Journal of the Society for Clinical Data Management

Aydin B, Kiely É, Ohmann C. Feasibility Assessment of Using CDISC Data Standards for in *vivo* and in *silico* Medical Device Trials. *Journal of the Society for Clinical Data Management*. 2023; 3(3): 3, pp. 1–7. DOI: https://doi.org/10.47912/jscdm.230

OPINION PAPER

Feasibility Assessment of Using CDISC Data Standards for *in vivo* and *in silico* Medical Device Trials

Burç Aydin*, Éanna Kiely† and Christian Ohmann*

This paper discusses the current applicable regulatory framework and feasibility of using CDISC data standards for *in vivo* and *in silico* (ie, research conducted by means of computer modeling and simulation) medical device clinical trials with an objective of adequately structuring clinical data generated through *in vivo* and *in silico* medical device trials using CDISC standards. The covered topics are global regulatory data requirements, guidance documents, application examples of CDISC standards for medical device trials, specific data conformity and verification/validation steps expected to be required for *in silico* device trials, and mapping scenarios of physics-based or physiological modeling data generated by *in silico* studies within the CDISC standards. A practical project approach is presented to address the opportunities, challenges, and multidisciplinary solutions for complementary *in vivo* and *in silico* clinical development of transcatheter aortic valve replacement devices with use of CDISC data standards. Continous discussion within the regulatory and CDISC standards frameworks, supported by computer modeling outputs and reuse of available clinical data generated by *in vivo* trials, is needed for successful use of CDISC standards in interdependent *in vivo* and *in silico* medical device trials.

Keywords: Medical device; clinical trial; CDISC; *in silico*; transcatheter aortic valve replacement

Introduction

It is the reliable and standardized clinical data behind a medicinal product that makes the evaluation and approval of a medicine or a medical device possible by the regulatory authorities. This regulatory procedure is a cornerstone to ensure the clinical safety and efficacy of medicinal products ultimately marketed for use by the medical community and by patients. Regulatory approval requirements primarily define which data elements should be collected and how they should be presented and analyzed. Within the context of this paper, the definition of *in silico* clinical trial is taken from the Avicenna Alliance as "*the use of individualised computer simulation in the development or regulatory evaluation of a medicinal product, medical device, or medical intervention*".[1]

Regulatory data requirements for medical device clinical trials

In vivo medical device trials

Medical device clinical trials in European Union (EU) are currently regulated by Regulation 2017/745 (also known as the 'EU Medical Devices Regulation' [EU MDR]) and are termed as 'clinical investigations' (ie, any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device). In EU MDR, 'clinical data' means information concerning safety or performance that is generated from the use of a device. Intracardiac devices are classified as Class III medical devices and their review demands (with certain exceptions) performing clinical investigations.[2] EU MDR provides the requirements for medical device clinical investigations under Annex XV Clinical Investigations, which are generally like the ones required by EU regulations for pharmaceutical randomized clinical trials. While EU MDR is the overarching European regulation for medical device clinical trials, regulatory overview of medical devices is managed by accredited notified bodies on a member state level with the scientific opinion sought from the European Medicines Agency (EMA) in case (a) medicines are used in combination with a medical device, (b) medical devices contain an ancillary medicinal substance, (c) a medical device is a companion diagnostic test, (d) medical devices are made of substances that are systemically absorbed, or (e) a medical device is categorized as a high-risk medical device.[3]

Currently, there is no Europe-wide mandate for any clinical data standard to be applied for the regulatory overview of a pharmaceutical or a medical device. European initiatives, however, exist at EMA and Heads of Medicines Agencies (HMA) levels to promote the use of standards to facilitate interoperability of data and possible

* European Clinical Research Infrastructure Network (ECRIN), Paris, France

† ClinBuild Clinical Data Services Limited, Cork, Ireland

Corresponding author: Christian Ohmann (christianohmann@outlook.de)

adoption of relevant Clinical Data Interchange Standards Consortium (CDISC) standards for collecting raw data in clinical studies.[4,5]

The medical device data requirements of the United States Food and Drug Administration (FDA) are managed by the Center for Devices and Radiological Health (CDRH). CDRH encourages manufacturers to use data and terminology standards in pre-market submissions and post-market reports for medical devices yet does not require the use of specific clinical data standards. Medical device clinical trial data are accepted by the CDRH in any format, including CDISC standards.[6] However, CDRH is expected to adopt an approach in the future for data standardization in medical device clinical trial data submissions and early adoption of clinical data standards by medical device developers could support process optimization, successful data submission, and timely regulatory review.[7–11] Of note on this possible change in the FDA policy for medical device clinical trial data submissions, the FDA Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) already require pharmaceutical clinical trials data to be presented in CDISC standards, along with controlled terminologies.[12]

In silico medical device trials

While 75 EU-funded research projects concerning *in silico* trials are ongoing in Europe, there is not yet a European framework or strategy for implementing *in silico* medical device trials.[13] In fact, a few of these projects are expected to support the European framework for *in silico* trials.[14,15] This paper itself is a similarly targeted assessment of the current and evolving framework.

The FDA has recently published draft guidance for the assessment of the credibility of *in silico* approach in medical device regulatory submissions.[16] While this guidance does not directly address any clinical data standard, it does provide an important framework for credibility assessment of different *in silico* clinical trial approaches, from defining the question of interest to generating the adequacy assessment and reporting, following the document 'Assessing Credibility of Computational Modeling through Verification and Validation: Application to Medical Devices', prepared by the American Society of Mechanical Engineers.[17] The FDA presents different evidence categories for *in silico* clinical data generation; two categories are relevant for medical device trials: Category 5 – Evidence generated using *in vivo* conditions to support the current context of use (for individual-level data and for comparison between model predictions and a clinical dataset) and Category 8 – Population-based evidence (no comparison is made on a patient-level basis). Relevance of each of these clinical evidence categories is considered within the verification and validation needs.[16]A reporting guidance document by the FDA is also available for reporting modeling studies in medical device submissions.[18]

As a section summary, data standards are not currently mandated for medical device clinical trial submissions in the EU or the United States yet regulators might be expected to adopt or to broaden the scope of clinical data standards. Inclusion of *in silico* medical device trials data into regulatory submission files also raises issues of data conformity and verification/validation with the corresponding *in vivo* medical device trials data. Use of clinical data standards for medical device trials has been presented by medical device developers in recent literature.[7–11] Interestingly, the FDA itself is currently partnered with the private sector to produce the first simulated human heart, the 'Living Heart'. Objectives of this project include *in silico* testing of new medical devices.[19] While other data standards could also be employed for medical device trials, CDISC standards represent the most advanced set availablefrom a regulatory point of view. The next section valuates the potential use of CDISC standards for the management of *in vivo* and *in silico* medical device trials data.

CDISC standards and medical device trials

CDISC is a standards development organization that manages data standards and controlled terminology for clinical research data management. These standards make standardized clinical data collection, organization, analysis, and review possible.[20] CDISC standards also include a tabulation standard for animal studies (Standard for Exchange of Nonclinical Data, [SEND]), study planning, data exchange, and descriptive dataset metadata (Define-XML). CDISC standards employ different domains for clinical trial data, such as medical history, adverse events, laboratory test results, and medical device properties. Domains are further grouped into classes, with most belonging to the following three: General Observation Classes of Interventions (Concomitant Medication and Exposure), Events (Adverse Events and Medical History) and Findings (Laboratory and Questionnaires). Domains and classes have associated variables, controlled terminologies, and business rules.[20] The structured model can support clinical researchers in becoming proficient with the standard. CDISC has implementation guides already in place for the SDTM and ADaM standards, for use in medical device clinical trials. This guidance covers seven medical device-related domains (for device identification, fixed and variable device properties, device tracking, and device-subject exposure), and complements other foundational CDISC standards.[21]

Since 17 December 2016, the FDA, CDER, and CBER require pharmaceutical submission data and metadata to be structured using CDISC standards, namely Study Data Tabulation Model (SDTM), Analysis Data Model (ADaM), SEND, and Define-XML.[22] The Japanese Pharmaceuticals and Medical Devices Agency requires CDISC standards for both pharmaceutical and medical devices submissions.[23] The Chinese National Medical Products Administration has made a recommendation to report data in CDISC standards.[24] While CDISC standards are mostly used by the pharmaceutical industry for regulatory submission purposes and have only been partially implemented in the academic world, CDISC now collaborates with Research Electronic Data Capture (REDCap) and OpenClinica initiatives to promote the adoption and use of CDISC and Clinical Data Acquisition Standards Harmonization

(CDASH) standards in academic clinical research as well.[25,26] An academic research community has also expressed interest in using CDISC standards for investigator-led clinical research without a regulatory mandate.[27]

The FDA has published guidance for industry on specifics of standardized study data and controlled terminologies for pharmaceutical submissions.[12,28] There are two major needs that are fulfilled by these technical requirements: (1) To facilitate and expedite the regulatory review process of the clinical data (using a study data standardization plan, data standards, and controlled terminologies); and (2) to conduct comparative analyses across studies. An additional benefit of data sharing and reuse is facilitated by applying the same data standards across different research groups.[29,30] For simulation and modeling purposes, data sharing is more than an ethical imperative: validation and improvement of the models require patient- and/or population-level clinical data over time from the studies within the therapeutic area, and any shared clinical data should be made interoperable to serve the purpose.[1,31] It is reasonable to expect that these regulatory and data sharing benefits would similarly apply to clinical data generated within medical device trials if clinical data standards are adopted for regulatory submission and data sharing procedures.

Limitations of CDISC Standards

While comprehensive, CDISC standards have some general and device-related limitations. As an example, the FDA states that ADaM structures do not support simultaneous analysis of multiple dependent variables or correlation analysis across several response variables. Conversion of legacy study data (data in a non-standardized format) to SDTM and ADaM formats could also raise traceability issues and may require extensive work on the data to conform to regulatory standards, depending on the complexity and available documentation of the source data.[22] Prospective application of CDISC standards is therefore a more appropriate procedure. As CDISC standards are not binding for medical device manufacturers, clear implementation of the standards has not been possible so far. Example implementation strategies and associated problems to be considered in advance have been shared in the literature.[7–11] Finally, CDISC standards do not address specific data management requirements for *in silico* trials; these specific aspects are further elaborated below.

Considerations for physics-based or physiological modeling data

CDISC standards have been developed for real-world clinical data, meaning that they help organize biologically or operationally obtained data. In *in silico* trials, however, data will be generated solely through simulation and modeling. While clinical components of these data could be managed using CDISC standards (assuming that data will be generated as one record per subject per parameter per timepoint), the physics-based or physiological data generated within a medical device simulation model could require a different structure and/or standard. An FDA guidance document provides a general outline for the reporting requirements of computational medical device modeling studies, without naming particular data submission requirements.[18] If new medical device standards were to be developed to support the modeling and submission of underlying physics-based or physiological data to regulatory bodies, a cross-functional team including CDISC experts could support on this task. The data could be mapped to CDISC SDTM and ADaM domains and datasets, and have additional metadata described in the Define-XML as needed. This approach could also help to map relatedness and causality links between medical device physics-based or physiological data and clinical events, findings, and interventions datasets.

Implementation issues and scenarios

From a technical perspective, implementing CDISC standards for the clinical data of a medical device trial should take the same approach and involve the same considerations whether the trial is *in vivo* or *in silico*. The key decision point is the anticipated purpose of conducting an *in silico* device trial: If the purpose is to validate the *in silico* trial model for supporting the regulatory submission of a new device, the reviewers will require a twin set of identical *in vivo* and *in silico* trials for validation purposes, depending on the novelty and the associated risks of a the new medical device. This assumption demands an *in silico* trial generating patient-level data and the same CDISC standards and considerations should apply for the *in vivo* as well as the *in silico* trial. The regulators will also require the same data approach from the Case Report Form (CRF) variables and format up to the analysis results and metadata to verify model validation and conduct patient-level comparative analyses. It will be ideal, therefore, to prospectively implement the *in silico* trial strategy into an actual and *in vivo* clinical development program of a medical device.

If the purpose of the *in silico* approach is to supplement the assumptions and findings of an *in vivo* trial (eg, extrapolation for patient populations with different baseline characteristics), an approach should be taken for generating population-level model and data. An *in silico* trial with population-level findings would be of limited use for regulatory purposes as the cross-comparison of *in silico* and *in vivo* clinical data would be restricted to the level of aggregated data.

In silico trials are expected to be accompanied by additional animal, human and/or cadaver studies within a regulatory submission package of a medical device (whether for model validation purposes or for parameters that could not be addressed by the *in silico* trial, or both).[32] As discussed above, CDISC standards (along with Controlled Terminologies) provide an interoperable and harmonized data framework for all of these study types. The FDA study data technical conformance guide provides a folder structure to organize clinical and non-clinical datasets from multiple studies within the same submission package.[28,33] Care should be taken to harmonize any custom term or domain created by the sponsor (if required) across the submission dossier.

Another potential challenge in *in silico* medical device trials would involve traceability and causality links with the underlying physics model.[34] For example, how would an *in silico* transcatheter aortic valve implantation (TAVI) medical device trial simulate the adverse event of procedural bleeding in a single patient? Would the adverse event have causal (ie, mathematical) connection to the underlying physics data or would it appear solely stochastically through statistical probability analysis? In any case, the *in silico* trial should clearly define individual elements of engineering and modeling outcomes and their relation to the clinical outcomes. CDISC standards (SDTM, ADaM, and Define-XML) could be employed to identify and map the metadata of these outcomes, just as they are used to identify the clinical ones. The Define-XML specification document provides methodology and examples, including use of supplemental files, for linking computational methods, algorithms, and code to a clinical variable.[35]

Full technical details of successful implementation of CDISC standards for TAVI medical device trials is beyond the scope of this paper and readers are advised to consult the references of previous publications.[7–11] Of special interest for TAVI trials, the Edwards Lifesciences group reported their successful implementation of CDISC standards for their TAVI trials and their involvement with the CDISC authors to work on CDISC implementation and the development of user guides[9] The last, but highly crucial, step would include direct and trial-/device-specific discussions with the regulators for the data requirements. The FDA emphasizes this point and advises that the discussions should be initiated at an early development phase.[28] EU authorities similarly offer expert panel consultation for all class III devices, and prior to the clinical investigation, the manufacturer may consult an expert panel with the aim of reviewing the manufacturer's intended clinical development strategy and proposals for clinical investigation.[2,3]

Discussion

This paper assessed the feasibility of using CDISC data standards for *in vivo* and *in silico* medical device trials from a regulatory requirements and data management perspective. TAVI medical device trials were taken as a use case for practical implications. For regulatory evaluation and approval procedures, clinical data submission requirements should be considered to be the same for *in vivo* and *in silico* medical device clinical trials for data validation, traceability, and interoperability purposes. These trials should be expected to be complementary to each other, possibly along with supplemental non-clinical or observational data, within the same submission package. While there are no binding regulatory frameworks in the United States and EU for clinical data submission of medical device clinical trials, the available FDA framework of CDISC standards and controlled terminologies for pharmaceuticals offers a viable and feasible option. CDISC standards and additional controlled terminologies should be considered as the most advanced clinical and non-clinical data tools from a regulatory and clinical development perspective for practical adoption into the data management structure of medical device trials. Use of CDISC standards for medical device clinical development could facilitate and expedite the regulatory review process, cross-study comparative analyses, clinical data sharing and use, and model validation and improvement. While this reasoning for CDISC standards is supported by available guidance documents and successful real-world TAVI medical device approval cases made available in the literature, adoption of CDISC standards for medical device trials is still an active research area and requires prospective consideration and built-in investment in a clinical data management program, ideally starting from the CRF development stage. Plans for providing standardized clinical data should be discussed with regulators at an early stage of a medical device clinical development program.

When compared to *in vivo* medical device trials, an *in silico* approach comes with specific opportunities and challenges for implementing CDISC standards. If validation of an *in silico* trial model is desired with the use of patient-level data along with *in vivo* clinical studies of a medical device, *in vivo* and *in silico* clinical development activities and elements, including data format and standards, should be prospectively harmonized within the same development program before any data collection begins. This approach should avoid traceability and interoperability problems. If the purpose of an *in silico* trial model is limited to supplementing an *in vivo* medical device trial, a population-level data generation model could be built. In this case, the statistical analysis plan and structure of datasets generated by the *in silico* approach require careful consideration to provide reliable supplementary outcomes while conforming with regulatory statistical principles. In both cases, an early discussion with regulators should again help medical device developers to design and implement an optimal *in silico* model within the clinical development activities of a medical device.

A unique challenge for *in silico* medical device trials will be the formatting and mapping of physics-based or physiological data generated by a medical device computational model. As medical device modeling studies mature, new data structures and standards could be required to present datasets of computational outputs linked with medical device trials to support regulatory submissions. CDISC metadata standards could be used for mapping model-generated data to CDISC, SDTM, and ADaM domains. Addressing this challenge will require the multidisciplinary work of subject matter experts in computational modeling, clinical research, and data management. CDISC community and research activities are ongoing for mitigation. Specifically, an ongoing European project called 'In-Silico testing and validation of Cardiovascular IMplantable devices (SIMCor)' is aiming to establish a computational platform for *in silico* development, validation, and regulatory approval of cardiovascular implantable devices.[36] One of the project's objectives to mitigate the challenges stated above is to contact medical device manufacturers

that are sponsoring TAVI clinical trials for which the possibility of anonymized patient-level data sharing was announced on clinical trial registries, and to request the reuse of trial metadata and anonymized patient-level data. If made available, the trial metadata will be used to build up template CRFs, SDTM, ADaM, and Define-XML files for pilot implementation of mapping between computational model-generated data and clinical outcomes, while anonymized patient-level data will be used to support computational model development, verification, and validation.[37] Additionally, the SIMCor project involves scientific and regulatory advisory boards to facilitate the formation of the desired multidisciplinary forum for advancement of *in silico* medical device trials methodology.

This feasibility assessment concludes that CDISC standards are an ideal foundation to start addressing harmonized clinical data management of *in vivo* and *in silico* medical device trials for regulatory approval procedures. This ssessment is limited to the scope of a single-use case of TAVI medical device trials;similar steps should be taken for different types of medical devices for which clinical trials for regulatory approval are required and an *in silico* clinical trial approach could provide added benefit. For specific disease areas, CDISC Therapeutic Area User Guides can support *in silico* medical device trials design and evaluation teams with disease-specific examples and guidance for CDISC standards implementation.[38] While the learnings from *in vivo* medical device trials using CDISC standards are relevant for *in silico* trials, continous regulatory discussion, multidisciplinary teamwork, and reuse of available trial metadata and clinical data are needed to overcome specific challenges and to successfully implement CDISC standards for complementary *in vivo* and *in silico* medical device trials.

Acknowledgements

The authors wish to thank Steve Canham (ECRIN) for his input.

Funding Information

This paper was prepared within the 'In-Silico testing and validation of Cardiovascular IMplantable devices (SIMCor)' project activities. This project received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101017578.

Competing Interests

BA is currently an employee of Aixial Group on behalf of Sanofi. This paper is not related in any way with BA's current role or employer. ÉK is an authorized CDISC Instructor and has performed consultancy work for CDISC. CO has no competing interests to declare.

Author Contributions

BA provided the first and the updated version of the manuscript. ÉK and CO reviewed the manuscripts and gave feedback to BA. ÉK provided input as CDISC specialist and CO as a previous head of a clinical trial unit. BA, ÉK and CO have been involved in the SIMCor project.

References

1. **Viceconti M, Henney A, Morley-Fletcher E.** in silico Clinical Trials: How Computer Simulation Will Transform the Biomedical Industry. January 2016. DOI: https://doi.org/10.18203/2349-3259.ijct20161408
2. **European Parliament and European Council**. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. *Official Journal of the European Union* 2017, 5.5.2017; L 117/1.
3. **European Medicines Agency.** Human regulatory – medical devices. Accessed February 21, 2022. https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices
4. **Heads of Medicines Agencies and European Medicines Agency.** HMA-EMA Joint Big Data Taskforce – summary report. February 13, 2019. EMA/105321/2019. Accessed February 22, 2022. https://www.ema.europa.eu/en/documents/minutes/hma/ema-joint-task-force-big-data-summary-report_en.pdf
5. **Heads of Medicines Agencies and European Medicines Agency.** European Medicines Regulatory Network Data Standardisation Strategy. December 16, 2021. EMA/447502/2021. Accessed February 22, 2022. https://www.ema.europa.eu/en/documents/other/european-medicines-regulatory-network-data-standardisation-strategy_en.pdf
6. **Food and Drug Administration.** Data Standards and Terminology Standards for Information Submitted to CDRH. Accessed June 3, 2022. https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/data-standards-and-terminology-standards-information-submitted-cdrh
7. **Smoak C.** CDISC Standards for Medical Devices: Historical Perspective and Current Status. *PharmaSUG* 2020, Paper MD-020. Accessed February 22, 2022. https://www.pharmasug.org/proceedings/2020/MD/PharmaSUG-2020-MD-020.pdf
8. **Hall P.** Successful US Submission of Medical Device Clinical Trial using CDISC. *PharmaSUG* 2020, Paper MD-041. Accessed February 22, 2022. https://www.pharmasug.org/proceedings/2020/MD/PharmaSUG-2020-MD-041.pdf
9. **Hall P, Karunasundera T, Maharjan S, Vegesna V.** Multiple Successful Submissions of Medical Device Clinical Trial in the US and China using CDISC. *PharmaSUG* 2021, Paper MD-044. Accessed February 22, 2022. https://www.pharmasug.org/proceedings/2021/MD/PharmaSUG-2021-MD-044.pdf
10. **Smoak C.** A Critique of Implementing the Submission Data Tabulation Model (SDTM) for Drugs and Medical Devices. *PharmaSUG* 2017, Paper DS25. Accessed February 22, 2022. https://

www.pharmasug.org/proceedings/2017/DS/PharmaSUG-2017-DS25.pdf

11. **Teli R, Sacco A.** Medical Device SDTM: A Real Case. *PHUSE EU Connect* 2019, Paper PP05. Accessed February 21, 2022. https://phuse.s3.eu-central-1.amazonaws.com/Archive/2019/Connect/EU/Amsterdam/PAP_PP05.pdf
12. **Food and Drug Administration.** Providing Regulatory Submissions In Electronic Format – Standardized Study Data Guidance for Industry. June 2021, revision 2. Accessed August 22 2023. https://collections.nlm.nih.gov/catalog/nlm:nlmuid-9918350982006676-pdf
13. **European Commission.** The Community Research and Development Information Service, (CORDIS). Search conducted with the keyword 'in silico trial', accessed February 21, 2022. https://cordis.europa.eu/search/en
14. **European Commission.** The Community Research and Development Information Service (CORDIS). In Silico World: Lowering barriers to ubiquitous adoption of In Silico Trials. Accessed February 21, 2022. https://cordis.europa.eu/project/id/101016503
15. **European Commission.** The Community Research and Development Information Service (CORDIS). A European standardization framework for data integration and data-driven in silico models for personalized medicine. Accessed February 21, 2022. https://cordis.europa.eu/project/id/825843
16. **Food and Drug Administration.** Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions – Draft Guidance for Industry and Food and Drug Administration Staff. December 2021. Accessed August 22, 2023. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/assessing-credibility-computational-modeling-and-simulation-medical-device-submissions
17. **American Society of Mechanical Engineers.** Assessing Credibility of Computational Modeling through Verification and Validation: Application to Medical Devices. 2018, V&V 40.
18. **Food and Drug Administration.** Reporting of Computational Modeling Studies in Medical Device Submissions Guidance for Industry and Food and Drug Administration Staff. September 2016.
19. Dassault Systèmes and the FDA Extend Collaboration to Inform Cardiovascular Device Review Process and Accelerate Access to New Treatments. Accessed February 21, 2022. https://www.3ds.com/newsroom/press-releases/dassault-systemes-and-fda-extend-collaboration-inform-cardiovascular-device-review-process-and-accelerate-access-new-treatments
20. **Clinical Data Interchange Standards Consortium.** CDISC Standards. Accessed August 22, 2023. https://www.cdisc.org/standards
21. **Clinical Data Interchange Standards Consortium.** Medical Devices. Accessed February 21, 2022. https://www.cdisc.org/standards/foundational/medical-devices
22. **Food and Drug Administration.** Data Standards Catalog v8.0 (02-15-2022) – Supported and Required Standards. Accessed February 23, 2022. https://www.fda.gov/media/156273/download
23. **The Japanese Pharmaceuticals and Medical Devices Agency.** Revision of Technical Conformance Guide on Electronic Study Data Submissions. January 2019, Notification No. 0124001. Accessed August 22, 2023. https://www.pmda.go.jp/files/000229468.pdf
24. **The Chinese National Medical Products Administration.** Guideline on the Submission of Clinical Trial Data. July 2020.
25. **Clinical Data Interchange Standards Consortium.** CDISC and REDCap Work Together to Foster More Meaningful Clinical Research for Academics. Accessed February 23, 2022. https://www.cdisc.org/news/cdisc-and-redcap-work-together-foster-more-meaningful-clinical-research-academics
26. **Clinical Data Interchange Standards Consortium.** CDISC and OpenClinica Collaborate to Drive Academic Clinical Research Forward. Accessed February 23, 2022. https://www.cdisc.org/news/cdisc-and-openclinica-collaborate-drive-academic-clinical-research-forward
27. **Takahara S, Saito TI, Imai Y, Kawakami T, Murayama T.** A use-case analysis of Clinical Data Interchange Standards Consortium/Study Data Tabulation Model in academia in an investigator-initiated clinical trial. *Nagoya J Med Sci.* 2022; 84(1): 120–132. DOI: https://doi.org/10.18999/nagjms.84.1.120
28. **Food and Drug Administration.** Study Data Technical Conformance Guide – Technical Specifications Document. March 2022, Version 4.9. Accessed August 22, 2023. https://www.fda.gov/media/153632/download
29. **Kush RD, Warzel D, Kush MA,** et al. FAIR data sharing: The roles of common data elements and harmonization. *J Biomed Inform.* 2020; 107: 103421. DOI: https://doi.org/10.1016/j.jbi.2020.103421
30. **Ohmann C, Banzi R, Canham S,** et al. Sharing and reuse of individual participant data from clinical trials: principles and recommendations. *BMJ Open.* 2017; 7(12): e018647. DOI: https://doi.org/10.1136/bmjopen-2017-018647
31. **Romero K, Ito K, Rogers JA,** et al. The future is now: model-based clinical trial design for Alzheimer's disease. *Clin Pharmacol Ther.* 2015; 97(3): 210–214. DOI: https://doi.org/10.1002/cpt.16
32. **Faris O, Shuren J.** An FDA Viewpoint on Unique Considerations for Medical-Device Clinical Trials. *N Engl J Med.* 2017; 376(14): 1350–1357. DOI: https://doi.org/10.1056/NEJMra1512592
33. **Food and Drug Administration.** Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product

Applications and Related Submissions Using the eCTD Specifications Guidance for Industry. February 2020. Accessed August 22, 2023. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications

34. **Bodner J, Kaul V.** A Framework for In Silico Clinical Trials For Medical Devices Using Concepts From Model Verification, Validation, And Uncertainty Quantification (VVUQ). *ASME VVS* 2021, VVS2021-65094. DOI: https://doi.org/10.1115/VVS2021-65094
35. **Clinical Data Interchange Standards Consortium.** Define-XML. Accessed February 23, 2022. https://www.cdisc.org/standards/data-exchange/define-xml
36. **European Commission.** The Community Research and Development Information Service (CORDIS). In Silico testing and validation of Cardiovascular Implantable devices. Accessed February 21, 2022. https://cordis.europa.eu/project/id/101017578
37. **Aydin B, Ohmann C.** SIMCOR Deliverable 10.1: In-silico trial impact assessment framework. *Zenodo.* December, 2021. DOI: https://doi.org/10.5281/zenodo.6353628
38. **Clinical Data Interchange Standards Consortium.** Therapeutic Areas. Accessed February 23, 2022. https://www.cdisc.org/standards/therapeutic-areas

How to cite this article: Aydin B, Kiely É, Ohmann C. Feasibility Assessment of Using CDISC Data Standards for in *vivo* and in *silico* Medical Device Trials. *Journal of the Society for Clinical Data Management*. 2023; 3(3): 3, pp. 1–7. DOI: https://doi.org/10.47912/jscdm.230

Submitted: 20 October 2022 **Accepted:** 04 August 2023 **Published:** XX Month 202X

Journal of the Society for Clinical Data Management is a peer-reviewed open access journal published by Society for Clinical Data Management.

OPEN ACCESS