



Regulation of IVDs



**U.S. FOOD & DRUG
ADMINISTRATION**

Kristian Roth, Ph.D.

Branch Chief

Bacterial Multiplex and Medical Counter Measures

Division of Microbiology

Center for *in vitro* Diagnostics and Radiological Health (CDRH)

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Definition:

“In Vitro Diagnostic Device”

“Reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. ... for use in the collection, preparation, and examination of specimens from the human body.”

[21 CFR 809.3]

Risk Based Regulatory Framework



Goals:

Get safe and effective devices to market as quickly as possible (premarket review).

Ensure that currently marketed devices remain safe and effective (postmarket enforcement).

Classification of *In Vitro* Diagnostics

Classifications for IVDs are based on the estimation of the degree of risk a patient is exposed to if a test returns a false result.

Class I: Lowest Risk PMN Exempt

Class II: Moderate Risk 510(k)

Class III: High Risk PMA

Unclassified devices: De Novo

Is there recommended follow up?
Will treatment be delayed?
Will treatment be inappropriate?

Is the specimen type appropriate
for the claim?

Intended Use of the Device

The “**Intended Use**” defines the device claims

- Who will be tested, where, and when
- What are the appropriate specimens
- How result(s) may be used in patient management

Evolving Landscape

- 2013: XPERT MTB/RIF ASSAY Down classification
 - does not provide confirmation of rifampin susceptibility since mechanisms of rifampin resistance other than those detected by this device may exist that may be associated with a lack of clinical response to treatment
 - presence of rifampin-resistance associated mutations of the *rpoB* gene is confirmed, specimens should also be tested for the presence of genetic mutations associated with resistance to other drugs
 - must be used in conjunction with mycobacterial culture to address the risk of false negative results and to recover the organisms for further characterization and drug susceptibility testing

Evolving Landscape

- 2014: XPERT MTB/RIF ASSAY
 - Assay result of “MTB NOT DETECTED” from either one or two sputum specimens is highly predictive of the absence of *M. tuberculosis* complex bacilli on serial fluorescent acid-fast sputum smears from patients with suspected active pulmonary tuberculosis and can be used as an aid in the decision of whether continued airborne infection isolation (AII) is warranted in patients with suspected pulmonary tuberculosis

Next steps:

Improved run time and sensitivity

Pediatrics

Further Evolution

- Leverage existing information of known quality
 - Peer reviewed data/ clinical trials data
- Change is not built into the 510(k) paradigm
 - Creative approaches are needed
- Tiered results reporting may be possible
 - High quality and low quality results
 - Biomarker model where probabilities are reported
- To move forward, a proposal is needed.

Principles of a Successful IVD Pre-Market Submission to FDA

- Clear & precise “intended use” (IU)
- Complete device description
- Scientific evidence supporting the IU
 - Clinical validity has been established
- Data establishing safety and effectiveness of the device
 - Compared to current well accepted method
- Good Mfg. Quality System in place



Consider using Pre-Submission Review (Pre-Sub)

Free protocol review by FDA

Specific sponsor questions and device IU determine the nature of FDA feedback

Allows informal discussion of potentially complicated questions regarding:

Regulatory pathway

Study design

Not binding on the FDA or sponsor

max 75 day review timeline

Interactive, flexible, confidential

Useful Sources of Information

Search: FDA Device Advice

Device Advice: Comprehensive Regulatory Assistance - FDA

www.fda.gov/MedicalDevices/DeviceReg... ▾ Food and Drug Administration ▾

Aug 9, 2016 - Welcome to Device Advice, the Food and Drug Administration's (FDA's) Center for Devices and Radiological Health (CDRH) web page for ...

Overview of Device Regulation

Overview of regulations for ... of
Medical Device Regulation ...

Investigational Device ...

An investigational device exemption
(IDE) allows the ...

Product Code Classification ...

The Product Classification Database
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