Logical Observation Identifiers Names and Codes for *In Vitro* Diagnostic Tests

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Guidance for Industry and Food and Drug Administration Staff

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For questions about this document, contact the Digital Health Unit in the Office of the Center Director at (301) 796-6900 or email: DigitalHealth@fda.hhs.gov.

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

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Preface

Public Comment

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Identify all comments with the docket number FDA-2017-D-6982. Comments may not be acted upon by the Agency until the document is next revised or updated.

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Guidance for Industry and Food and Drug Administration Staff

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 or Office responsible for this guidance as listed on the title page.

I. Introduction

The Food and Drug Administration (FDA or Agency) recognizes that with the increasing implementation of electronic health records (EHR), there has been a greater demand to standardize the way that *in vitro* diagnostic (IVD) tests are coded. Efforts to harmonize and standardize information captured and stored in electronic healthcare systems carry important implications for public health, including expediting access to patient diagnostic information for healthcare providers, reducing burdens on laboratories for connecting new diagnostic systems to Laboratory Information Systems (LIS), and facilitating the use of healthcare information for decision support tools, in addition to many more potential uses.

Information from IVD tests form a significant proportion of all EHRs. Laboratories commonly associate a LOINC® (Logical Observation Identifiers Names and Codes; owned, developed, and curated by the Regenstrief Institute)[1] code with each test being performed by a laboratory. For each IVD test, LOINC provides a unique numeric code associated with test attributes that identify the type of IVD test such as the component, property, time, system, scale and method.[2] At present, LOINC is the IVD coding system that is most widely used by clinical laboratories and EHRs, and is the IVD coding standard recommended by the Office of the National Coordinator for Health Information Technology (ONC) in the U.S. Department of Health and Human Services (HHS) as an essential part of meaningful use. LOINC is a partially FDA-

[1] *See* http://loinc.org/
[2] https://loinc.org/get-started/loinc-term-basics/

recognized consensus standard, where the recognition is limited to IVD tests. To review the classes of LOINC that are currently not recognized by FDA, see the FDA Recognized Consensus Standards Database Web site.[3]

It is important to distinguish between LOINC codes and Unique Device Identifiers (UDIs). The LOINC coding system identifies the type of laboratory test being performed, and the UDI identifies a specific model/version of a regulated laboratory device made by a specific manufacturer.[4] This guidance neither addresses nor affects the requirements related to the assignment of UDIs for regulated devices.

FDA's guidance documents, including this guidance, 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 guidance means that something is suggested or recommended, but not required. Similarly, the use of "should not" in this guidance does not suggest or create an independent legal prohibition, but indicates a recommended practice.

II. Background

The essential role of semantic interoperability in healthcare information technology has been well recognized.[5] Executive Order 13410 defines interoperability as "the ability to communicate and exchange data accurately, effectively, securely, and consistently with different information technology systems, software applications, and networks in various settings, and exchange data such that clinical or operational purpose and meaning of the data are preserved and unaltered."[6] FDA's "Study Data Technical Conformance Guide" further defines semantic interoperability as "the ability of information shared by systems to be understood, so that nonnumeric data can be processed by the receiving system. Semantic interoperability is a multi-level concept with the degree of semantic interoperability dependent on the level of agreement on data content terminology and other factors. With greater degrees of semantic interoperability, less human manual processing is required, thereby decreasing errors and inefficiencies in data analysis. The use of controlled terminologies and consistently defined metadata support semantic interoperability."[7]

The unambiguous and consistent representation of laboratory tests is essential for achieving many of the potential benefits of electronic health records. Semantic interoperability is essential for developing decision support algorithms that can access and seamlessly aggregate data from multiple systems. For instance, in the context of infectious diseases, semantically interoperable EHR systems can allow for more efficient tracking of outbreaks or significant public health

[3] *See* recognition consensus standards page for LOINC at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/detail.cfm?id=32889.
[4] *See* http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/UniqueDeviceIdentification/.
[5] *See* the shared nationwide interoperability roadmap at https://www.healthit.gov/sites/default/files/hie-interoperability/nationwide-interoperability-roadmap-final-version-1.0.pdf.
[6] *See* Executive Order 13410, Promoting Quality and Efficient Health Care in Federal Government Administered or Sponsored Health Care Programs, available at https://www.gpo.gov/fdsys/pkg/FR-2006-08-28/pdf/06-7220.pdf
[7] *See* "The Study Data Technical Conformance Guide," available at https://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM384744.pdf

threats by providing access to evaluable real-time IVD test information from multiple geographic locations. Consistent representation also allows EHR databases to be used to study diagnostic assays without having to adjust for different coding schemes at individual sites. Examples of studies using EHR databases might include post marketing studies that address the need for rapid nucleic acid assays to be routinely followed by conventional confirmatory methods, or studies that assess IVD performance in different clinical environments. Potential analysis of standardized data holds great promise for providing access to real-world evidence that may be useful for future regulatory actions. Unambiguous and consistent representation of IVD tests in EHRs can also minimize potential errors as information is transmitted across systems (for example, by ensuring that the correct units for test results are always maintained), helping to minimize patient risks as systems become increasingly interconnected.

Semantic interoperability should be considered as a specific application of general interoperability. FDA's support of the adoption of a uniform LOINC coding system for IVD tests is consistent with other FDA efforts in promoting aspects of medical device interoperability.[8]

III. Scope

As FDA seeks to encourage consistency in the coding of IVD tests, this guidance addresses questions regarding the distribution of LOINC codes by IVD test manufacturers to users, primarily clinical laboratories and software vendors. This guidance is restricted to the appropriate use of LOINC codes for specific types of IVD tests, and does not address the coding of test results for interoperability, for example, through the use of response sets within coding systems such as SNOMED-CT (Systematized Nomenclature of Medicine – Clinical Terms) or LOINC. It also does not address unique device identification (UDI), which identifies individual devices as required by statute and regulation.[9]

IV. LOINC Coding of IVDs

A. Is LOINC-coding mandated by FDA for IVD tests?

No. LOINC, or any similar coding system for IVD tests, is voluntary and not required by FDA.[10] FDA, however, strongly encourages the use of consensus standards for coding of IVD tests and specifically recognizes the utility of LOINC for this purpose.[11]

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[8] *See* "Medical Device Interoperability," available at http://www.fda.gov/medicaldevices/digitalhealth/ucm512245.htm.

[9] *See* http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/UniqueDeviceIdentification/.

[10] As stated earlier, this guidance neither addresses nor affects UDI requirements.

[11] *See* recognition consensus standards page for LOINC at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/detail.cfm?standard__identification_no=32889.

B. Should manufacturers include LOINC codes in device labeling?

FDA supports the voluntary inclusion of LOINC codes for IVD tests in labeling if the information is accurate and consistent with the approved or cleared indications for the device. FDA does not intend to perform premarket review of LOINC codes that manufacturers may choose to provide to clinical laboratories or to other users. However, device labeling remains generally subject to other requirements of the Federal Food, Drug, and Cosmetic Act, including misbranding and adulteration.

Manufacturers may choose to include LOINC codes in printed labeling or to include a reference to a location external to the labeling that lists or otherwise provides LOINC codes for the IVD test. For example, labeling could include a hyperlink to a web site with a table of LOINC codes associated with the manufacturer's test(s). LOINC codes incorporated directly into devices – for example, LOINC codes included with device output that is directly transferred to an external system such as an LIS – may be subject to quality system requirements applicable to the device.

C. What are FDA's views on manufacturers providing LOINC codes for uncleared or unapproved indications for use?

In general, LOINC codes provided by the manufacturer should be consistent with FDA-cleared or FDA-approved Indications for Use for that IVD test. A manufacturer's dissemination, through, for example, inclusion in printed labeling or on manufacturer website, of a LOINC code that suggests an unapproved or uncleared indication for use may be considered evidence of a new intended use and result in the device being considered adulterated and/or misbranded under the FD&C Act.[12]

However, FDA understands that a clinical laboratory or other persons may make individual, unsolicited requests to manufacturers for LOINC codes for specific uncleared or unapproved indications for use. In that event, where the manufacturer's response provides the appropriate LOINC coding for the specific circumstance named in the request or identifies the need for a new LOINC code to address the clinical use referenced in the request, FDA does not intend to consider that response as evidence of the firm's intent that the product be used for unapproved or uncleared uses.[13]

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[12] *See* sections 501(f)(1), 502(o), 513(f)(1), and 515 of the FD&C Act (21 U.S.C. 351(f)(1), 352(o)), 360c(f)(1), and 360e). S*ee also* FDA's guidance for industry *Drug and Device Manufacturer Communications with Payors Formulary Committees, and Similar Entities – Questions and Answers* available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm537347.pdf

[13] *See, e.g.*, FDA's draft guidance *Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices Practices* available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm285145.pdf. When final, this guidance will represent FDA's current thinking on this topic.

This guidance does not alter the requirements for when IVD tests are required to submit a new premarket notification submission (510(k)) or new Premarket Approval Application (PMA). Additionally, this guidance does not affect requirements applicable to clinical laboratories under other statutes or regulations currently in place.

D. Does FDA recommend a specific format for distributing LOINC codes?

No. There is no specific FDA recommended format for distributing LOINC codes. FDA acknowledges that LOINC codes may be displayed as simple text in a table format, or in structured formats such as Java Script Object Notation (JSON) or Extensible Markup Language (XML).

However, FDA strongly encourages the use of an FDA-recognized consensus standard as the mechanism to communicate or disseminate the LOINC codes provided by manufacturers or others (for example, the Regenstrief Institute), to laboratories or other end users. The LOINC transmission document for IVDs (LIVD) standard is one communication standard explicitly developed for this purpose by the IVD Industry Connectivity Consortium.[14] Standardized formats can facilitate a laboratory's ability to adopt new LOINC codes, incorporate updates or changes to existing LOINC codes, and maintain a database of LOINC codes applicable for local use. FDA recommends that manufacturers follow developments in this area as standards for electronically transmitting recommended LOINC codes are modified or expanded, or as new standards emerge, as these may further contribute to greater semantic interoperability within and across laboratories.

[14] See http://ivdconnectivity.org/livd/