New Developments at the FDA – Final LDT Rule, Harmonization of ISO 13485, Memo on Reclassification of Certain Assays, and More

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Disclaimers

Agenda and,
What Does It All Mean?

- IVD Pilot for Certain Oncology Drugs
- MCDs
- Down Classification of Some CDx tests and Other IVDs
- Harmonization of ISO 13485 and FDA QSRs
- RUO/IUO Kit Use in CLIA Labs
- Final LDT Rule and Potential Legislation

2023 Pilot for Certain Oncology Drugs Used with Certain IVD Tests

- Announced June 21, 2023 “…to provide greater transparency regarding performance characteristics that certain oncology biomarkers used for selection of oncology drug products should meet” in an effort “to support better and more consistent performance of LDTs resulting in better drug selection and improved care…”
- Oncology Drug Developers can apply
- Data is collected on any tests used for drug selection to inform the reviews of the oncology drug submission

Multi Cancer Detection Assays

- Dozens of assays are in development
- Some have launched clinically as an LDT
- None have been FDA approved
- The FDA is highly likely to approve assays that accurately detect cancers, especially for cancers that are without a formal screening program
- Reimbursement challenges

Down Classification of Some CDx Tests and Other IVDs

- On January 31, 2024 the FDA made known its decision to initiate a reclassification process for most IVDs that are currently Class III to Class II
- The FDA has prior exempted more than 1,000 IVDs from FDA review
- FDA reclassified HCV on November 19, 2021. Per Timothy Stenzel….'Today's action allows manufacturers of….HCV tests….to seek marketing clearance…rather than…a PMA"…
- In 2023, FDA began the process of reclassifying HBV and certain other IVDs to class II

Harmonization of ISO 13485 and FDA QSRs

- The FDA through the International Medical Device Regulators Forum (IMDRF) has been advocating for international harmonization of regulatory oversight
- The Medical Device Single Audit Program (MDSAP) has seen considerable and growing success
- Filling in the gaps between ISO 13584 and Quality System Regulation (QSR) was announced January 31, 2024 in a Final Rule leading to the new Quality Management System Regulation (QMSR)
- This will ease work for those test developers who operate both in the US and Internationally

RUO Reagent and Kit Use in CLIA Labs

- The use of RUO reagents and kits in test development is commonplace and can be in line with FDA regulations, if certain items are followed
- Test developers can incorporate RUO reagents and kits into their tests as long as they take responsibility for the full validation and oversight of their use (stay tuned)
- Developers of RUO reagents and kits would be wise to pay close attention to the 2013 FDA Guidance on research use only (RUO) and investigational use only (IUO) products

Final LDT Rule and Potential Legislation

- The Final rule was announced on 4/29/2023, in force 60 days after publishes. Makes one change to the definition of an IVD product “including when the manufacturer of these products is a laboratory.”
- Phaseout Period (by end of each period)

  1 Year – comply with MD(AE) reporting and reporting of corrections and removals

  2 Years – comply with labeling, registration and listing, and investigational use requirements

  3 Years – QS [v light, light and full] – records and sometimes design controls and purchasing controls

  3.5 Years – comply with high risk (class III) premarket review requirements (PMA)

  4 Years – comply with moderate and low risk premarket review requirements moderate and low
- Enforcement Discretion (ED) continues for Forensic, HLA, PH Surveillance and pre-1976 type LDTs (manual)
- Excluded from ED – EUAs, DTC (stay tuned for more details) and donor screening

Preliminary Thoughts

- Looks like (nearly) everyone got something, more on this later
- Exclusions – DoD, VA, Integrated Health Systems, Unmet needs, Tests launched prior to Rule, NYS approved
- NYS may be swamped for a long long time
- The FDA will likely very busy for a long time with Pre-Subs and Q-Subs seeking specific clarifications
- EUAs – PHL provisions (see two new draft guidances)
- Lawsuits - ???
- Legislation
- Possible that no LDT lab would have to submit to FDA?
- Status of RUO Kits developed for Clinical Labs

Thank you