Identification of Medicinal Products — Implementation and Use

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

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TABLE OF CONTENTS

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Identification of Medicinal Products — Implementation and Use Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION AND SCOPE

This guidance is for sponsors, applicants, and registrants who are involved in the regulatory submission of medicinal product[2] data. The guidance supports the development and implementation of the International Organization for Standardization (ISO) Identification of Medicinal Products (IDMP) standards for substances, terminologies, and other information for use throughout the global medicinal product development lifecycle.[3] The purpose of these standards is to enable improved accuracy, completeness, and consistency in the international exchange of medicinal product information among stakeholders.

The five IDMP standards, along with their corresponding technical specifications, were developed within the ISO network member organizations.[4] The standards, initially published by ISO in 2012, provide a framework to uniquely identify and describe medicinal products with consistent documentation and terminologies to provide for the reliable exchange of product information between global regulators, manufacturers, suppliers, and distributors. This framework includes data models, terms, definitions, and some controlled vocabulary code lists.

This guidance explains FDA's position and progress on aligning the Agency's standards to IDMP standards, which the Agency supports, to identify and describe marketed medicinal products with the exception of investigational medicinal products,[5] with the goal of harmonizing the standards for the international exchange of medicinal product data.

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[1]This guidance has been prepared by the Office of Strategic Programs in the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2017-D-6821 (available at https://www.regulations.gov/docket?D=FDA-2017-D-6821). See the instructions in that docket for submitting comments on this and other Level 2 guidances.

[2] ISO 11615 defines *medicinal product* as "…any substance or combination of substances that may be administered to human beings (or animals) for treating or preventing disease, with the view to making a medical diagnosis or to restore, correct or modify physiological functions." However, for purposes of this guidance, *medicinal product* will be used as a general term to describe human drug, biologic, and combination products as defined in FDA statutes and regulations. Blood and blood components used for transfusion are excluded.

[3]See https://www.fda.gov/industry/fda-resources-data-standards/identification-medicinal-products-idmp.

[4]See https://www.iso.org/home.html.

[5]See https://www.iso.org/standard/70150.html.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required

II. THE ISO IDMP STANDARDS

A. Substance Identification — ISO 11238

The ISO 11238[6] standard specifies the data elements and structures for unique identification and exchange of regulated information on substances.[7] It defines substances that are present in medicinal products in a scientifically consistent manner. The standard also includes information on specified substance levels, for example, grade, manufacturer, manufacturing, and quality information. The implementation of specified substance levels may depend on the type of substance and the particulars of a specific substance.

B. Dose Forms, Units of Presentation, Routes of Administration, and Packaging — ISO 11239

The ISO 11239[8] standard specifies the data elements and structures for unique identification and exchange of regulated information on pharmaceutical dose forms,[9] units of presentation, routes of administration, and packaging.

Each pharmaceutical dose form has six associated characteristics — state of matter, basic dose form, release characteristics, transformation, intended site, and administration method. The characteristics allow for pharmaceutical dose forms to be more easily identified, and for related pharmaceutical dose forms to be identified together more easily and in different ways. The ISO 11239 standard uses selected dose form characteristics for various use cases, such as global pharmaceutical product identification.

C. Units of Measurement — ISO 11240

The ISO 11240[10] standard defines the data elements and structures for unique identification and exchange of units of measurement. It specifies rules for standardized and machine-readable documentation of quantitative composition and strength of medicinal products; defines technical

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[6] See https://www.iso.org/standard/69697.html.
[7] For purposes of this guidance, substance refers to the medicinal product ingredients and moieties.
[8] See https://www.iso.org/standard/55032.html.
[9] According to the ISO 11239 standard, the *pharmaceutical dose form* can refer to the administrable dose form or the manufactured dose form. The standard defines *manufactured dose form* as the pharmaceutical dose form of a manufactured item, and an *administrable dose form* as the dose form that is administered to the patient, with or without any transformation of the manufactured dose form. The terms "dose forms" and "dosage forms" are used interchangeably throughout this document.
[10] See https://www.iso.org/standard/55033.html.

specifications for representation of units of measurement in coded form; and provides structures and rules for mapping between different unit vocabularies and language translations. The standard also specifies that for electronic data exchange of units of measurement, a single common reference vocabulary should be used.

D. Medicinal Product Identification — ISO 11615

The ISO 11615 specifies a unique Medicinal Product Identification (MPID) that is assigned regionally to each authorized medicinal product and can be supplementary to the existing authorization number.[11] The standard also specifies the data elements and their structural relationships for unique identification and exchange of regulated medicinal product information. Data elements that identify and characterize a medicinal product include:

- Medicinal product name[12] (authorized by regulatory agency)
- Clinical particulars (e.g., indications, contraindications)
- Pharmaceutical Product (e.g., substance, dose forms, routes of administration)
- Packaged medicinal product
- Marketing authorization (e.g., authorization number, application information, Marketing Authorization Holder)
- Manufacturer/establishment
- Versioning (e.g., regulated documents by region)

E. Pharmaceutical Product Identification — ISO 11616

The ISO 11616[13] standard specifies the data elements and structures for unique global identification and exchange of regulated pharmaceutical product information. The Pharmaceutical Product Identifiers (PhPIDs) are generated using the following attributes to link similar products across regions: active substance(s), strength(s)/reference strength(s),[14] and administrable dosage form(s). Global unique identifiers for the preceding attributes should be identified to enable the generation of global PhPID.

III. BENEFITS OF IDMP IMPLEMENTATION AND USE

Medicinal products are important components of health care and having accurate information about these products is important to ensuring patient safety. The interoperability of information systems and standards across the healthcare sector is important to reduce the risk of errors in data entry and interpretation, and to facilitate the use of advanced analytics to identify global medicinal product safety issues, including potential counterfeit products across global markets.

The IDMP standards should serve as common standards (for data elements and structure) for improved data sharing. These are internationally accepted standards for consistent

[11] See https://www.iso.org/standard/70150.html.
[12] Medicinal product name can be either an invented/trade name/proprietary name, a common/nonproprietary or proper name, a scientific name, or any other applicable descriptor.
[13] See https://www.iso.org/standard/70044.html.
[14] Reference strength is used as a reference from which the strength of a medicinal product is described.

documentation, coding, and exchange of product information among regulators, manufacturers, suppliers, and distributors. Further, their utility can be seen beyond regulatory purposes (e.g., in e-health records, and e-prescribing).

A. Drug Safety and Pharmacovigilance Using Common Substance and Product Identification

Global adoption of the IDMP standards can improve both drug safety efforts and pharmacovigilance by uniquely identifying and uniformly exchanging the IDMP medicinal product and substance identifiers between regulators in Individual Case Safety Reports (ICSRs) using the International Council for Harmonisation (ICH) E2B(R3) format.[15] As noted above, the use of the IDMP standards for ICSRs has potential to improve data quality and efficient processing by regulators, which may lead to improved accuracy of signal detection to associate adverse events and product quality defects to single or multiple products and substances globally.

B. Medicinal Product Traceability for Global Supply Chain Integrity

IDMP identifiers contain information, including the proprietary name, common name (e.g., nonproprietary or proper name), pharmaceutical dose form, strength(s), package size(s), and batch identification of the medicinal product. These identifiers may provide for greater visibility of the supply chain and lead to improved traceability and supply chain integrity to help protect patients from receiving poor quality or illegitimate products, like counterfeits.

C. Regulatory Registration and Exchange of Medicinal Product Information

The implementation and use of the IDMP standards should allow the identification and exchange of medicinal product information independent of registration origin. Some foreign countries operate under agreements that support the mutual recognition of product authorizations; therefore, it is beneficial to identify the same medicinal products authorized in different countries. Further, some countries may purchase medicinal products authorized by another regulatory authority and the full identity of those products may be unclear. The lack of clarity can also be problematic when one country requires marketing authorization/registration/licensing and another country does not. This is also problematic when a patient has a prescription from one country and wants to fill it in a different country. The implementation of the IDMP standards should provide more clarity in identifying pharmaceutically similar products across regions to support the mitigation of medicinal product shortages.

[15] See the guidances for industry *E2B(R3) Electronic Transmission of Individual Case Safety Reports (ICSRs) Implementatin Guide — Data Elements and Message Specification* (April 2022); *Appendix I (B) to the ICH E2B(R3) ICSRs Implementation Guide — Backwards and Forwards Compatibility* (April 2022); and *FDA Regional Implementation Guide for E2B(R3) Electronic Transmission of Individual Case Safety Reports for Drug and Biological Products* (April 2022). We update guidances periodically. For the most recent version, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

IV. FDA APPROACH TO THE IDMP STANDARDS

FDA supports the use of the IDMP standards to identify and describe medicinal products (excluding investigational medicinal products) and to facilitate the international exchange of medicinal product data.

In 2013, FDA established an internal committee to determine the conformance of FDA standards to the ISO IDMP standards. Over several years, the committee analyzed the structure, format, and content of the Unique Ingredient Identifier (UNII);[16,17] SPL (Structured Product Labeling) Pharmaceutical Dosage Form Terminology;[18] Unified Code for Units of Measure (UCUM), and National Drug Code (NDC) [19] to assess their conformance to ISO 11238, ISO 11239, ISO 11240, and ISO 11615, respectively. FDA's internal committee determined that the Agency's standards conform to the ISO IDMP standards for regional use. For global implementation of ISO 11616 (PhPIDs), global identifiers for substances and dose (dosage) forms will need to be defined. In the following sections, the FDA standards that conform to the ISO IDMP standards are discussed.

A. Unique Ingredient Identifier

ISO 11238 substance identification provides an information model to define and identify substances within medicinal products or substances used for medicinal purposes. The ISO 11238 standard identifies five types of substances: chemicals; proteins; nucleic acids; polymers; and structurally diverse materials, such as viruses, cells, and tissues (as well as mixtures). FDA has determined that the UNII code conforms to the ISO 11238 standard.

The UNII is an alphanumeric identification consisting of nine randomly generated alphanumeric characters and a check character. The UNII code is permanently assigned to the substance and can be used to identify the substance in each medicinal product.

Unique identification of substances[20] should enhance the regulatory review of active and inactive substances in submissions and should facilitate an understanding of the relationships to other substances and products from a quality, safety, and medicinal product use perspective.

FDA, in collaboration with the National Center for Advancing Translational Sciences (NCATS/National Institutes of Health (NIH)), has developed an ISO 11238-compatible Global

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[16] See https://www.fda.gov/industry/structured-product-labeling-resources/uniis-preferred-substance-names-and-their-identified-synonyms.
[17] See https://www.fda.gov/industry/fda-data-standards-advisory-board/fdas-global-substance-registration-system
[18] See https://thesaurus.cancer.gov/ncitbrowser/ConceptReport.jsp?dictionary=NCI_Thesaurus&version=21.04d&code=C54456&ns=ncit.
[19] See https://www.fda.gov/drugs/drug-approvals-and-databases/national-drug-code-directory.
[20] The use of the term "substance" or "substances" in this guidance is intended to be synonymous with the terms "component", active ingredient" and "inactive ingredient" as defined in 21 CFR 210.3. FDA regulatory determinations related to complex substances are based on current Agency standards and may not align with international substance standards in some cases.

Substance Registration System (GSRS). The GSRS software[21] and a public dataset are freely distributed by NCATS/NIH to enable companies and other interested parties to search for registered substances in the public domain and to identify substances in a manner consistent with ISO 11238.

B. SPL Pharmaceutical Dosage Form Terminology

ISO 11239 specifies the data elements and structures for unique identification and exchange of regulated information on pharmaceutical dose forms.[22] The standard does not specify that a region must map its dose form terms to a central terminology. FDA uses different dosage form terminologies for various use cases (e.g., SPL Pharmaceutical Dosage Form Terminology and United States Pharmacopeia (USP) Pharmaceutical Dosage Forms[23]).

As stated in section II.E, substance, administrable dose form, and strength are inputs into the generation of the PhPID. However, there is no global central dose form terminology that can be used for global PhPID. FDA is collaborating with regulators, standards development organizations, and other stakeholders to develop and finalize a solution that uses pharmaceutical dose form characteristics, in addition to substance and strength, to generate the global PhPID.

C. Unified Code for Units of Measure

ISO 11240 Units of Measurement specifies rules for the usage and coded representation of units of measurement for exchanging information about quantitative medicinal product characteristics such as strength.

The Unified Code for Units of Measure (UCUM) is a terminology standard that provides a system of coding units of measurement used in international science and medicine.[24] UCUM provides a single coding system for units of measurement that is unambiguous in electronic data exchange and assigns a concise meaning and definition to each defined unit code. It facilitates unambiguous electronic communication of quantities together with their units. UCUM is the ISO 11240-compliant standard for units of measurement for most medicinal products.

In September 2019, FDA announced the adoption of the most current set of the UCUM codes.[25] UCUM is the supported terminology standard and code system used for units of measurement in drug establishment registration and drug listing, and it is also recommended for use in the content of product labeling provided in regulatory submissions to the Center for Biologics Evaluation and Research and the Center for Drug Evaluation and Research.

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[21] See https://gsrs.ncats.nih.gov/ and https://precision.fda.gov/uniisearch.
[22] For the purposes of this guidance, the focus of the ISO 11239 standard is on dose (dosage) form.
[23] https://www.usp.org/
[24] See https://ucum.org/trac/wiki/adoption/common.
[25] See the *Federal Register* notice, "Electronic Submissions; Data Standards; Support for Unified Code for Units of Measure" (84 FR 47308, Sep. 9, 2019), available at https://www.federalregister.gov/documents/2019/09/09/2019-19346/electronic-submissions-data-standards-support-for-unified-code-for-units-of-measure).

D. National Drug Code

As discussed above, the ISO 11615 standard specifies a unique MPID that is assigned regionally to each authorized medicinal product and can be supplementary to the existing authorization number. FDA will continue to use the NDC as the unique identifier for U.S. medicinal products.

The NDC is composed of a labeler code, product code, and package code. The concept and specifications to assign labeler code, product code, and package code are comparable with the ISO 11615 concept and specifications for Marketing Authorization Holder Code, Medicinal Product Code, and the Package Description Code. Adding the two-letter Geopolitical Entities, Names, and Codes (GENC)[26] standard "US" country code[27] to the NDC results in a code comparable to the ISO MPID.

V. PHASED APPROACH TO GLOBAL IMPLEMENTATION

FDA is collaborating with various stakeholders, such as international standards development organizations (e.g., ISO, HL7 (Health Level 7 International)), regulatory agencies, and nongovernmental organizations to resolve issues that are impeding IDMP implementation beyond local or regional boundaries. FDA is working with these stakeholders to initiate and conduct projects leading to the establishment of a framework for the global implementation of the ISO IDMP standards and the maintenance of global identifiers. FDA intends for the framework to ensure that global PhPIDs and substance identifications are accessible to stakeholders for global drug safety and pharmacovigilance, global supply chain integrity and reliable exchange of product information, and that it will enhance the global availability of safe and effective medicinal products. FDA envisions that following the establishment of such a framework, global implementation of the IDMP standards should be conducted using a phased approach.

Further guidance and/or technical specifications will be provided, as needed, for global implementation of the IDMP standards.

[26] See https://nsgreg.nga.mil/genc/discovery.
[27] The two-letter GENC country code for US is the same as the two-letter ISO 3166-1 alpha 2 country code for US.