The Standard for the Exchange of Nonclinical Data (SEND): Challenges and Promises

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Abstract
The Standard for the Exchange of Nonclinical Data (SEND) is an implementation of the Study Data Tabulation Model for nonclinical studies that enables the U.S. Food and Drug Administration (FDA) to modernize and streamline the review process. As a result, patients may benefit from speedier approval of new drugs. However, SEND implementation and compliance can be challenging and require effective cooperation between pharmaceutical companies and contract research organizations. In order to improve Society of Toxicologic Pathology (STP) members’ awareness about SEND, including the steps, obstacles, and mistakes to avoid in its implementation while applying for FDA approval, the Career Development and Outreach Committee of the STP sponsored a career development lunchtime series panel discussion entitled “The Standard for the Exchange of Nonclinical Data (SEND): Challenges and Promise” in conjunction with the STP 37th Annual Symposium. The presentations and discussion at this workshop provided perspectives of experts including pathologists and information technology professionals familiar with the SEND submission process and FDA reviewers. This article is designed to provide brief summaries of their talks as well as the questions asked during this well-received panel discussion.

Keywords
SEND, SDTM, nonclinical studies, drug approval, FDA

The Study Data Tabulation Model (SDTM), established by the Clinical Data Interchange Standards Consortium (CDISC), provides a standard for organizing and formatting data to streamline processes in the collection, management, analysis, and reporting for both clinical and nonclinical studies (The Study Data Tabulation Model 2013). The Standard for Exchange of Nonclinical Data (SEND) is the implementation of the SDTM for nonclinical studies (Standard for Exchange 2016). The goal of SEND is to establish an industry standard for the content and structure of nonclinical data submitted to the U.S. Food and Drug Administration (FDA) in electronic format, eventually phasing out paper submissions. Controlled terminology is required by the FDA as a part of the standardized electronic format in study data standards like SEND and SDTM. Organizations, including CDISC and International Harmonization of Nomenclature and Diagnostic Criteria (INHAND) for lesions in rats/mice and nonrodent species are working on standardizing terminology in the field of toxicologic pathology (Keenan et al. 2015). Submission of data in the SEND-compliant formats is required by the FDA for new drug applications (NDAs), biologics license applications (BLAs), and abbreviated new drug applications (ANDAs) submissions since December 2016 and for investigational new drug (IND) studies since December 2017 (Study Data Standards 2017).

The SEND Implementation Guide (SENDIG) 3.0 currently supports single-dose general toxicity, repeat-dose general toxicity, and carcinogenicity studies for NDA/ANDA, BLA, and IND submissions. Safety pharmacology and reproductive toxicology are out of scope for SEND 3.0 but will be supported in future versions of SEND. Recently published SENDIG 3.1 contains a subset of safety pharmacology, including respiratory and cardiovascular studies (Standard for Exchange 2016). The SEND Developmental and Reproductive Toxicology...
Implementation Guide (DARTIG) 1.0 for embryo fetal development has also been recently published. DARTIG 1.0 is not yet required but has been released to allow development and validation of tools ahead of implementation (Standard for Exchange 2016). The main promise of SEND is to reduce the NDA examination time by enabling the FDA to receive, process, review, and archive submissions more efficiently and effectively. SEND implementation and compliance, however, can be challenging and require effective cooperation between pharmaceutical companies and contract research organizations (CROs). Continuously evolving SEND standards present challenges to the industry, including data management and information technology (IT) support, quality assurance (QA), and integration of data from multiple test sites.

The Career Development and Outreach Committee (CDOC) of the Society of Toxicologic Pathology (STP) sponsored the Career Development Lunchtime Series Panel Discussion entitled “The Standard for the Exchange of Nonclinical Data (SEND): Challenges and Promise” as part of the activities at the 2018 STP annual symposium in Indianapolis, IN. The panel discussion provided an active platform to discuss challenges and promise associated with SEND and included perspectives of pathologists and IT professionals familiar with the SEND submission process from pharmaceutical companies/CROs, self-employed consultants, and FDA reviewers familiar with reviewing SEND data. Panelists representing pharmaceutical companies/CROs/consultants included: Audrey Walker—Associate Director of Electronic Submissions at Charles River Laboratories (CRL); Kathleen Funk, DVM, PhD, DACVP—President/Senior Pathologist at Experimental Pathology Laboratories (EPL); and Charlotte Keenan, DVM, PhD, DACVP, FIATP—Principal Consultant/Pathologist at C.M. Keenan ToxPath Consulting. Reviewers representing FDA included Imran Khan, PhD—Pharmacologist/Toxicologist at U.S. FDA/Center for Drug Evaluation and Research (CDER) and LuAnn McKinney, DVM, DACVP—Pharmacologist/Toxicologist CDER at U.S. FDA/CDER. The article that follows provides brief summaries of talks by the aforementioned panelists as well as the representative questions asked during the 2018 STP CDOC panel discussion. This article reflects the views of the authors and should not be construed to represent the views or policies of the FDA or pharmaceutical companies/CROs.

**SEND: Challenges and Promises in a Big CRO**

Audrey Walker (CRL) presented an overview on challenges, prospects, and promises of implementing SEND in a big CRO like CRL. Audrey has been in the IT industry for over 25 years and has worked with preclinical data for over 20 years. She led the validation and implementation of SEND data for submission compliance for CRL and continues to lead the team today. Audrey also provides guidance to sponsors and labs trying to implement SEND. In 2007, Audrey joined the CDISC SEND team as coauthor of the CDISC SEND Implementation Guides 3.0 and 3.1 and is also a member of the CDISC Global Governance Group, the SEND Extended Leadership Team, Core Team, and Controlled Terminology Team. In 2009, Audrey received the Super Performance Award from the CDISC group in appreciation for her outstanding contribution to the overall CDISC mission. In 2011, Audrey received the Leveraging Collaboration Award as a member of the CDISC SEND team from the FDA.

**Challenges**

Challenges that CRL encountered were many and the complexity was magnified due to our global footprint. We quickly realized that harmonization across our sites would be key in order to be successful, and so we began the journey of reviewing terminology and processes in order to align with CDISC as closely as possible. This was a process that took many years to accomplish and we continue to harmonize where possible as the process evolves.

The effort to review and update data collection processes to align with CDISC SEND was very labor intensive and disruptive to multiple CROs. Continuously evolving SEND standards presents a challenge to the industry, including data management and information technology (IT) support, quality assurance (QA), and integration of data from multiple test sites.

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The effort to review and update data collection processes to align with CDISC SEND was very labor intensive and disruptive to daily operations. CRL reviewed practices from the animal arrival, to in-life, through to necropsy and histopathology data collection. Although everyone acknowledged the importance of the effort, the amount of changes needed in order to streamline the process were many and the learning curve was steep. Training and informational sessions were held with staff continuously throughout the implementation to communicate what SEND was and why these changes were occurring. Charles River now collects more data online than we ever have before!

Another challenging task that was essential to the completion of our compliance journey was the mapping of Charles River terminology to CDISC SEND terminology. Through many collaborative sessions between the SEND team and our scientists, we mapped over 10,000 terms for our original go live and continue to update these mappings as terminology is updated.

As we became closer to completing the validation of our system, we began to pilot with a number of sponsors. This exercise was crucial in solidifying our internal processes for SEND creation and also clarifying how we would transfer this new deliverable to our sponsors. A new challenge became evident as we worked through different scenarios. Multisite studies! How were we going to handle data being provided by test sites outside of CRL? It quickly became evident that SEND knowledge and capabilities differed greatly across the industry. Through collaborative sessions with all parties involved, we have defined our process and frequently educate our sponsors and other interested parties on our best practices.

Should QA be involved with SEND data sets or not, was a big debate internally as well as externally. This debate continues today. Whether SEND should be included in the protocols is another debate that continues within industry. A possible future state may be that the FDA will become accustomed to the SEND data sets and eventually announce they no longer need the individual animal listings and that the SEND data sets...
will replace them. At this point, the SEND data sets would become subject to QA audit and study director review and, therefore, be included as standard within the protocols/study plans. [Note: This is the opinion of Audrey Walker’s and not that of CRL.]

SEND will continue to change and improve as the industry uses the model and submits data to the FDA. Issues are starting to come to light that point to areas that need further clarification and the CDISC team is updating the implementation guides accordingly. SEND is new to all including the FDA, so there will be updates and further clarifications as we continue this journey. We are all learning, and are all in it together, so we all need to work together as partners to make this important initiative succeed.

**Prospects and Promises**

With SEND data sets, both sponsors and the FDA can review the data more efficiently and effectively. Once you start to review data electronically, you will not want to go back to paper PDF review. It is only a matter of time before everyone will have visualization tools to review the data and will have forgotten what it was like to review data in PDF paper form. [Note: This is the opinion of Audrey Walker.]

Many sponsors are creating data warehouses to mine their SEND data. As this format becomes easier to produce the expectation of receiving SEND data sets before the finalization of the study will become the norm. With the data in a warehouse, you can mine across a compound, across species, compound class; the sky is the limit.

The benefit Charles River has seen from SEND has been the urgency it created for us to harmonize processes and glossaries across the safety assessment unit. Due to the numerous process changes made, we encounter fewer data issues than we did before the inception of SEND. Moving forward, Charles River will continue to change processes as new guidance documents are released. We will continue to evaluate the collection of data electronically. We will continue to train staff both technical and scientific about new SEND initiatives as they are released. We look forward to the new era of electronic SEND data.

**SEND: Challenges and Promises in a Small CRO**

Dr. Kathleen Funk (EPL) provided an overview on challenges, prospects, and promises of implementing SEND in a small CRO like EPL. Dr. Funk, is a board certified pathologist and President of EPL, Inc., a CRO that handles preclinical histopathology, primary and peer review evaluations, and consultations for a wide variety of companies and institutions. EPL does not have an in-life facility; consequently SEND issues that directly concern in-life data are not encountered. However, EPL generates SEND data that must be incorporated into the larger SEND files generated from in-life studies, and this is accomplished by working closely with other preclinical CROs. As it relates to SEND, Dr. Funk’s responsibilities include managerial and business decisions that involve the deployment of resources, while SEND package generation is accomplished by EPL IT personnel and trained technicians.

**Challenges**

Challenges and obstacles overcome in implementing SEND at EPL are three-fold and classified as technical, internal, and client-related issues. The technical considerations are that the SEND software is still nascent and we had to overcome some implementation obstacles. Furthermore, the SEND software is evolving rapidly, resulting in more frequent software updates, each requiring new validation efforts.

Internal issues include the disruption to the flow of our internal business processes and the fact that we had to develop standard operating procedures and decide when we would create the SEND files in the reporting process. While IT was necessarily involved in SEND implementation, we also had to create a new position and decide the personnel who would best fit this position’s job requirements. We discussed what the role of quality control (QC) and QA would be and decided that there is no role for QA since we would generate the SEND files after the final audit of the tables and narrative. It was decided that QC would review the Study Data Reviewers Guide (SDRG) and validation report. QA would not be involved at all since the SEND data are put together after their review is complete. This decision appears to be the consensus of the QA industry. We acknowledge that training will be ongoing as the standards evolve and validation activities will be more frequent as the standards evolve. Another internal issue is that it still is difficult to predict how much time a given study will take to generate an error-free SEND report.

Client-related issues include the fact that some clients are unfamiliar with SEND and sometimes don’t know whether they need SEND files. Additionally, since we are a histopathology CRO with no in-life component, not all aspects of the SDRG apply to EPL. We have decided to be proactive and inquire before a study is undertaken whether SEND files will be required and what domains do the client want us to generate. The bulk of our work focuses on the following domains: demographics (which contains animal information), microscopic findings (MI), macroscopic findings, and related records (RELREC, which is where correlated findings are identified). We have found we need to suggest the domains as RELREC, dealing with microscopic correlations, as this has often been overlooked by clients as a SEND file they would like to have generated. We also have requests for SEND files from older studies that were input into a non-SEND pathology data capture system. This request particularly segues into the question of how much to bill for SEND files. Another client-related issue is getting the proper information from our client. For example, USUBJID, which is the unique subject identifier for an animal, requires a specific naming convention, which we do not always know. An example of this problem would be if an animal number is supposed to be DRV-1M001 and we are told it should be DRV1M001 (without the dash). When we have
received improper animal identification, our SEND files will have a compatibility problem when the data sets are combined, or harmonized with the in-life SEND package. We have encountered animal identification issues that were more time-consuming to resolve since our pathology capture database was set up with incorrect animal identifiers.

Prospects and Promises

What has worked well at EPL is that the control terminology has not given us much trouble. Most of the issues we run into involve study-specific, nonstandard tissue names which we explain in the SDRG. Our processes are working well and since we generate mostly files in the MI data set, we can focus on that and turn studies around quickly. A nice by product of the SEND effort is that validation procedures have become more efficient. We know that at least one of our SEND data sets has been submitted successfully to FDA as part of a larger SEND package for a successful NDA.

Going forward, EPL will continue to cement our internal processes, perform cross-training and increase overall awareness of SEND, and solicit more feedback from clients on our data submissions.

SEND and INHAND: Challenges and Prospects in Pharmaceutical Industries

Dr. Charlotte Keenan (C.M. Keenan ToxPath Consulting) provided an overview of collaboration between SEND and INHAND and the challenges, prospects, promises of implementing SEND in the pharmaceutical industry. Dr. Keenan received her Veterinariae Medicinae Doctoris from the University of Pennsylvania School of Veterinary Medicine and did her pathology residency in the army at the Walter Reed Army Institute of Research. Dr. Keenan is a Diplomate of the ACVP and a Fellow of the International Academy of Toxicologic Pathology. Dr. Keenan has over 30 years of experience in the pharmaceutical industry and is currently an independent consultant in toxicologic pathology. Dr. Keenan is Chair of the INHAND Global Editorial Steering Committee (GESC).

During 2012, INHAND GESC representatives Charlotte Keenan and Dawn Goodman attended meetings with representatives of the FDA CDER, CDISC, and the National Cancer Institute (NCI) Enterprise Vocabulary Services (EVS) to initiate integration of INHAND terminology as the preferred terminology for SEND. The collaboration between SEND and INHAND is based on the FDA’s interest in utilizing published, peer-reviewed data standards. Drs. Keenan and Goodman serve as members of the CDISC SEND Controlled Terminology committee to assist in providing guidance on base processes and modifiers associated with the INHAND published terminology. Any questions raised on terminology are reviewed by the full GESC and/or appropriate INHAND working group for resolution. The GESC may also call on experts in the field to assist in any aspect of their role as a “Scientific Advisory Board.”

Challenges

From the perspective of the pharmaceutical industry, developing standardized terminology for microscopic pathology is quite challenging. Anatomic pathology is primarily a descriptive science with many “shades of gray.” The current requirements of the SEND model dictate that the diagnosis be segmented into defined fields. Pathologists may view this as restrictive and not compatible with how their company’s data entry lexicon is organized. However, data collection systems can be interfaced with SEND extract software, such that the diagnosis can be mapped to the appropriate SEND fields. INHAND representatives work closely in a positive collaboration with the SEND Controlled Terminology committee to ensure that INHAND terms are mapped appropriately and new terms are reviewed and added, or modifications made, if needed, to existing INHAND and SEND terms.

Prospects and Promises

On the positive side, delivering standardized data will lead to efficiencies in regulatory submissions, providing one standard used by sponsors and vendors. When data are submitted in a standardized format, it can be searched within a study, across studies within a program, or across different programs. It will allow regulatory reviewers to more effectively review the submission and communicate any questions more specifically to the sponsor. Sponsors will also be developing tools to maintain internal data from SEND extracts. The collaboration between the INHAND GESC, FDA CDER, CDISC, and EVS represents a renewed endeavor to harmonize nonclinical data for regulatory submission, enhancing communication between pathologists, toxicologists, and regulatory scientists worldwide.

SEND at CDER/FDA

Dr. Imran Khan (CDER, FDA) provided an overview of prospect and challenges of SEND at FDA. Dr. Khan received his PhD in pharmacology from Medical University of South Carolina. He was a Research faculty at the School of Medicine, UCSD from 1998 to 2008. He moved to the FDA as a Pharmacology/Toxicology Reviewer at CDER in 2008.

Challenges

Actually, there are no identifiable disadvantages to data submission in SEND format as it pertains to its utilization by the pharmacology/toxicology reviewers. However, there are some challenges in having the pharmacology/toxicology reviewer become familiar with the SEND submissions and utilizing the visualization/analytical tools to view the submitted data. To mitigate these potential challenges, CDER/FDA has implemented several training courses for pharmacology/toxicology reviewers to get familiar with SEND and the visualization tools. In addition, pharmacology/toxicology reviewers from individual divisions are volunteering and providing their input in the designing of the visualization tool as well as beta testing.
the software as it is being developed with the ongoing feedback from the reviewers.

Prospects and Promises

The SEND is a standard format for sponsors to submit nonclinical study. It allows presentation of nonclinical data in a consistent and predictable manner. It facilitates automated analyses of data and the use of analytical and review tools. Currently, SEND data are accepted for single-dose toxicity studies, repeat-dose toxicity studies, and carcinogenicity studies. The SEND submissions contain the study report in a PDF format, a nonclinical study data reviewer’s guide, a define file and data sets related to the studies noted above. After validation of the SEND submission by the Office of Computation Sciences, the reviewers at CDER have access to the SEND submission; however, they require a visualization tool to access and view the data. The visualization tool, which is a software that can be developed by any software company (not unique to FDA), allows the reviewer to create consistent tables and visualizations that facilitate communications within and across review teams. Currently, the tools allow reviewers to visualize representations of change from control, to “drill down” into summary data, and quickly locate all study endpoint data for individual animals. Therefore, the reviewers have more time to focus on science, spend less time digging out data for individual animal from line listings, and thus use more of their time to conduct a more thorough scientific review of the submission.

SEND-related Questions

Some of the most relevant SEND-related questions asked during panel discussion are listed below along with the answers:

Question: How are special stains mapped in the SEND-compliant lexicon?

Reply: Special stains can be mapped to the MIMETHOD variable.

Question: Since FDA pharm/tox reviewers will be using the SEND data set during their review and so rely on those data to draw conclusions, then:

1. Will the FDA consider the SEND data to be raw data?

Reply: FDA does not consider SEND data as the raw data.

2. When FDA compliance auditors review a particular study at a test facility, will they also be reviewing the SEND data?

Reply: This would be under the purview of the Office of Compliance; however, from a general point of view SEND data following submission is validated by the Office of Computational Science.

Question: What is your procedure for mapping a new finding not already present in the SEND-compliant lexicon? What are the logistics of doing it? Is the pathologist able to add a new term, and if he/she does create one, who does the mapping and when? Does it happen in real time as each study’s pathology is completed or not until a SEND file is created?

Reply: Speaking for CRL the lexicons are governed by the glossary committee, any new term goes through governance. If a new CDISC term is deemed needed, we will put a request to CDISC for a new term. The term is added and documented as an extra term in the Study Data Reviewers Guide until published by CDISC.

Question: Where/how did the SEND lexicon come from? Who created them originally? Have all SEND-compliant terms come from INHAND? How do they map to each other and how do they differ? Some INHAND papers have not been published yet—so what happens in these cases?

Reply: The initial list for the SEND codelist of nonneoplastic (NONNEO) microscopic pathology contains terms from published INHAND organ systems. There is a SEND Controlled Terminology Committee, composed of industry sponsor pathologists and data management specialists, along with 2 representatives from the INHAND Global Editorial Steering Committee, who review and map INHAND terms to SEND-compliant format. Some terms on the NONNEO codelist may look different from how they have been presented in the INHAND publications. Terms on the NONNEO codelist are mostly generic and can be used across tissues, where appropriate. INHAND published terms have been modified to fit the SEND standard in some cases by being broken into base process and modifiers. For example, the INHAND term Necrosis, zonal would be separated into NECROSIS for population in MISTRESC (Microscopic Standardized Result) and ZONAL in MIDISTR (Microscopic Distribution). Tissue-specific terms from INHAND are included on the NONNEO codelist when it is important to use the exact term representing a spectrum of tissue changes (e.g., chronic progressive nephropathy). In the process of mapping terms from INHAND to SEND, some inconsistencies have been noted for the same term across several organ systems (e.g., thrombus vs. thrombosis). These will be harmonized using the new change control process and the most current INHAND terminology will be available on the goRENI website. The SEND list will continue to grow as INHAND publishes additional organ systems.

Question: When does a pathologist know if a term is not SEND-compliant? If this happens after the study/pathology report is finalized, then an amendment is needed. What if the study pathologist is on vacation or this correction is not done in a timely manner? What can be done to satisfy/help the sponsor in these cases?

Reply: Upon completion of the SEND extract, there should be a listing of those terms that are not SEND-compliant. An amendment would only be needed if the pathologist and study director determined it is important to adjust the term to something that is SEND-compliant. Otherwise, the original diagnoses should be submitted along with an explanation in the Study Reviewer’s Guide defining the terminology that was used. Going forward, of course, it would be helpful to have the pathology terms in the data entry system map to SEND-compliant terms.
Speaking for CRL the lexicons are governed by the glossary committee, so the pathologist can only choose from the standardized list. If there is something that is study–specific, they can choose to add a new term to that specific study. If this term is something that will become standard, then the new term goes through governance. If a new CDISC term is deemed needed, we will put in a request to CDISC for a new term. The term is added and documented as an extra term in the Study Data Reviewers Guide until published by CDISC.

**Question:** There are pathologic changes that exist in continuum, for example, degeneration → necrosis → regeneration. Therefore, some pathologists prefer the single diagnostic term to describe these events, for example, degeneration/necrosis/regeneration. How do they map in SEND or to what specific diagnosis they will map? What if there are more than 2–3 slashes (/) in a single diagnosis?

**Reply:** This situation was reviewed in SEND several years ago and a consensus was reached that two terms separated by a slash would be acceptable. However, each individual term must also be in the SEND list with its own definition. More than one slash will not be accepted.

**Question:** Do FDA reviewers pull out the original file to see the original diagnosis made? Can they pull out the diagnoses by a “modifier”? Will they be able to see if the findings are background or test article-related?

**Reply:** Reviewers can see the controlled terminology entries and the pathologist’s preferred terms. The terms can be sorted by any column. Background or test would be explained by the pathologist in the signed dated pathology report.

**Question:** Is there any case in which SEND submission is rejected even if the data are validated by software like “Pinnacle 21”? To what extent do we have to assure the quality of SEND data?

**Reply:** Data can pass the Pinnacle 21 validator, but that does not mean it is good data, it also takes someone to review the data to make sure it makes good scientific sense and that data accurately reflects the study plans, amendments, deviations, and reports.

**Question:** For what purpose are “define files” used?

**Reply:** The define file is essentially like the table of contents for the study submission. It details what domains were submitted, what variables were submitted, and any metadata, comments, or computational methods for those variables.

**Question:** Diagnoses related to reproductive organs/system or sexual maturity are not included in INHAND or SEND. How do they map?

**Reply:** For now, tissue-specific diagnoses that relate to maturity (sexual and skeletal) will be added in SEND. For example, GROWTH PLATE OPEN has recently been added. There is also discussion underway in a SEND committee on macroscopic and microscopic domains to provide a “tissue” that would capture an overall assessment of the animal’s maturity.

**Question:** How and when does the FDA use SEND data? What does the FDA do with the SEND data?

**Reply:** First FDA reviews the study report along with summary tables submitted by the sponsors. The SEND data are then used by FDA to relook at any findings or to create tables for their own reviews. The SEND data are considered by FDA as an original data set which always belongs to the clients.

**Question:** Does FDA read across SEND data from different studies or is a data set from one study compared with other similar studies?

**Reply:** FDA doesn’t read across studies and every study is considered to be complete on its own.

**Question:** Can sponsors submit data at draft or at interim?

**Reply:** The SEND submission rule does not only apply to final study reports. SEND data sets are required when the study report is submitted, even when it is an audited draft report or an interim study report. If there are changes to the SEND data sets requiring resubmission with the final study report, resubmit the updated data sets using the “replace” operator. Information about using the “replace” operator to update data sets can be found in Section 7.1 of the Study Data Technical Conformance Guide (https://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM384744.pdf). SEND data sets would not need to be resubmitted with the final report if there were no changes to the data set from the audited draft report.

**Question:** PDF files are so difficult to read. Why are they still used?

**Reply:** FDA read pdf first. Pdf reports contain discussion, descriptions, interpretations of the data and results including adjustments of adversity. SEND listings are the line listings of findings.

**Question:** Is there a way to know retrospectively when (date/year) a “term” became SEND-compliant? How do you record this?

**Reply:** The listing of INHAND terms in goRENI indicates if a term is new or modified. A Word document of INHAND terms is available on the goRENI website and this document also shows when a term has been modified. A current listing of SEND terms and all past terms are available on the NCI website: https://www.cancer.gov/research/resources/terminology/cdisc. There are quarterly updates to this terminology list.

**Question:** What if the initial pathology data was not recorded electronically? How are these mapped to the SEND lexicon?

**Reply:** Retrospectively enter it within you pathology system. If you do not have a pathology system, it will be a lot of work to convert this data manually. One could potentially find a company who does SEND Data Conversion Services to convert the data into SEND format. There are quite a few vendors that provide this service.

**Author Contributions**

All authors (SC, AW, KF, CK, IK, KM) contributed to conception or design; data acquisition, analysis, or interpretation; drafting the manuscript; and critically revising the manuscript. All authors gave final approval and agreed to be accountable for all aspects of work.
in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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