such a biorepository. Registering a cell line with an international registry such as hPSCreg or Cellosaurus automatically generates a persistent and unique identifier, a practice that has already been demonstrated to reduce the risk of ambiguity and increase the integrity of FAIR principles (findable, accessible, interoperable, and reusable) and data management (Bandrowski et al., 2016; Kurtz et al., 2018; Luong et al., 2011), important even if the lines themselves have restricted availability. Registries link a cell line's unique identifier with provenance and characterization information creating a digital identity that can be referenced globally. It also helps to ensure that derivatives (such as genetically modified transgenic reporter lines, gene edited isogenic lines, or subclones that have distinct properties) are linked to the originating line. This process does not preclude the use of "in-house" names for newly generated lines, but it does de-risk the ambiguity inherent with similarly named lines. While there is currently no international registry designed for primary tissues, or cells that are propagated from those tissues (e.g., organoids), in cases where data are generated and placed in the public domain, there is a need for an unambiguous digital identity.

Pluripotency and the undifferentiated state

The precise definition of pluripotency has evolved over the years from early studies on embryonal carcinoma (EC) cells as the stem cells of germ cell tumors and teratocarcinomas, through isolation of embryonic stem cells from the blastocysts of early embryos, and to the reprogramming of somatic cells back to induced pluripotent stem cells (iPSCs). In each case, such pluripotent stem cells (PSCs) may have certain features reflecting their origins, but the one feature common to them all is the ability to differentiate and give rise to all the somatic cells of an adult organism. It is important to recognize that this provides for a functional definition of pluripotency, and therefore designating a cell line as pluripotent requires clear evidence that it can generate differentiated cells that correspond to derivatives of each of the three germ layers.

Traditionally, researchers have used the ability of human PSCs to produce teratomas containing tissues corresponding to all three germ layers in immunodeficient mice as a definitive test of pluripotency. However, the cost and animal welfare concerns are making this assay impracticable in many jurisdictions, while *in vitro* systems for monitoring differentiation are now very well developed with several studies showing that these can provide equivalent information about differentiation capacity (The International Stem Cell Initiative, 2018), thus obviating the need for the teratoma assay.

While the characterization of a cell line as pluripotent requires functional evidence of its capacity to differentiate, such assays are not always practicable or necessary for monitoring cell lines that have already been proved to be pluripotent or when large panels of new human iPS cell lines are derived using established methods. In these situations, the use of markers of the undifferentiated cells is informative. However, the expression of such markers must be properly interpreted. While they are typically characteristic of undifferentiated PSCs, their expression does not prove pluripotency. Many of the markers commonly used can also be expressed by various differentiated cell types and cancer cells, which are clearly not pluripotent, and some have been reported lost from cells that retain pluripotency. Further, genetic and epigenetic variations may lead to a pluripotent cell losing some or all of its capacity to differentiate, a phenomenon most obviously seen in germ cell tumors that are composed entirely of EC cells

without evidence of differentiation; these are known as "nullipotent" stem cells that, nevertheless, express all the common markers of PSCs. Consequently, although some of the markers may function and be required for pluripotency, their expression is not proof of a pluripotent phenotype. They should not be described as "pluripotent markers," an incorrect usage that has crept into the literature: they are only markers of undifferentiated cells and then only when analyzed in an appropriate context. The undifferentiated state and pluripotency are distinct properties, but both are needed to be a pluripotent stem cell. In circumstances where it is impracticable or deemed unnecessary to fully characterize a stem cell line by differentiation assays, it may be described as putatively or presumptively pluripotent if it expresses markers characteristic of PSCs and it has been derived by an established method expected to generate PSCs.

Genomic characterization

Stem cells have been hailed as powerful models of development and disease due to their ability to propagate *in vitro* without the need for transformation or immortalization. Capturing the donor cell genotype, whether "wild type" or disease specific, has been a key advantage of stem cell-based models of development or disease compared to other cell types that cannot propagate in culture for long periods of time. Nonetheless, like any cells in culture, stem cells are susceptible to the acquisition of genetic changes, ranging from single nucleotide variants to large karyotypic abnormalities (Andrews et al., 2022; Halliwell et al., 2020). PSCs are particularly vulnerable to specific recurrent genetic changes (Andrews et al., 2022; Draper et al., 2004; The International Stem Cell Initiative, 2011) that may affect behavior of stem cells and differentiated derivatives and thereby impact the results of experimental use. For this reason, it is important to monitor the genetic composition of a cell culture over time to help ensure the validity of any data collected.

While characterizing the genome at the MCB level or at the initiation of experiments is essential, cell cultures should be monitored, ideally over the time span of experimental use. This becomes more critical as the length of culture (number of populations doublings) increases, particularly because experience shows that variants can become detectable and take over culture very rapidly, sometimes within 4 or 5 passages (Olariu et al., 2010; The International Stem Cell Initiative, 2011). If the experimental time course exceeds 10 passages, monitoring during the experimental period is recommended. Assessing the genome after a major manipulation event or other bottleneck, e.g., cloning events or gene editing, is also recommended, as the significant selection associated with these events may inadvertently also result in the selection of cell lines that have acquired genomic changes. Finally, to ensure that culture materials maintain the expected genome throughout the experimental process, checking the genetic composition at the end of experiments is ideal.

The manner in which the genome is queried is at the discretion of the researcher, as different approaches may be more relevant based on context (see Section 3.0 and Appendix 5 of the Standards document). It is important to recognize that each method has its advantages and shortcomings, and it is essential that details of the assessment are reported to allow other scientists a precise understanding of the methods used to aid in their evaluation of the data as presented (see "reporting" section, below). It is necessary to understand that an unexpected finding of a genetic variant does not necessarily compromise the results or ability to publish, as long as it is fully described. In fact, quite the opposite, it is only through publication of these findings that we will be able to understand and evaluate whether they have any effects.

Model systems

Organoids and organ-on-chip technologies (also referred to as microphysiological systems or MPSs) are rapidly advancing as complex models that represent different aspects of human organs and tissues, with promise to reproduce human physiology such that they are predictive of interventions in the human body. They often contain multiple cell types derived from stem cells, grown in 2D or 3D formats, in some cases including microfluidic flow to mimic, for example, blood circulation. Many models are already physiologically relevant and reliable, albeit simplified, tissue representations.

Crucial to ensuring that these human model systems are widely adopted by academia and industry is confirming their reproducibility between developers and end users, as well as individual laboratories and operators. Because this is a rapidly evolving field, with new and ever more complicated methods being developed, it is essential that these model systems are fully described in publications in which they are used, and that controls and quality metrics are considered when planning and executing experiments.

An important consideration in generating any model is the quality of its components and appropriate metrics to assess the quality of the model itself. Components may include stem cells and derivatives themselves, culture reagents and vessels, and in the case of MPS, materials, dimensions, design, and for example where relevant, flow rates in microfluidic devices. Thus, as with basic characterization of pluripotent stem cell lines, the starting cell type, whether it be pluripotent or tissue-derived stem cells, should be fully assessed and described in resultant

publications and registries. This includes not only donor details where possible (genotype, clinical characteristics, donor background, etc.) but also tissue of origin with as much detail as possible regarding specific anatomical site of origin. Because of aging, acquisition of mutations, and environmental insults, tissue heterogeneity can impact the type of cells isolated, especially an issue with regard to tumor cell isolation.

In addition to the model itself, any assays that report the behavior of cells in the model should be fully characterized and benchmarked to native tissue. Since such assays serve to both validate the model system itself and provide a readout of physiology and disease phenotype, it is vital that such assays are described in full. Only if measures are fully validated will comparisons between experimental groups, for example between diseased states or after interventions, be meaningful and interpretable.

There are many variables that can affect the reproducibility of model systems, including but not limited to the stem cell input (e.g., sex, ethnic background, derivation method, growth and differentiation protocols) and the system itself (e.g., oxygen tension). The impact of these variables should be tested by performing replication studies across cell lines and users to ascertain the validity of the model and its readouts. In addition, all experiments must be properly powered and sample sizes chosen such that robust conclusions can be made on the outcome. In studying disease states, it is also important to include appropriate and sufficient non-diseased samples to establish base lines for controls. Possible batch-to-batch, clone-to-clone, and line-to-line variability also have to be considered. When including healthy control lines, such as for baseline measurements or generating allelic series on isogenic backgrounds, it is important to consider how "healthy" has been defined: has SNP analysis for polymorphisms been carried out for disease traits or predisposition? Was donor age considered, particularly with regard to diseases that manifest later in life (for example, unaffected family members)?

Ensuring reproducibility involves not only careful replication within a laboratory, but also ensuring that sufficient details are provided to enable others to perform the same experiments successfully. This includes reporting details of the starting cellular material, culture conditions, and assays. Where devices are used for the model, preference is for commercial (validated) systems that can be easily obtained by other users, or when made in-house, recognized manufacturing techniques should be used where possible. Where not possible, sufficient details of the manufacture of the device and its benchmarking should be included, as described in the reporting section, below.

It is important to know to what extent a model system captures human (patho)physiology. It is unlikely at the present time that any model recapitulates all features of human tissues, but the model may be fit for purpose if it reflects those relevant for a particular application. Where possible, models should exhibit established native cellular morphological and functional traits. Morphological assessment should confirm the shape, structure, form, and/or size of target cells, with alterations in the morphology of cells, potentially indicative of changed cellular function, such as during stem cell differentiation, tumor formation, and cell-pathogen interactions. Cell functionality should similarly recapitulate *in vivo* cellular processes underpinning the fundamental activities (intra- and intercellular) and role of a target cell or tissue, such as metabolism, proliferation, respiration, diffusion, osmosis, active transport, ion flux, motility, and electrophysiology. Thus, the combination of morphology and function evaluation should be used to assess the validity of the model system.

Ideally, phenotypes identified in a model should be relevant to the human disease, and efforts should be made to corroborate cell and molecular features with those in patients with the disease, through comparison with postmortem tissue, relevant patient cells or tissues, or published data. Assessment of cell-specific markers can be performed by common immunophenotyping methods or transcript analysis. Quality control assessment should be performed for any assays on the model system to determine the specificity of a given phenotype and avoid nonspecific effects due to general cell health. Finally, disease models with genetic perturbations or derived from patients with a genetic condition should be checked and confirmed to carry the relevant genetic mutation and any off targets or other mutations explicitly disclosed.

Reporting

The accurate and detailed reporting of experiments is critical to the interpretation of the results and the reproducibility of the work. While a seemingly obvious recommendation, the inability to replicate preclinical research has been estimated to cost 28 billion US dollars annually (Freedman et al., 2015). Many fields have addressed this issue through subject-specific reporting standards e.g., materials design analysis reporting (MDAR) checklist (https://osf.io/bj3mu) or journal-specific standards, e.g., https://journals.biologists.com/DocumentLibrary/DEV/Checklist.pdf. International initiatives have formed to house such standards to facilitate good research practices: https://www.equator-network.org/. To improve the reproducibility of preclinical research using human stem cells, the ISSCR has developed a "checklist": Reporting Practices for Publishing Results with Human Pluripotent and Tissue Stem Cells (see https://www.isscr.org/standards-document and SnapShot, this issue).

The checklist is at the core of the standards as it is intended to provide scientists, reviewers, and editors with a

template for the essential information that should be included in any publication with human stem cells. It draws from the recommendations in the document to establish nine reporting categories, most of which are unique to human stem cells, although some relate to practices commonly shared with research more widely, such as basic culture principles.

Part and parcel of accurate reporting is the attention to details and the transparency of protocols and references. Material sections of manuscripts are increasingly relegated to supplemental materials and references to methods are found in the citation of a citation, which itself may not be fully transparent in the methods. The National Academy of Sciences Engineering and Medicine's report on this topic calls for the inclusion of "a clear, specific, and complete description of how the reported results were reached. Reports should include details appropriate for the type of research, such as a clear description of all methods, instruments, materials, procedures, measurements, and other variables involved in the study; a clear description of the analysis of data and decisions for exclusion of some data or inclusion of other; and discussion of the uncertainty of the measurements, results, and inferences" (https://nap.nationalacademies.org/catalog/25303/reproducibility-and-replicability-in-science).

Ultimately, like other checklists used by journals, this is a tool for the stem cell community to improve the reliability and reproducibility of reported research.

IMPLEMENTATION AND CONCLUSIONS

The primary goal of drafting the standards was to create a set of practical recommendations that establish the minimum characterization and reporting criteria for basic research using human stem cells. Although standards have been previously proposed for repositories, distribution centers, and clinical applications (Hao et al., 2020a; 2020b; International Stem Cell Banking Initiative, 2009; Stacey et al., 2013; Zhang et al., 2022), these standards were not focused on the issues of laboratory research with human pluripotent and tissue stem cells. There was also an aspirational component to the development of laboratory standards, a natural consequence of the need to shift or improve current standard practices, some of which may be insufficient to ensure the rigor and reproducibility of research (Anderson et al., 2021). The challenge to the committee was to establish a balance so that these standards are practicable enough that they can be implemented broadly, and that the community recognizes their value (aspirational) and adopts them for the common good of the field.

Some of the recommended practices are already being implemented, although not uniformly. It is becoming more common for funders and journals to require the authentication of cell lines in grant applications and publications. Despite the now well-known example of many tumor cell lines being contaminated by HeLa cells (Horbach and Halffman, 2017), in a recent analysis by the International Journal of Cancer, at least 5% of papers used misidentified human cell lines (Souren et al., 2022). This issue is not unique to tumor-derived cell lines as work from WiCell shows a similar trend in PSC lines submitted for banking (https://www.wicell.org/media.acux/c1efdf25-89b1-4df5-8508-9d74687130ef).

The registration of new PSC lines is also becoming increasingly required by funders and journals. For example, the European Commission requires that any PSC lines used in EU-funded research be registered in hPSCreg, to confirm appropriate ethical provenance. This can provide researchers confidence that a particular line was properly consented for their jurisdiction, donor restrictions and requirements are being adhered to within the laboratory, and any requirements of funding bodies, local governance, and/or national jurisdictions are being met. Laboratories working with tissue stem cells and their derivatives are also encouraged to adopt nomenclature rules that allow digital traceability (Kurtz et al., 2018).

For these standards to be effective in elevating the quality of research, they must be adopted by the scientific community. While overall these recommendations were designed to be technically and financially practicable for any laboratory, they are not without cost. However, the costs associated with the recommended characterization strategy are minimal when compared to the overall costs of research and may ultimately save research dollars by reducing the need for repeating experiments and by helping to ensure the validity of results. Paramount to the adoption is the recognition that their value to a laboratory and the field is worth the relatively minimal investment. From a funding perspective, grantees should include associated costs in budgets as a necessary part of research activities. Further, funders can and should require proof of basic characterization and provide the financial resources necessary to properly conduct these assays and better ensure the validity of results, particularly where the use of public funds is concerned.

The acknowledgment of these standards by journals will also encourage adoption. Many journals already have checklists focused on improving reporting, such as the MDAR, https://osf.io/bj3mu, or a proprietary checklist, https://journals.biologists.com/DocumentLibrary/DEV/Checklist.pdf. Similarly, a checklist for stem cell research has been developed as part of this initiative. While there is no expectation that journals police its enforcement, it can be a very valuable tool for editors, reviewers, and authors to evaluate manuscripts submitted for publication.

Finally, there is an ongoing educational requirement to raise awareness and acceptance of these standards. This

document, while building on the work of other groups such as the International Stem Cell Initiative and the International Stem Cell Banking Forum (Stacey and Healy, 2021; The International Stem Cell Initiative, 2018), is the first of its kind to focus on best practices for research laboratories using human stem cells. Continued outreach and updating will be a gradual process that is ultimately dependent upon the community. The obligation of conducting rigorous and reproducible science rests with the collective efforts of the scientific community (scientists, funding agencies, journal editors, and others). We believe these standards, when fully adopted, will set researchers up for success, improve the quality of basic preclinical research, and ultimately strengthen the pipeline of therapies for patients.

ACKNOWLEDGMENTS

The ISSCR and the Task Force would like to thank the many reviewers of the document who took the time to provide valuable feedback. We would also like to thank Eric Anthony for his work in establishing this initiative.

CONFLICT OF INTERESTS

This work was supported by the Burroughs Wellcome Fund, the Doris Duke Charitable Foundation, and the Simons Foundation Autism Research Initiative. Additional support to authors provided by the Arto Hardy Family (to J.M.C.); The Novo Nordisk Foundation Center for Stem Cell Medicine, which is supported by the Novo Nordisk Foundation (NNF21CC0073729 to K.B.J. and C.L.M.); the Medical Research Council Professor Award (G1100526/2 to A.G.S.); the Medical Research Council (MR/X000028/1 and MR/X007979/1 to I.B.); the UK Regenerative Medicine Platform (MR/R015724/1 to I.B.); The Francis Crick Institute, which receives its funding from Cancer Research UK (CC0199 to L.E.H.); the UK Medical Research Council (CC0199 to L.E.H.); the Wellcome Trust (CC0199 to L.E.H.); the Medical Research Council (MC_UP_1201/9) and the European Research Council (ERC STG 757710) (M.A.L.); the Korean Fund for Regenerative Medicine (funded by Ministry of Science and ICT) and Ministry of Health and Welfare, Republic of Korea (RS-2022-00070674, to J.S.); and the National Research Foundation of Korea grant funded by the Korean government (MSIT) (no. 2020M3A9E4037903 to J.S.). For the purpose of Open Access, the author has applied a CC BY public copyright licence to any Author Accepted Manuscript version arising from this submission (L.E.H.).

P.A. receives royalty income from the Wistar Institute, Philadelphia, PA, derived from the sale of the TRA series of monoclonal antibodies under license from Wistar, specifically, TRA-1-60, TRA-1-81, TRA-2-49, TRA-2-54, and TRA-1-85 and is a member of the scientific advisory board of TreeFrog Therapeutics. I.B. is a member of the scientific advisory board of WiCell. N.B. is CSO of NewStem Ltd. M.H. is co-inventor of several patents related to organoid technology. M.A.L. is an inventor on several patents related to cerebral organoids, is co-founder and member of the scientific advisory board of a:head bio, and is a member of the scientific advisory board of the Roche Institute for Translational Bioengineering. T.L. is a co-inventor and receives a share of royalties on various hPSC media- and culture-related patents currently owned and licensed by the Wisconsin Alumni Research Foundation (WARF). C.L.M. is an associate editor *Stem Cell Reports*. M.F.P. is the editor-in-chief of *Stem Cell Reports*, is a member of the ISSCR board of directors and the International Stem Cell Initiative, and receives compensation for services as editor-in-chief of the journal. J.S. is the founder and CEO of iPS Bio, Inc. Y.S. has the following additional affiliations: Graduate School of Pharmaceutical Sciences, Nagoya City University; Graduate School of Pharmaceutical Sciences, Osaka University; Graduate School of Pharmaceutical Sciences, the University of Tokyo; Faculty of Pharmaceutical Sciences, Tohoku University; and Life Science Technology Project, Kanagawa Institute of Industrial Science and Technology.

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