Introduction: COVID-19

The impact of COVID-19 is widespread and implicates a broad array of legal issues.

To assist our clients in navigating this unprecedented situation, we have created a COVID-19 Task Force and assembled a COVID-19 Toolkit.

Please see our COVID-19 Toolkit and reach out to any of us or the Covington COVID-19 task force at COVID19@cov.com.

COVID-19 Toolkit: Legal and Business Considerations
Introduction: COVID-19

This slide deck focuses on FDA regulatory issues medical device manufacturers are and will be facing during the COVID-19 public health emergency.

- Premarket Considerations
- Postmarket Considerations
- Emergency Use Authorization and Related Policies
- Diagnostic Considerations: IVDs and LDTs
- Digital Health
- Key EU Considerations
Premarket Considerations
How will premarket interactions and reviews be affected?

- All eligible FDA employees are teleworking, and in-person meetings have been canceled.
- Pre-submission and informational meetings are being transferred to conference calls or webex/video conferencing.
- Advisory Committee (Panel) meetings are being postponed.
- Review times may increase for premarket submissions.
What can I do in response to delays?

- Be patient and maintain positive relationships with reviewers
- Provide complete responses
- Ensure slide decks for meetings and video conferences are thorough and detailed
- Build anticipated delays into product development timeline
How should I handle COVID-19 disruptions to my clinical study?

Ensuring the safety of trial participants is paramount

<table>
<thead>
<tr>
<th>Study Protocol</th>
<th>Policies and Procedures</th>
<th>Final Clinical Study Report</th>
</tr>
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<tbody>
<tr>
<td>• Engage early with investigators and IRB to consider changes to protocol</td>
<td>• Informed consent</td>
<td>• Description of implemented contingency measures</td>
</tr>
<tr>
<td>• Prospectively define procedures to prioritize reporting of deviations that may impact the safety of subjects</td>
<td>• Study visits &amp; procedures</td>
<td>• List of affected participants &amp; description of how participation was affected</td>
</tr>
<tr>
<td>• Consult with review division regarding protocol modifications for the collection of effectiveness endpoints, or changes that affect data management and/or SAP</td>
<td>• Data collection</td>
<td>• Analyses &amp; discussions addressing impact of contingency measures on safety and effectiveness results</td>
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<tr>
<td>• Carefully document protocol changes and deviations</td>
<td>• Personnel (e.g., due to travel limitations, quarantine)</td>
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<td></td>
<td>• Adverse event reporting</td>
<td></td>
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<td></td>
<td>• Monitoring procedures</td>
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<td></td>
<td>• Quarantine measures</td>
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<tr>
<td></td>
<td>• Measures to deal with COVID-19 illness</td>
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For more information, see Covington’s client alert: FDA Releases Guidance on Clinical Trial Conduct During COVID-19 Pandemic
Postmarket Considerations
Are there any changes to FDA’s facility inspection schedule?

**Foreign Inspections**
- As of March 10, routine surveillance inspections postponed until May
- Alternative FDA tools
  - Increased import screening, examinations, and sampling at ports
  - Expect delays in FDA’s ability to generate and mail hard-copy Notices of FDA Action (release notices, sampling notices, etc.)
  - Reliance on mutual recognition agreements with other governments
  - Inspection record requests in lieu of onsite inspection

**Domestic Inspections**
- As of March 18, all domestic routine surveillance facility inspections are temporarily postponed
- All domestic “for cause” inspection assignments will be evaluated and will proceed if mission critical
- Alternative FDA tools
  - Inspection record requests in lieu of onsite inspection
How do I best utilize my limited quality resources?

Use a risk-based approach to prioritize quality operations

Assess patient risk of incomplete or delayed activities

• Update risk management file (RMF) to include recent complaints, adverse events, non-conformances, and health hazard evaluations (HHE)
• Document rationale for prioritization
• If patient risk unacceptable, take appropriate action
How do I maintain QSR compliance if understaffed?

- Ensure procedures, work instructions, and/or process aides are easily accessible throughout the organization in case employees are tasked with unfamiliar activities.
- Ensure clear access to QSR element owners or a “go-to” person for any QSR related questions.
- Conduct frequent check-ins with staff.
- Consider whether processes can be streamlined without compromising compliance.
How do I keep up with MDR Reporting timelines?

- Maintain normal MDR Reporting processes to maximum extent possible
- If not possible due to high employee absenteeism then:

  Document:
  - Declaration of pandemic high absenteeism and/or other factors (e.g., an increase in adverse event reporting) that prevent firm from meeting deadlines
  - FDA Guidance: “Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During a Pandemic” (March 2020); see also Covington’s client alert on the guidance.

  Submit 5-day reports as required by MDR regulation
  - Submit deaths within 30 calendar days
  - Maintain records of serious injury and malfunction reports

  Submit MDRs for “stored” serious injuries and malfunctions within 6 months of restoration of processes to pre-pandemic state
What if I cannot conduct internal audits?

Document internal audit waivers

- Use compliance history of previous audits, including significance of findings

In absence of supplier audits, develop alternative plan for supplier control, e.g.,

- Use document review (desk audit)
- Increased sampling
- Validate supplier manufacturing process
Do I have to notify FDA if personnel contract the virus?

There is no requirement to report the health of personnel to FDA. But state or local boards of health may have notification requirements.

Conduct a health hazard assessment and document any product impact. Clean and sanitize the facility.

Evaluate SOPs regarding control of personnel with communicable diseases and facility cleaning/disinfection.

In addition, interview affected persons, determine which other employees they interacted with, and notify other affected personnel, consistent with applicable privacy laws.
How is FDA enforcing against COVID-19 product promotion?

On March 9, FDA and FTC jointly issued Warning Letters to seven companies for making false and misleading claims that their products could prevent, treat, or cure COVID-19.

Cross-agency task force established to “closely monitor for fraudulent products related to COVID-19.”

On March 20, FDA issued a press release concerning unauthorized fraudulent COVID-19 test kits, including kits marketed to test for COVID-19 in the home. FDA has not yet authorized any test for this particular intended use.

The Agency referenced the Warning Letters issued on March 9 and said it expects additional actions will be forthcoming. FDA is increasing enforcement at ports of entry, including International Mail Facilities, and created an email address for the reporting of fraudulent products.
Emergency Use Authorization and Related Policies
What is an Emergency Use Authorization (EUA)?

- FDCA § 564 gives FDA the authority to authorize the introduction into interstate commerce of unapproved medical products, or unapproved uses of approved medical products when there is a public health emergency related to a chemical, biological, radiological, or nuclear (CBRN) agent.
When can FDA issue an EUA for COVID-19?

For FDA to issue an emergency use authorization (EUA) for a particular product, three things must happen:

1. HHS determines a public health emergency exists
   - HHS made determination on Feb. 4, 2020

2. HHS declares circumstances exist justifying emergency use
   - Feb. 4, 2020 declaration for *in vitro* diagnostics
   - Mar. 2, 2020 declaration for personal respiratory protective devices
   - New declaration needed for any additional product types

3. FDA grants EUA for specific products
   - FDA must determine that four criteria are met for each product (see next slide)
Is my product eligible for an EUA for COVID-19?

- FDA may issue an EUA for an individual product if the following four criteria are met:
  - The CBRN agent or infectious disease at issue is capable of causing a serious or life-threatening disease or condition
  - Based on the totality of the scientific evidence available, the product "may be effective" in diagnosing, treating, or preventing the serious or life-threatening disease or condition
  - The known and potential benefits of the product, when used to diagnose, prevent, or treat the disease or condition outweigh the known and potential risks of the product
  - There is no adequate, approved, and available alternative to the product
How do I request an EUA for COVID-19?

What should my request include?
- Description of product, intended use, and current approval status
- Need for product and alternatives
- Available safety and effectiveness data and risk-benefit discussion
- Manufacturing controls and GMP status
- “Fact Sheets” for HCPs and recipients and instructions for use

Where do I send my request?
- E-mail request to CDRH cdrhemcm@fda.hhs.gov
  - With e-mail alert to: EUA.OCET@fda.hhs.gov

When will FDA respond to my request?
- No set process or time period for FDA action on EUA request; driven by number of factors
- FDA has shown extraordinary level of responsiveness
If I receive an EUA, what does that mean?

- Subject to conditions of the EUA, which may include:
  - Requirements to inform administering HCPs and recipients of product of key information (“Fact Sheet”), including:
    - Product subject to an EUA
    - Significant known benefits and risks
    - Alternatives
    - Description of product
  - Requirements to monitor and report adverse events
  - Limitations on distribution, administration, and advertising
- Authorization ends when HHS determines circumstances that justified declaration have ended (or product receives approval/clearance)
What is my liability for an EUA-authorized product?

Manufacturer of device authorized under EUA is eligible for liability immunity under the Public Readiness and Emergency Preparedness Act (PREP Act)

- Mar. 10, 2020, HHS issued a PREP Act declaration for COVID-19 covered countermeasures
- Declaration created liability immunity for manufacture, testing, development, distribution, administration and use of covered countermeasures
- Covered countermeasures include any device used to treat, diagnose, cure, prevent, or mitigate COVID-19 or the transmission of SARS-CoV-2
When does an EUA end and what happens then?

- **Authorization ends when HHS determines circumstances that justified declaration have ended (or product receives approval/clearance)**

- **Products can no longer be distributed or used for conditions authorized under EUA**
  - *Except*, may continue use in any patient who began treatment before termination, to the extent found necessary by the patient’s attending physician

- **Manufacturers must manage disposition of products** (e.g., return or disposal)

- **Further distribution and use must be in compliance with either FDA premarket review requirements or investigational device requirements**
Has FDA granted any EUAs for COVID-19?

13 EUAs issued for diagnostics tests as of Mar. 20, 2020

NIOSH-approved disposable filtering facepiece respirators
What is the scope of the EUA for respirators?

- FDA authorized for use in healthcare settings:
  - All disposable filtering facepiece respirators (FFRs) approved by NIOSH as non-powered air-purifying particulate FFRs
  - FFRs that were NIOSH-approved but have since passed the manufacturers' recommended shelf-life
- Currently authorized respirators listed [here](#)
  - Includes N95, N99, N100, P95, and R95 filtration class respirators
  - FDA also maintains list of respirators that are eligible for authorization, contingent upon submission of a request from CDC, the manufacturer, or strategic stockpiler to FDA
- Masks, face shields, and other products that are not NIOSH approved are not within this EUA and would require separate EUA
Will FDA issue an EUA for ventilators?

- FDA stated interest in working interactively with manufacturers of ventilatory support devices that are not currently legally marketed in the U.S. to facilitate EUA
  - Submit information (contact info; labeling; information regarding foreign marketing authorization, compliance with recognized standards, QSR compliance status; and compatibility of power supply) to CDRH-COVID19-Ventilators@fda.hhs.gov

- FDA welcomes opportunity to work with manufacturers who have not previously been engaged in medical device manufacturing and have capability to increase supply of ventilator support devices
  - Send email to CDRH with proposed approach
What flexibility is FDA offering outside of the EUAs?

- FDA is collaborating with manufacturers and/or has issued policies to increase supply of:
  - Personal protective equipment (PPE), in particular surgical masks and surgical or isolation gowns
  - Patient monitoring devices
  - Ventilators and other respiratory devices
- FDA may consider granting expedited review to PPE manufacturers for premarket submissions or manufacturing site changes
  - Manufacturers can contact FDA regarding plans to increase availability of PPE
Can I make changes to patient monitoring devices without FDA review?

- Enforcement policy permits modifications to FDA-cleared non-invasive patient monitoring devices (e.g., cardiac monitors, ECG, NIBP) without a new 510(k)
  - Statements related to COVID-19 patients
  - Indications or claims regarding use in home setting
  - Hardware or software changes to increase remote monitoring capabilities
- Considerations
  - Changes to indications, claims or functionality cannot present undue risk (e.g., device cannot be intended to determine when patients need immediate clinical intervention)
  - Changes to hardware and software must not directly affect the physiological parameter measurement algorithms
Can I make changes to ventilators without FDA review?

- Enforcement policy permits modifications to the indications, claims, functionality, or to the hardware, software, or materials of FDA-cleared ventilators and other respiratory devices, e.g., to allow alternative supplier or more flexible sourcing, where no undue risk. Examples:
  - Use of ventilators outside of cleared use environment, and use of oxygen concentrators for primary supply when medically necessary and clinically appropriate
  - Modifications to motors, batteries, or other electrical components, and introduction of filtration to minimize aerosolization

- Enforcement policy also allows changes in the indicated shelf life and use duration where no undue risk, e.g., where devices are used according to healthcare institutional protocols, or useful life is limited to the occurrence of malfunction or visible soiling

- Validate changes and document in DMR and change control record, and label devices in accordance with enforcement policy
Where can I find more information?

- FDA Emergency Use Authorization [website]
- FDA FAQs on Shortages of Surgical Masks and Gowns
- FDA Guidances
Diagnostic Considerations: IVDs and LDTs
## What are the current pathways for COVID-19 tests?

<table>
<thead>
<tr>
<th>IVDs</th>
<th>High-Complexity LDTs</th>
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<tbody>
<tr>
<td><strong>EUA Pathway</strong></td>
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</tr>
<tr>
<td>- Template available on FDA website</td>
<td>- Generally same as IVD EUA pathway, <strong>but</strong> developer must include language on test report that test is validated but FDA review is pending</td>
</tr>
<tr>
<td>- May begin kit distribution after notifying FDA of validation completion</td>
<td>- FDA does not intend to object to use of a modified test when validated via bridging study to EUA-authorized test</td>
</tr>
<tr>
<td>- Manufacturer must: (1) provide instructions for use &amp; (2) post data concerning performance characteristics on company website</td>
<td>- <strong>State Pathway (e.g., NYSDOH)</strong></td>
</tr>
<tr>
<td>- Submit EUA within 15 business days of validation</td>
<td>- EUA is not required; no FDA interaction</td>
</tr>
<tr>
<td>- Submit modifications as EUA amendment</td>
<td>- Test must be developed under the legal authorities and established processes of the state in which lab resides</td>
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In addition to the above, FDA offers an alternative pathway for serology tests not intended as the sole basis to diagnose or inform infection status.
What EUAs for COVID-19 diagnostics has FDA granted?*

<table>
<thead>
<tr>
<th>Date (2020)</th>
<th>Assay</th>
<th>Entity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb. 4</td>
<td>2019-nCoV Real-Time RT-PCR Diagnostic Panel</td>
<td>CDC</td>
</tr>
<tr>
<td>Feb. 29</td>
<td>New York SARS-CoV-2 Real-time RT-PCR Diagnostic Panel</td>
<td>Wadsworth Center, NYSDOH</td>
</tr>
<tr>
<td>Mar. 12</td>
<td>cobas SARS-CoV-2 Test</td>
<td>Roche Molecular Systems, Inc.</td>
</tr>
<tr>
<td>Mar. 16</td>
<td>Panther Fusion SARS-CoV-2</td>
<td>Hologic, Inc.</td>
</tr>
<tr>
<td>Mar. 16</td>
<td>COVID-19 RT-PCR Test</td>
<td>Laboratory Corporation of America</td>
</tr>
<tr>
<td>Mar. 17</td>
<td>Lyra SARS-CoV-2 Assay</td>
<td>Quidel Corp.</td>
</tr>
<tr>
<td>Mar. 17</td>
<td>Quest SARS-CoV-2 rRT-PCR</td>
<td>Quest Diagnostics Infectious Disease, Inc.</td>
</tr>
<tr>
<td>Mar. 18</td>
<td>Abbott RealTime SARS-CoV-2 assay</td>
<td>Abbott Molecular</td>
</tr>
<tr>
<td>Mar. 19</td>
<td>Simplexa COVID-19 Direct</td>
<td>DiaSorin Molecular LLC</td>
</tr>
<tr>
<td>Mar. 19</td>
<td>ePlex SARS-CoV-2 Test</td>
<td>GenMark Diagnostics, Inc.</td>
</tr>
<tr>
<td>Mar. 20</td>
<td>COVID-19 genesig Real-Time PCR assay</td>
<td>Primerdesign Ltd.</td>
</tr>
<tr>
<td>Mar. 20</td>
<td>Xpert Xpress SARS-CoV-2 test</td>
<td>Cepheid</td>
</tr>
</tbody>
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*Current as of Mar. 20, 2020: Several laboratories are offering specimen testing and awaiting EUA approval under FDA’s guidance.
What other considerations should I keep in mind?

- **Interacting with FDA**
  - 24/7 hotline
  - Use of EUA templates

- **Interacting with state public health departments**

- **CLIA considerations**
  - Requirements (e.g., personnel) for high-complexity laboratories
  - Temporary testing locations

- **Alternative sources of materials**
  - Reagents, extraction kits, swabs, etc.

- **Fraudulent tests and FDA enforcement**
Digital Health
Do I need FDA review for my COVID-19 digital health product?

Is product subject to device regulation?

- Not a device or subject to enforcement discretion
  - No FDA premarket review required

- Regulated as a device
  - Classification exempt from 510(k)
    - No FDA premarket review required
  - Classification requires premarket review
    - Submit 510(k), de novo or PMA
    - Submit EUA request
Is my COVID-19 telemedicine product regulated?

- The following software functions are not subject to device regulation:

  "Allow patients or health care providers to interact through email, web-based platforms, video, or other communication mechanisms (but are not specifically intended for medical purposes)."

  "Allow health care providers to communicate in a secure and protected method (for example using a HIPAA compliant app to send messages between health care providers in a hospital)."

  "Specifically marketed to help patients document, show, or communicate to providers regarding potential medical conditions," including software "that serves as a videoconferencing portal specifically intended for medical use and to enhance communications between patients, health care providers, and caregivers."
Is my COVID-19 triage or diagnosis software regulated?

Software intended to support providers in making decisions around COVID-19 may be clinical decision support exempt from device regulation under FDCA § 520(o)(1)(E) if the software:

- Enables the health care professional to independently review the basis for the recommendation, such that it is not the intent that such health care professional rely primarily on the recommendation to make a clinical diagnosis or treatment decision regarding an individual patient and

- Is not intended to acquire, process, or analyze a medical image or a signal from an *in vitro* diagnostic device or a pattern or signal from a signal acquisition system
If my product is a device, how can I make it available?

- Request EUA
  - HHS has not yet issued a declaration that circumstances exist justifying emergency use of software products
    - Can submit EUA request in anticipation of appropriate HHS declaration
  - EUA requests needs to demonstrate:
    - Sufficient performance and accuracy to show product “may be effective”
    - Benefit outweighs risks
    - No alternatives available
Key EU Considerations
General comments

- Many of the U.S. considerations will also apply to the EU, including:
  - COVID-19 disruptions to clinical investigations
  - need for appropriate utilization of resources
  - impact on internal audits
  - regulation of digital health (including software) products
- In the EU, there is no premarket review and approval of devices so interactions with regulators less likely to be relevant
- However, existing challenges with notified body engagement will inevitably worsen
Is there an emergency use authorization?

No EU-wide emergency use authorization to allow non-CE marked medical devices (including IVDs) to be placed on the market

- MDR (effective May 26, 2020) introduces greater scope for EU-wide coordination

Requires a case-by-case assessment at the Member State level

- National competent authorities have their own exceptional use rules for approval to supply non-compliant medical devices
  - Typically apply on humanitarian grounds
  - Usually intended for the treatment of a single named patient
- National laws may also have scope for broader exemptions
Will the implementation of the MDR be delayed?

Medical Devices Regulation (EU) 2017/745 comes into effect on May 26, 2020

Industry is lobbying to delay implementation and/or extend scope of transitional arrangements
- Lack of notified bodies was already a problem
- COVID-19 is adding to lack of available resource for conformity assessments

No official communication from European Institutions to date

Companies should continue to work towards MDR effective date of May 26, 2020
Impact on the supply chain

- Under the existing Medical Devices Directive, there is limited regulation of supply chains, so adjustments to supply chains may be straightforward.
- MDR will introduce greater regulation of “economic operators,” including importers and distributors.
- Increased regulation of supply chain may make it more difficult to react to COVID-19 related disruption, particularly for importers, which will be identified on product labeling.
Resources and Contact Information
Resources

- **COVID-19 Legal and Business Toolkit**: upcoming briefing calls and on-demand audio briefings; practical guidance; thought leadership on updates; and details on our COVID-19 task force
  - Reach out to our COVID-19 task force at COVID19@cov.com

- **Life Sciences Briefing Call**: our experts on global business offer an assessment of the complex concerns that life sciences industry companies should have at top of mind
  - Download the audio recording

- **Checklist for Technology Solutions for COVID-19**: to assist companies that are developing technology solutions to help predict, mitigate or contain the spread of COVID-19, our cross-practice digital health team has put together a checklist of considerations
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