Structured Product Labeling Indexing

Background

Structured Product Labeling (SPL) is a Health Level Seven document markup standard accredited by the American National Standards Institute (ANSI) and adopted by the Food and Drug Administration (FDA) as a mechanism for exchanging product information electronically. Product information provided by companies in SPL format may be accessed from the FDA Online Label Repository (labels.fda.gov) and the National Library of Medicine DailyMed web site (dailymed.nlm.nih.gov). Health information suppliers download the SPL documents for use in a variety of electronic health care systems. As a product information exchange standard, SPL directly supports the Department of Health and Human Services' mission and the FDA's mission in providing the public with accurate, science-based information in an electronic and easily accessible format to maintain and improve patient safety.

The product information indexing initiative has the goal of enhancing access to the electronic product information provided by the companies (see the *Guidance for Industry: Indexing Structured Product Labeling)* Indexing refers to the creation by FDA of one or more files with machine-readable annotations that can be linked to the product SPL provided by the company. These machine-readable tags in SPL format allow the information to be easily incorporated, based on assigned codes, into electronic health records, e-prescribing systems and clinical decision support systems for rapid searching, sorting and access of relevant product information needed to make critical health care decisions and enhance patient care. Indexing files are available for download by the public from the National Library of Medicine's DailyMed website. The plan is for phased implementation of indexing. Currently, Pharmacologic Class and Billing Unit indexing files are available.

Pharmacologic Class Indexing

Pharmacologic class is defined based upon any individual or combination of the following three attributes of the active moiety: mechanism of action (MoA), physiologic effect (PE) and chemical structure (CS). Furthermore, if appropriate, FDA identifies the established pharmacologic class (EPC) for each approved medical product according to the principles outlined in the *Guidance for Industry and Review Staff: Labeling for Human Prescription Drug and Biological Products – Determining Established Pharmacologic Class for Use in the Highlights of Prescribing Information.*[1] An EPC is represented by a term or phrase that is

scientifically valid and clinically meaningful based on the MoA, PE and/or CS related to the therapeutic effect(s) for the approved indication(s).

An active moiety may be assigned an EPC, MoA, PE, CS, all four of these standardized indexing concepts, or any combination of these standardized indexing concepts depending on the scientific validity and clinical meaningfulness of these concepts in association with the active moiety. The source of the pharmacologic class standardized indexing concepts is the Department of Veterans Affairs' National Drug File Reference Terminology (NDF-RT). Each concept has a unique standardized alphanumeric identifier code.

Beyond the therapeutic effects, substances may also have other scientifically valid and clinically meaningful effects that may not be related to the approved indications. These "non-therapeutic effects" may be important for the safe and effective use of medical products, including drug interactions and safety assessments based upon appropriate considerations, such as enzyme induction/inhibition. For example, the effect of a substance on cytochrome P450 liver enzymes used by the body to break down chemicals can significantly increase or decrease the concentration of other substances in the body leading to toxic or sub-therapeutic effects, respectively. Therefore, active moieties are also being indexed with pharmacologic class concepts that represent the scientifically valid and clinically meaningful "non-therapeutic effects."

Pharmacologic class index files can be downloaded by the public from the National Library of Medicine's DailyMed website. On this website, one can also perform a search based on a pharmacologic class, currently listed as "Drug Class" as one of the search functions, followed by selecting a specific product within the identified pharmacologic class in order to access other information, such as the product's dosing and indications. The pharmacologic class index files are in SPL format and are regularly maintained and updated by the FDA. Electronic systems can parse data from these files, and build customized search and sort functions based on pharmacologic class, which can then link to other product information.

National Council for Prescription Drug Programs Billing Unit Indexing

The National Council for Prescription Drug Programs (NCPDP) developed the Billing Unit Standard to assist in consistent and accurate billing of pharmaceutical products. Information on the NCPDP Billing Unit Standard may be found at http://www.ncpdp.org/PDF/BUS_overview.pdf. The Billing Unit Index file contains the National Drug Code (NDC) and the corresponding NCPDP Billing Unit (GM, ML or EA). A Billing Unit Index file is created when a Billing Unit designated by

NCPDP for a specific NDC is available for a packaged product included in a product SPL file submitted by the drug company.

The billing unit index files are in SPL format and are regularly maintained and updated by the FDA. Billing Unit Indexing files can be downloaded by the public from the National Library of Medicine's DailyMed website.

Substance Indexing

A Substance is defined by a unique set of identifying characteristics described in the ISO /FDIS 11238 ISO/FDIS: Health Informatics - Identification of Medicinal Products Data Elements and Structures for the Unique Identification and Exchange of Regulated Information on Substances. Identifying characteristics vary depending on whether the substance is a chemical, protein, nucleic acid, polymer and/or structurally diverse. For example, chemical substances and mixtures of chemical substances are defined by one or more chemical structures. Each chemical structure is represented by the MOLFILE and accompanied by the IUPAC International Chemical Identifier (InChI). The molecular structure of proteins and nucleic acids is represented using a single letter notation. Each biological species is represented by its scientific name and the naming authority. Other characteristics include physicochemical properties and terminological classifiers.

Each Substance Index File contains information on a single substance identified by a Unique Ingredient Identifier (UNII) assigned by the FDA Substance Registration System. The file includes the UNII, the identifying characteristics and a hash code computed based on the identifying characteristics.

Substance Index Files are published on DailyMed and are regularly maintained and updated by the FDA.

Product Concept Indexing

A Product Concept Index File includes the product concepts found in a representative reference SPL and the drug applications associated with the product concepts. Currently, animal products, over-the-counter products, homeopathic products, compounded products, and biologic products regulated by CBER are excluded. Product concepts are characterized by dosage form, active ingredient/active moiety, strength and basis of strength. Product indexing files will be used to validate incoming SPL to ensure data elements are being listed consistently by sponsors and will be a basis for linking other SPL indexing initiatives.