User Profiles - Government and Standards Organizations

NCI EVS has extensive partnerships with government and standards organizations beyond NIH to develop terminology standards, content, technology, and operational support. Such partnerships are designed to directly support NCI's cancer research mission, improving regulatory, federal and community practices in ways that contribute to the conduct and sharing of cancer research while also having a positive impact on the wider biomedical community. The following collaborations are included in this section:

U.S. Food and Drug Administration (FDA)

FDA has worked with EVS since 2001, with formal Memoranda of Understanding starting in 2004, to develop and harmonize terminology content, standards and systems in areas of mutual interest such as drugs, devices, patient safety, and clinical trials. FDA has chosen EVS and NCI Thesaurus (NCIt) for developing and publishing many important terminology sets; some 15,000 FDA terms in over 20 defined subsets are now maintained in NCIt and required for regulatory reporting and other purposes. These include:

- **Structured Product Labeling (SPL):** Standard terminology for Drug Establishment Registration (Regulated Product Submission), Drug Listing and the Content of Labels. 16 NCIt subsets used for submission of proposed labeling by all manufacturers using electronic formats. There are 9,466 establishments from over 100 countries that use the SPL terminology in order to comply with federal regulations to list their products. There are approximately 40,000 subscribers to the FDA's SPL LISTSERV, and this is one of the primary mechanisms to inform users of changes to the SPL terminology that is maintained by NCI. FDA does not track the number of hits against the FDA Resources for Data Standards page and its sub pages, but they suspect that the number of hits is very high; when firms do not select the correct NCIt code, their submitted SPL file will not pass validation.

- **Unique Ingredient Identifier (UNII)** codes are being developed by FDA to uniquely identify all ingredients used in marketed medications in the United States, as well as substances in biologics, foods and devices. Each UNII is assigned based on molecular structure or other immutable characteristics. FDA provides a full set of published UNII codes and a search page on a Web site now hosted by the National Library of Medicine (NLM) and updated approximately monthly.

  EVS collaborated with FDA on the launch and early publication of UNII codes. More than 12,000 UNII codes have been included in corresponding NCIt concepts, and more continue to be added each month, although NCIt no longer provides comprehensive representation of all UNII concepts. Most of these 12,000 concepts were included in NCIt because of their therapeutic and other interest for cancer and related research, and they are extensively annotated with definitions, chemical formulae, CAS registry numbers, synonyms, and other information to help support such research. Files providing UNIIs that have matching NCIt concept codes are available for download in Excel and text formats.

- **CDRH Device Event Problem Codes:** NCIt subsets used for the reporting of medical device problems to FDA. CDRH is responsible for ensuring the safety and effectiveness of medical devices and eliminating unnecessary human exposure to man-made radiation from medical, occupational and consumer products. Approximately 200 organizations from some 3,000 different reporting locations report to the CDRH using NCIt terminology. CDRH receives approximately 35,000 submissions per month that are based on NCIt terminology.

- **Individual Case Safety Report (ICSR):** NCIt subsets used for adverse event reporting. Proposed regulations for electronic submissions will create similar levels of use for these subsets.

- **eCTD (electronic Common Technical Documents):** Standard terminology for regulatory forms required by the Center for Drug Evaluation and Research (CDER).

- **Drug Submissions**: Beginning June 1, 2009, FDA no longer accepts paper submissions for drug establishment registration and listing unless a waiver is granted. Moving from a paper-based format to an electronic system will improve the timeliness and accuracy of the submissions. This is not possible without the terminology provided by NCIt. Of 22,246 New Drug related Submissions from October 2009 - September 2010, (63%) were in electronic format submissions that required terminology from NCIt.

- **Stability**: NCIt provides terminology for FDA and HL7 Stability Data Standards, including human pharmaceuticals, animal drugs and medical devices that are in regulatory submissions, amendments, supplements and annual reports.

EVS resources and systems are also used in FDA efforts such as the **Janus Clinical Trials Repository (CTR) Project** , a standards-based repository of subject level clinical trial data to support regulatory review and patient centered outcomes research (PCOR).

For more information, visit the NCI website FDA terminology resources.

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2. Reed TL, Kaufman-Rivi D.
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Clinical Data Interchange Standards Consortium (CDISC)

CDISC is an international, non-profit organization that develops and supports global data standards for medical research. CDISC is working actively with EVS to develop and support controlled terminology for a wide spectrum of clinical and nonclinical studies.

CDISC terminology is being widely adopted as a standard for study coding and data submissions. In the United States, draft FDA guidance on regulatory submissions (see Study Data Technical Conformance Guide) recommends CDISC terminology as a set of controlled terms that meet the FDA requirements for the implementation of the CDISC standards. As part of the General Considerations of Controlled Terminology regarding CDISC, the Guide states: "Sponsors should use the terminologies and code lists in the CDISC Controlled Terminology, which can be found at the NCI (National Cancer Institute) Enterprise Vocabulary Services."

CDISC terminology goes through an extensive process of content development and public review before it is declared ready for release. All CDISC controlled terminology – more than 10,000 terms – is maintained and published as NCI Thesaurus (NCIt) subsets, as part of a partnership started in 2002. The main terminology efforts encompassed by the CDISC-EVS partnership are shown below:

- **Study Data Tabulation Model (SDTM)** is an international standard for clinical research data, and is approved by the FDA and Japan's Pharmaceuticals and Medical Devices Agency (PMDA) as a standard electronic submission format. EVS maintains and distributes SDTM controlled terminology as part of NCIt. More information is available at CDISC's SDTM Web page. SDTM has been downloaded more than 14,000 times in over 90 countries, primarily for institutional use. More than 270 commercial organizations use SDTM, as do numerous academic, non-profit and research organizations.

- **Questionnaire (QS) and Functional Test (FT) Terminology** contains standardized, controlled terminology for commonly used questionnaires and functional tests in biomedical and therapeutic area research. EVS maintains and distributes Questionnaire controlled terminology as part of NCIt. More information is available at CDISC's Questionnaire Web page. Questionnaire terminology can be used for both collection (CDASH) and submission (SDTM) data sets.

- **Clinical Data Acquisition Standards Harmonization (CDASH)** develops clinical research study content standards in collaboration with sixteen partner organizations including NCI. EVS maintains and distributes CDASH controlled terminology, a subset of SDTM, as part of NCIt. More information is available at CDISC's CDASH Web page.

- **Analysis Data Model (ADaM)** supports efficient generation, replication, review and submission of analysis results from clinical trial data. EVS maintains and distributes ADaM controlled terminology as part of NCIt. More information is available at CDISC's ADaM Web page.

- **Standard for Exchange of Non-Clinical Data (SEND)** extends Study Data Tabulation Model (SDTM) for non-clinical studies. SEND guides the organization, structure and format of standard nonclinical tabulation data sets for interchange between organizations such as sponsors and CROs and for submission to a regulatory authority such as the FDA. NCI EVS maintains and distributes SEND controlled terminology as part of NCIt. It now includes some 1,000 additional terms beyond the SDTM terminology that is also part of the SEND standard. More information is available at CDISC's SEND Web page.

The CDISC Shared Health and Research Electronic Library (SHARE) project aims to create a global, electronically accessible library of CDISC standard metadata that can be used to improve biomedical research and its link with healthcare. The SHARE metadata repository (MDR) provides a dynamic environment where the relationships between and among CDISC metadata and controlled terminologies are published at a level of granularity that is user-defined and in forms that are both human and machine readable. The SHARE MDR is built using CDISC and BRIDG metadata and terminology that is coded and maintained in the EVS NCIt environment. More information is available at CDISC's SHARE Web page.

For more information, visit the NCI website CDISC terminology resources.

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Coalition for Accelerating Standards and Therapies (CFAST)

CFAST is a joint initiative of the Clinical Data Interchange Standards Consortium (CDISC) and the Critical Path Institute (C-Path), with steering committee participation from the US Food and Drug Administration (FDA), the National Cancer Institute Enterprise Vocabulary Services (NCI EVS) and TransCelerate BioPharma (TCB). Its purpose is to create therapeutic area-specific data standards to support clinical research in areas of particular importance to public health. Section XII of the Prescription Drug User Fee Act V (PDUFA V) provides the directive for FDA support for this Data Standards for Therapeutic Areas initiative. More information is available on the CFAST Web pages of CDISC and C-Path , and on the FDA Therapeutic Areas Web page.

Therapeutic area teams follow a CFAST-approved process that incorporates stakeholder inputs and public review to produce therapeutic area user guides, questionnaire supplements and controlled terminology. Controlled terminology goes through an extensive process of content development and public review before it is declared ready for release. All controlled terminology developed by the therapeutic area teams is published as part of the CDISC controlled terminology standards.

For more information on CDISC controlled terminology, visit the NCI website CDISC Terminology resources.

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National Council of Prescription Drug Providers (NCPDP)

NCPDP is a not-for-profit, ANSI-accredited, Standards Development Organization with over 1,600 members representing virtually every sector of the pharmacy services industry. NCPDP creates and promotes the transfer of data related to medications, supplies, and services within the healthcare system through the development of standards and industry guidance. In 2009, NCPDP decided to partner with EVS to use NCIt subsets to support two of those standards, employed by some 200 vendors serving approximately 15,000 pharmacies nationwide:

- **NCPDP SCRIPT Standard** supports messages for new prescriptions, prescription changes, refill requests, prescription fill status notification, prescription cancellation, medication history, and transactions for long term care environments. Many large providers such as First DataBank and Surescripts, the nation's largest e-prescriber, use this standard. Surescripts alone connects thousands of pharmacies across the US, and is connected to the largest network of payers and Medicaid Fee for Service payers nationwide.

- **NCPDP Telecommunication Standard** supports the electronic communication of claims and other transactions between pharmacy providers, insurance carriers, third party administrators, and other responsible parties. It is the standard used for eligibility, claims processing, reporting and other pharmacy industry communications, as designated in HIPAA. More than 4 billion claims are processed each year using this standard.

For more information, visit the NCI website NCPDP Terminology resources.

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Federal Medication Terminologies (FMT)

Work started in 2002 as an interagency collaboration between NCI EVS, FDA, VHA, and NLM – joined later by AHRQ, CMS, DoD, and EPA – to improve the exchange and public availability of medication information with coordinated development of terminology standards. The initial FMT terminology set has been endorsed by U.S. Federal standards efforts including the National Committee on Vital and Health Statistics (NCVHS), Consolidated Health Informatics (CHI), the Healthcare Information Technology Standards Panel (HITSP), and the Office of the National Coordinator for Health Information Technology (ONC) within the Department of Health and Human Services (HHS).

For more information, visit the NCI Website Federal Medication Terminologies resources.

U.S. Environmental Protection Agency (EPA)

EPA joined in the Federal Medication Terminologies (FMT) collaboration. EPA has also developed an EPA Science Vocabulary that utilizes substantial content from NCI Thesaurus, particularly for definitions, in addition to content from numerous EPA glossaries and other documents, and from other terminologies such as the Human Disease Ontology. It will be made publicly available in December 2014.

Veterans Health Administration (VHA)

VHA has worked closely with EVS since 2002. Under an ongoing Memorandum of Understanding, VHA works with EVS on collaborative terminology policy and products, including content collaboration and publication of the VA's National Drug File Reference Terminology (NDF-RT), used by both agencies as a drug information reference resource.

The VHA also performed a thorough comparison of the functional capabilities of LexEVS to those of other terminology servers. The VA provided the results to the VKC, which transformed the matrix into a document that can be used by potential adopters of LexEVS as they evaluate the capabilities of the system. This is an example of a valuable contribution from the community that is not code-based; in an open source model, contributions of documentation can be as important as contributions of code.

Medical Dictionary for Regulatory Activities (MedDRA)

MedDRA is an international terminology for coding and regulatory reporting of drug and device adverse events. MedDRA is an International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) standard, adopted by FDA and many other agencies. MedDRA is used by more than 3,000 regulatory, industry and academic subscribers from 60 countries, and has been translated into 11 languages.

EVS manages the MedDRA license for NIH, and publishes multiple versions through LexEVS, the NCI Term Browser, and other means. EVS maintains multiple versions of MedDRA on its servers and browsers to support validation and interpretation of data encoded with those versions.

Over 10 years, EVS has performed numerous mapping comparisons between MedDRA and NCI terminologies including NCI Thesaurus (NCIt), PDQ, CTEP SDC, and CTCAE, as part of ongoing efforts to promote compatibility and data translation between these sources. NCI Metathesaurus maintains mappings between MedDRA and more than 70 other biomedical terminologies, providing a rich source of additional description of MedDRA terms and supporting data translation and analysis.

EVS and the MedDRA Maintenance and Support Services Organization (MSSO) are working with the UK Medicines and Healthcare products Regulatory Agency (MHRA) on use of the EVS Mapping Tool to develop an initial proof-of-concept mapping from SNOMED CT to MedDRA, focusing on high frequency adverse event terms to test the possibility of automated conversion of EHR data to support more proactive identification of potential signals with drugs that have gained marketing approval.

EVS and the MSSO have worked with NICHD, FDA, and other partners in developing a specialized set of pediatric adverse event terminology for use in research and care, as a part of the larger Pediatric Terminology Subset in NCIt and also for inclusion and distribution as part of MedDRA. For more information, visit the NCI website pediatric terminology page.

EVS has made numerous contributions to updates of MedDRA terminology. EVS conducted a comprehensive review of the over 8,500 terms in MedDRA's Neoplasm classification, suggesting changes initially presented to a special Blue Ribbon Panel meeting in 2011. NCIt is used as the primary reference terminology for updates to MedDRA neoplastic terminology. The MedDRA Browser now includes more than 10,000 link-outs to full-text term definitions in NCIt.

World Health Organization (WHO)

The International Classification of Diseases (ICD) is the global standard diagnostic classification for all general epidemiological and many health management purposes, and has many clinical uses. WHO work on the International Classification of Diseases 11th revision (ICD-11) is using NCI Thesaurus (NCIt) as an important source of cancer-related terminology, relationships, and other features such as definitions. EVS has helped facilitate access to and reuse of NCIt content, as well as expert review and suggestions on some draft ICD-11 content; the oncology-specific ICD-O is also being influenced by NCIt's in-depth characterization of cancers and other neoplasms.

WHO is also taking advantage of EVS-supported open source terminology tooling in its work. In June 2009, WHO requested a Classification Markup Language (ClaML) LexEVS data processing program that could be used to render ICD-10 in preparation for, and as the foundation of, ICD-11. Stanford University's Protégé and related terminology editing tools are also a vital component of WHO efforts.

Health Level 7 (HL7)

EVS supports terminology content for the Regulated Clinical Research Information Management (RCRIM) committee of HL7, and for other committees as appropriate including Patient Safety, Pharmacy, Clinical Genomics, and the Clinical Interoperability Council.

CareLex

CareLex™ (http://www.carelex.org/) is a publicly funded not-for-profit enterprise working to improve information interoperability in health sciences to accelerate delivery of new therapies to patients. To achieve this, CareLex actively partners with the biopharmaceutical industry, researchers, contract research organizations (CROs), technology experts, allied professionals, and government regulators to develop and manage open source technologies and advance global standards for clinical trials data interoperability.

EVS has worked with CareLex since 2013 to help develop and publish terminology for their electronic Trial Master File (eTMF) Standards Initiative. This terminology is maintained and distributed as part of NCI Thesaurus (NCIt), and can be found at http://evs.nci.nih.gov/ftp1/CareLex/About.html .

The Taiwan Cancer Registry

The Taiwan Cancer Registry, a population-based cancer registry founded in 1979, uses NCI Thesaurus terminology. Hospitals with greater than 50-bed capacity that provide outpatient and hospitalized cancer care are recruited to participate in reporting all newly diagnosed malignant neoplasms to this registry.

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