In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only

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Distribution of In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only

Guidance for Industry and Food and Drug Administration Staff

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For questions regarding this document contact Elizabeth Mansfield, by phone at (301) 796-4664, or by email at elizabeth.mansfield@fda.hhs.gov. For questions relating to devices regulated by CBER, contact the Office of Communications, Outreach and Development, CBER at 301-827-1800 or 800-835-4709.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of In Vitro Diagnostic Device Evaluation and Safety

Center for Biologics Evaluation and Research

Outline of Presentation

- **Definitions of RUO and IUO products**
- **FDA Concerns Regarding Distribution of RUO and IUO Labeled IVD Products**
- **Regulatory Requirements for RUO and IUO Products**
- **Labeling and Distribution of RUO and IUO Products**
- **FDA's compliance approach**
- **Summary**

RUO IVD Products

An RUO product is an IVD product that is in the laboratory research phase of development and is being shipped or delivered for an investigation that is not subject to investigational device regulation, 21 CFR part 812

Examples of RUO IVD Products

- Tests that are in development to identify test kit methodology, kit components and analytes to be measured

- Instrumentation, software, or other electrical/mechanical components under development to determine correct settings, subcomponents, subassemblies, basic operational characteristics and possible use methods

Examples of RUO IVD Products : Cont'd…..

- Reagents under development to determine production methods, purification levels, packaging needs, shelf life, storage conditions, etc.

- Other types of products for use in non-clinical research

IUO IVD Products

An IUO product is an IVD product that is being shipped or delivered for product testing that is not subject to the Investigational Devices regulation prior to full commercial marketing

Examples of IUO IVD Products

- IVD products under investigation that are being evaluated in comparison studies that use archived or fresh specimens to determine performance characteristics

- Used in studies to collect supporting data for device premarket application

FDA Concerns Regarding Distribution of RUO and IUO Labeled IVD Products

- Use of unapproved/uncleared IVD products labeled as RUO or IUO in clinical diagnostic use

- These products have unproven performance characteristics and may have inadequate manufacturing controls to ensure consistent manufacturing of the finished product

FDA Concerns Regarding Distribution of RUO and IUO Labeled IVD Products – cont'd…..

- Healthcare providers and patients are unaware that these products are for RUO or IUO, i.e. not intended for clinical dx.

- Misleads the healthcare provider and may cause serious harm to patients

Regulatory Requirements for RUO Products

RUO products are exempt from

- Premarket notification and premarket approval, i.e. 510(k) and PMA
- Compliance with Quality Systems regulation
- Registration and Listing
- Exempt from IDE regulation

Regulatory Requirements for RUO Products: Labeling

- Should not be represented as an effective IVD product

- All labeling must bear the following statement which is prominently placed:

"***For Research Use Only.***

Not for Use in Diagnostic Procedures."

Regulatory Requirements for IUO Products

IUO products are exempt from

- Premarket notification and premarket approval as long as they are appropriately labeled
- Compliance with Quality Systems regulation, if exempt from Investigational Devices regulation
- Registration and listing

Regulatory Requirements for IUO Products: Labeling

All labeling must bear the statement, which is prominently placed:

"***For Investigational Use Only. The performance characteristics of this product have not been established***"

Distribution of RUO and IUO Products

Practices considered to be inconsistent with RUO/IUO labeling:

- Inclusion of any performance claims
- Providing instructions for clinical interpretation
- Providing clinical information
- Providing aid or assistance to the clinical laboratory in validation/verification of a test that uses RUO/IUO labeled IVD products
- Product names or descriptors that claim or suggest the IVD product may be used for any clinical diagnostic use including a clinical investigation subject to IDE regs.

Practices Considered Inconsistent with RUO/IUO Labeling, cont'd…

- Claims or suggestions that clinical laboratories can validate the test through their own procedures and subsequently offer it for clinical diagnostic use as a laboratory developed test

- Solicitation of business from clinical laboratories; for example, a manufacturer who produces only products labeled RUO whose sales force makes routine calls to clinical laboratories that do not perform research

Practices Considered Inconsistent with RUO/IUO Labeling, cont'd…

Past history of distribution of a product intended for clinical diagnostic use as an analyte specific reagent (ASR), but the product is now labeled as RUO or IUO, without any change in distribution practices such as advertising to and solicitation of business from clinical laboratories

Practices That May Be Consistent With RUO/IUO Labeling

- Providing basic instructions for correctly using the product in a research manner (for example, mixing proportions, incubation times, storage conditions, etc.)
- Providing instructions for use by the manufacturer for IUO labeled IVD products that are the subject of a clinical investigation
- Providing general support services - general repair or maintenance and general non-diagnostic use-specific technical support

Practices That May Be Consistent With RUO/IUO Labeling, cont'd…..

Software Labeled RUO or IUO

Stand-alone software that is designated as an IVD or software that is a component or accessory to an IVD labeled as RUO or IUO may be distributed for research or investigational use to entities conducting research or investigations with the software

FDA's Compliance Approach

- The RUO/IUO guidance is intended for the manufacturers and distributors of IVDs

- Manufacturers must comply with all applicable requirements under the FFD&C Act and FDA regulations for those IVDs that are intended for clinical diagnostic applications

FDA's Compliance Approach – cont'd

FDA will consider the totality of the circumstances concerning a manufacturer's sale and distribution of a product labeled as RUO or IUO before determining non-compliance, i.e. FDA does not generally intend to focus on an isolated incident or aspect when determining compliance

User Certification Program

- Manufacturers may ask users to certify that they will not use RUO/IUO products in a manner inconsistent with the labeling for these devices

- This would be one factor that may be considered when assessing the circumstances surrounding the distribution and use of RUO or IUO product. This is acceptable but not sufficient

Reasons for Compliance Actions

- **Distribution of a Misbranded Device (FFDC&A Sec 502)**
  - False and misleading labeling
  - Failure to register
  - Failure to provide directions for use and warnings

An IVD product that is labeled RUO or IUO but is not intended for research or for investigational purposes is considered misbranded

- **Distribution of an Adulterated Device (FFDC&A Sec 501)**
  - Failure to obtain premarket approval

Summary

- FDA issued this guidance as a reminder to manufacturers of RUO and IUO IVD products of the distribution and labeling requirements applicable to these devices

- FDA expects manufacturers to follow this guidance

- If there are questions regarding the RUO/IUO designation of an IVD product, please contact OIR/FDA

Thank you!

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