Pharma Intelligence
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Commercial, Regulation, Compliance and FDA News on Coronavirus

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Abbott Rolls Out COVID-19 Antibody Test

Executive Summary
Abbott has launched its first COVID-19 antibody test to help determine if a person has been previously infected with the virus. The diagnostics giant said it intends to ship a total of 4 million tests in April.

Abbott Laboratories Inc. has launched a new antibody test to identify people who have been infected with COVID-19.

Abbott's SARS-CoV-2 IgG test is the third COVID-19 diagnostic developed by the company. Last month, it launched a real-time polymerase chain-reaction test, Abbott m2000 RealTime SARS-CoV-2 test, and a rapid, point-of-care test for its ID NOW platform (Also see "Abbott Launches Five-Minute POC Rapid COVID-19 Test" - Medtech Insight, 28 Mar, 2020.)

The new test identifies the IgG antibody, a protein produced by the body's immune system in the late stages of coronavirus infection. The test will initially be available on Abbott's Architect i1000SR and i2000SR laboratory instruments which can run up to 200 tests per hour.

Abbott said it expects to ship a total of 4 million tests in April and expand laboratory antibody testing to the detection of the IgM antibody.

Abbott will initially make the test available by following the U.S. Food and Drug Administration's notification without an emergency use authorization pathway established in new guidelines announced on 16 March. Abbott said it plans to file for an EUA with the FDA and for a CE Mark in the European Union. Multiple companies, including Becton Dickinson & Co.., Cellex Inc. and Ortho-Clinical Diagnostics Inc. are launching serology tests to detect SARS-CoV-2 antigens or antibodies under the new guidelines. (Also see "COVID-19: Nanomix Wins BARDA Funding For Mobile Point-Of-Care Assay" - Medtech Insight, 8 Apr, 2020.)

Antibody testing will be a critical step in tackling the coronavirus pandemic as tracking the population that has already been infected may allow some people to return to work and help re-open the economy.

The UK's Medicines and Healthcare products Regulatory Agency published specifications for at-home and point-of-care serology COVID-19 tests after none of the self-tests acquired by the UK government met its standards. (Also see "UK Publishes COVID-19 Self-Test Specifications" - Medtech Insight, 9 Apr, 2020.)

The Belgian government has banned self-tests, including antibody tests, as it considers these test insufficiently accurate to be used in the pandemic. (Also see "Belgium Bans COVID-19 Antibody Self-Tests But UK Goes Ahead" - Medtech Insight, 31 Mar, 2020.)

Medtech Insight is tracking the global diagnostic pipeline of COVID-19 tests. See our COVID-19 test tracker for a full listing.

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‘Hunker Down, Expect The Worst And Hope For The Best’: Investment Analyst Advises Medtech Businesses To Cut Costs

Executive Summary
Maxim Jacobs, managing partner at Edison Investment Research, urges medtech companies to be financially prudent as the COVID-19 pandemic worsens. Cancellations of routine surgeries are creating a huge strain on device businesses which could continue for months.

As hospitals prioritize COVID-19 patients, masses of elective and routine procedures have been cancelled, creating a black hole of revenue for device business.

Maxim Jacobs, managing partner at Edison Investment Research told Medtech Insight companies must strategize how to cut unnecessary costs and preserve capital to compensate for lost sales during this period of low procedure volumes and uncertainty. “Not only are sales going down to almost zero for many of these companies, clinical trial timelines are being pushed out which means of course more funding stress as companies don’t have enough money to see the year through,” said Jacobs.

“There are companies that are usually reasonable in terms of their expenditure so they won’t have much to cut, but then there are some big spenders that assume the market will always be open.” His advice for companies is to “hunker down, be prepared for the worst and hope for the best. We are in uncharted waters. Try and be as offensive with your financial and commercial decisions as you possibly can.”

Companies that are dependent on the procedures that can be most easily deferred, such as orthopedic or ophthalmological procedures, will likely see a bigger impact from COVID-19. (Also see “Wall Street Tries To Guess The Impact Of Pandemic On Medtech Revenues” - Medtech Insight, 24 Mar, 2020.)

Jacobs said many medical device managers may not have experience with previous recessions since the last one was over a decade ago. “Decide what do I really need for [the] business and the urgency of that need,” he advised. “Can it hold off? You want to make sure that if it’s still bad in June, you have money. Being as conservative as possible is the best way to go.”

No Winners

Despite some medtech companies ramping up production of in vitro diagnostic (IVD) tests and ventilators, Jacobs said he sees no financial winners from the pandemic. With the economic impact so difficult to measure, Jacobs said no company should rely on any revenue boom out of COVID-19.

“Some of the small companies may benefit if they have an IVD test that catches on but for the larger companies, I don’t think these sales will move the needle that much,” he said. “We don’t know the full implications of this but if it sparks a significant recession/depression that has a global character to it, then for example in the US people might lose their insurance and then won’t necessarily be able to pay the deductibles for future procedures.”

He warned companies should be ready for a long wait to see their stock prices improve. “There’s still a lot we don’t know about the virus itself. Is there a risk of re-infection, is it going to be seasonal? We know that in the 1918 pandemic, the first round was not as bad as the second round which occurred later in the year.”

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With social distancing measures and closures, business could potentially resume by June, but companies have no certainty of that, he said.

"You've fallen off a ship and you don't know when you're going to be rescued. You need to have a raft."

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Wall Street Tries To Guess The Impact Of Pandemic On Medtech Revenues

Executive Summary
As the pandemic unfolds with an uncertain outcome, US securities analysts that cover publicly traded medtech companies are developing mathematical models to estimate the impact of the COVID-19 pandemic on medtech companies.

US securities analysts are trying to estimate the impact of the COVID-19 pandemic on the performance of medtech companies by building mathematical models that account for disruption of supply chains and the widespread deferral of elective procedures.

Following the outbreak of COVID-19 in China at the end of 2019, most medtech companies addressed the impact of COVID-19 during their most recent sales and earnings reports. Much of that discussion was about disruption to supply chains in Asia. For example, Boston Scientific Corp. announced it expected the outbreak would have a $10m to $40m impact on its first-quarter sales, due to deferred procedures and disruptions to its supply chains in China. (Also see "The Cost Of Coronavirus: Medtech Market Wins And Losses" - Medtech Insight, 28 Feb, 2020.)

Since then, the number of patients with COVID-19 has continued to rise around the world, especially in Europe and North America. Analysts are now focused on the increasing number of hospitals around the world that are deferring elective procedures to make room for an expected wave of COVID-19 patients. Also, hospitals may choose to defer capital purchases while they try to manage the surge of COVID-19 patients. (Also see "US Hospitals Cancel Elective Surgeries, Team Up With Medtechs To Find Remote-Monitoring Solutions" - Medtech Insight, 17 Mar, 2020.)

"Having evaluated and analyzed the risks and potential range, scope and duration of these issues on our universe, we believe the potential impact may vary significantly, based on regional exposures and revenue mix of each company," Credit Suisse analysts Matt Miksic and Vik Chopra wrote in a 6 March report on the impact of the pandemic on the medtech companies they cover.

Companies that are dependent on the procedures that can be most easily deferred, such as orthopedic or ophthalmological procedures, will likely see a bigger impact from COVID-19. For example, Credit Suisse predicts the COVID-19 outbreak could reduce Zimmer Biomet Holdings Inc.'s 2020 sales by more than 20% versus estimates before the outbreak, because many orthopedic surgeries will being postponed.

Analysts will likely have to adjust their forecasts at least weekly as they get new information from physicians. For example, on 6 March, Credit Suisse reported that it expected the impact of COVID-19 may have relatively little impact on Edwards Lifesciences Corp. because most of Edwards' revenues come from transcatheter aortic valve replacement (TAVR), which is usually an urgent procedure that cannot be delayed indefinitely.

But in a 19 March report, Miksic and Chopra reported that at least one surgeon that performs TAVR told them that "most" TAVR and transcatheter mitral repair cases can be deferred. The exact impact on the volume of these procedures completed in 2020 is unknown, but Miksic and Chopra expect these cases will "catch up" when the pandemic subsides.

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Wells Fargo analyst Larry Biegelsen expects that most of the deferred procedures will still be completed, which will mitigate impact of the deferrals over the long term. "While our analysis does not assume any catch-up from procedures postponed during the COVID-19 pandemic, we believe a majority of postponed procedures will eventually be done once the pandemic subsides," Biegelsen wrote in a 15 March report.

Several analysts have conducted small surveys of physicians to get a clearer picture of which procedures are being deferred to make resources available to treat COVID-19 patients.

On 10 March, Jefferies analysts conducted a survey of 62 interventional cardiologists, orthopedic surgeons and anesthesiologists to evaluate procedure volume trends in response to the COVID-19 outbreak.

At the time of that survey, the impact of COVID-19 on procedure volumes had been minimal, but 23% of the doctors surveyed said they expected a reduction in procedure volumes because of the pandemic and 55% expected deferrals and cancellations to increase.

About 29% of interventional cardiologists reported a change in procedure volume related to the pandemic while only 13% of anesthesiologists reported a change in their procedure volume. About 23% of orthopedic surgeons said their procedure volume had changed.

"Most [doctors surveyed] also noted their institutions are preparing for a reallocation of resources as a result of the virus. Most procedures are likely to be shifted out as opposed to cancelled outright. But over the near term, [companies] with less elective exposure are best positioned," Jefferies analyst Raj Denhoy wrote in a 10 March report.

That survey was finished five days before the US Surgeon General, the American College of Surgeons and other medical societies formally called for all non-essential procedures to be delayed, Denhoy pointed out in a 15 March report. "While most cases are likely to be shifted out as opposed to canceled outright, a concern for device companies is their ability to withstand a protracted turn-down from a cash perspective," he explained.

On 22 March, Wells Fargo analysts announced the results of a similar survey of 117 US-based physicians across nine specialties and 14 procedures. On average, the physicians in that survey expect to postpone 75% of the surveyed procedures during the COVID-19 pandemic.

The respondents expect to postpone about 68% of cardiovascular procedures and 82% of orthopedic procedures, with 84% of the procedures being performed within four months of the pandemic subsiding.

Although they expect more orthopedic surgeries to be deferred than cardiovascular surgeries, the survey respondents expect most of the postponed orthopedic procedures to be performed faster than the postponed cardiovascular procedures.

"[According to the respondents] the most common reason for a patient not having his/her procedure done once the pandemic subsides was due to the patient finding an alternative treatment, although with cardiovascular procedures, the most common reason tended to be due to the patient passing away," Wells Fargo's Biegelsen explained.

Grey Sky Vs. Blue Sky

Because of the volatility in the industry and the rapid pace of news related to the pandemic, Credit Suisse analysts published the "framework" they are using to understand the potential impact

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of the pandemic on companies' sales and earnings in addition to the specific sales estimates for each company.

"Our scenario analysis provides a reasonable framework for where estimates can go," Miksic and Chopra wrote.

For each company, Credit Suisse's model produced a "blue sky" best case scenario where the pandemic has a minimal impact on the company's revenues, a "grey sky" estimate where the impact is more severe, and a "base case" representing a middle point between the blue sky and grey sky estimates. (See chart below)

Credit Suisse believes the revenue impact of COVID-19 beyond 2020 will be modest, with procedure volumes stabilizing by the first quarter of 2021.

Impact Of COVID-19 On Medtech Company Sales

Credit Suisse's base case, best case and worst case estimates of COVID-19's impact on the 2020 revenue of selected medtech companies.

Company	Original 2020 Sales Estimate	Revised 2020 Sales (Base Case)	Best Case	Base Case	Worst Case
Abbott Laboratories	$34,057	$32,199	-0.9%	-5.5%	-12.6%
Alcon	$7,699	$7,054	-1.8%	-8.4%	-18.2%
Baxter International	$11,678	$11,171	-1.0%	-4.3%	-9.2%
Boston Scientific	$11,879	$10,794	-1.9%	-9.1%	-20.1%
Edwards Lifesciences	$4,881	$4,687	-0.9%	-4.0%	-8.7%
Globus Medical, Inc	$850	$798	-1.3%	-6.2%	-13.7%
Integra LifeSciences	$1,563	$1,494	-0.9%	-4.4%	-9.5%
Johnson & Johnson	$85,704	$80,800	-1.4%	-5.7%	-12.1%
Medtronic	$32,321	$29,730	-1.8%	-8.0%	-17.2%
NuVasive	$1,233	$1,148	-1.5%	-6.9%	-15.3%
Organogenesis Holdings Inc	$281	$271	-0.7%	-3.6%	-7.4%
Stryker	$4,694	$4,223	-1.0%	-5.0%	-11.3%
Zimmer Biomet Holdings, Inc	$8,185	$7,397	-2.1%	-9.6%	-21.4%

Source: Company, Credit Suisse estimates

Wells Fargo provided Medtech Insight with "base case" and "best case" estimates for the 2020 revenues of companies they cover. (See chart below)

The base case estimates assume that the outbreak will be most disruptive in China in February and March and afflict the rest of the world from mid-March through May. Wells Fargo's best-case scenario assumes the world largely recovers by the end of April.

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Under these assumptions, the median impact to medtech companies' 2020 sales would be -9.1% in the base case and -5.4% in the best case.

Wells Fargo's Coronavirus Impact Analysis

Estimates of the potential impact of COVID-19 on the 2020 revenue of companies covered by Wells Fargo analysts.

Base Case | Best Case

Company	Original FY2020 Sales Estimate	Adjusted FY2020 Estimate	Absolute Impact	Percentage
Abbott Laboratories	$34,069	$32,053	-$2,016	-5.9%
Alcon	$7,803	$7,319	-$484	-6.2%
Axonics Modulation Technologies	$95	$87	-$9	-9.3%
Baxter International (1)	$11,934	$11,749	-$186	-1.6%
Becton, Dickinson & Co (2)	$17,656	$17,250	-$406	-2.3%
Boston Scientific	$11,934	$10,826	-$1,109	-9.3%
Cooper Companies (3)	$2,803	$2,732	-$71	-2.5%
Edwards Lifesciences	$4,833	$4,416	-$417	-8.6%
Glaukos Corporation	$292	$263	-$29	-10.1%
Globus Medical, Inc	$852	$749	-$103	-12.1%
Inspire Medical Systems	$119	$108	-$11	-9.4%
Integra LifeSciences	$1,569	$1,489	-$80	-5.1%
Intuitive Surgical	$5,025	$4,604	-$421	-8.4%
Johnson & Johnson	$85,726	$81,834	-$3,892	-4.5%
Medtronic (4)	$31,991	$29,041	-$2,950	-9.2%
Merit Medical	$1,053	$945	-$109	-10.3%

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Nevro Corp.	$436	$393	-$43	-9.9%
Novocure Ltd.	$451	$442	-$9	-2.0%
NuVasive	$1,230	$1,076	-$154	-12.5%
Penumbra	$640	$623	-$17	-2.6%
SeaSpine Holdings	$178	$156	-$21	-12.0%
Shockwave Medical	$76	$69	-$7	-9.6%
Stryker	$15,979	$14,545	-$1,433	-9.0%
Teleflex Incorporated	$2,789	$2,584	-$205	-7.4%
Wright Medical	$996	$870	-$126	-12.7%
Zimmer Biomet Holdings, Inc	$8,222	$7,252	-$970	-11.8%

**Current WF forecasts*
1) Baxter enterprise value calculated as per our estimate of debt, cash and minority interest as of 2019-end and current share count estimate
2) Becton Dickinson- FY ending September
3) Cooper - FY ending October
4) Calendar Year 2020 data for MDT

Source: Company reports; Wells Fargo Securities, LLC estimates; FactSet

Biegelsen pointed out that the stock prices of the companies Wells Fargo covers declined by a median of 22.7% between 19 February and 15 March, while the S&P 500 overall declined 19.9% during this period. "[This decline] suggests to us that the market is already pricing in at least 2.5 months of impact outside of China," he wrote.

Wells Fargo's estimates are a "rough guess" based on the impact of COVID-19 in China and February and the analysts' conversations with physicians, Biegelsen cautioned. "It's important to note that some companies have not provided much color yet on the potential impact, so we've had to make assumptions for those companies."

He also points out that Wells Fargo's model does not account for potential offsets from COVID-19 that may bring in more revenue for medtech companies that make products needed to treat patients with the disease. (Also see "COVID-19: US Auto Giant General Motors Wants To Make Ventilators, Trump Says; Ford And Tesla Also Express Interest" - Medtech Insight, 20 Mar, 2020.)

For example, Medtronic announced on 18 March that it has increased production of ventilators by more than 40% and is on track to more than double its capacity to manufacture and supply ventilators in response to the crisis. (Also see "Ventilator Firms Across Europe Ramp Up

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Production To Meet 'Unprecedented' Demand" - Medtech Insight, 18 Mar, 2020.)

Medtronic manufactures the Puritan Bennett 980 and Puritan Bennett 840 high-performance ventilators for high-acuity settings at its facility Galway, Ireland. The facility currently employs 250 people dedicated to manufacturing ventilators. The company plans to rapidly add at least 250 more, adding additional shifts and operating the factory 24/7.

Companies Can Weather The Storm, For Now

While much of the focus of securities analysis has been on COVID-19's impact on medtech companies' bottom lines and stock prices, Jefferies analysts ran a "stress test" on each of the medical device companies it covers to evaluate the cash position of each company to determine if any are at risk of insolvency.

"All companies in our coverage are very well capitalized and none appear at risk," Jefferies' Denhoy wrote on 15 March. (See chart below)

To prepare for the expected sales downturn, some companies have "extended maturities" – negotiated later due dates for certain debt repayments. For example, Zimmer Biomet has a $1.5bn in term loans due to mature in 2020, but the company recently announced a strategy to push those maturities to 2026 and 2030. Other companies will likely have to reduce spending, Denhoy suggested.

Denhoy agrees with other analysts that the most important variable related to COVID-19 will be the number of non-essential medical procedures that are deferred to free up health care resources to treat COVID-19 patients.

Jefferies stress-test model assumes that one quarter of all non-essential procedures will be delayed, with a "liberal view of what could be considered a non-essential or able to be delayed procedure," Denhoy explained.

"The good news is US medtech is in great shape with most companies having very strong balance sheets; hence we do not see any obvious going-concern risks across our coverage," Denhoy concluded. "However, we do see select companies that have high elective procedure exposure coupled with low/negative [free-cash flow] profiles or maturities due next year as facing potential liquidity risks."

Denhoy pointed out the stress test model shows LivaNova is facing a potential deficit of about $140m due to its low cash balance. However, the model's estimate for LivaNova's free cash flow is "artificially low" due to recent higher-than-usual "one-off costs," so "spending discipline should get them through." (Also see "LivaNova's Vagus Nerve Stimulator Earns CE Mark For Treating Depression" - Medtech Insight, 10 Mar, 2020.)

During its 26 February fourth-quarter 2019 earnings call, LivaNova did not include any impact of COVID-19 in its 2020 sales and earnings guidance because it did not have any manufacturing in China and its operations in Italy had not yet been affected. The company's next earnings call is scheduled for 29 April.

Denhoy highlighted Penumbra Inc. and Abbott Laboratories Inc. as examples of companies that are relatively well-prepared for this crisis.

Although not covered in Jefferies' analysis, Denhoy pointed out that Penumbra "is relatively insulated" because almost all the procedures that use its products to treat stroke or peripheral thrombus are urgent and non-elective.

Abbott is the most diversified company that Jefferies covers, which makes it a good pick for a company that can perform relatively well during

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the crisis, Denhoy wrote. "It has exposure to some elective/semi-elective procedure volumes – medical devices are [about] 30% of revenue – but the balance of revenue is less exposed."

For example, Abbott's diabetes business "is safe as the technologies are needed in the treatment of the disease," and Abbott's diagnostics business should be "more immune to volume compression," Denhoy explained.

Abbott recently announced plans to deliver 150,000 polymerase chain reaction tests for SARS-CoV-2, the virus that causes COVID-19, to existing customers in the US and eventually provide up to one million tests per week. The tests run on Abbott's m2000 RealTime automated system. (Also see "Abbott Receives Emergency Use Authorization For COVID-19 Test" - Medtech Insight, 19 Mar, 2020.)

"By our exposure model, the company is well capitalized and should weather the storm well," Denhoy concluded.

Jefferies' 'Stress Test' Summary

Jefferies' analysts "stress tested" medtech companies exposed to elective procedures to determine their liquidity/solvency risks.

Company	2019 Gross Profit ($m)	2019 Free Cash Flow ($m)	Procedure Delay Impact On Free Cash Flow($m)	Estimated 2020 Cash Position ($m)
Medtronic	$19,729	$5,873	-$3,995	$18,466
Abbott Laboratories	$16,693	$4,498	-$2,128	$5,510
Boston Scientific	$6,879	$1,375	$1,393	$545
Edwards Lifesciences	$3,193	$925	-$647	$2,133
Abiomed	$640	$208	-$106	$901
LivaNova	$704	-$116	-$99	-$153
Stryker	$9,382	$1,542	-$1,431	$3,787
Zimmer Biomet*	$5,107	$1,063	-$1,034	$647
Wright Medical**	$700	-$58	-$168	-$115
NuVasive	$724	$112	-$174	$152
Orthofix Medical	$354	$13	-$72	$12
Intuitive Surgical	$3,099	$1,173	-$473	$5,976
Alcon	$3,639	$367	-$464	$793
ResMed	$1,462	$390	-$205	$390
Teleflex	$1,493	$334	-$265	$370
Hologic	$1,698	$540	-$238	$674
Varian	$1,397	$314	-$21	$1,018
Integra	$905	$162	-$93	$268
AccuRay	$163	-$34	-$2	$63

**Zimmer Biomet recently refinanced $1.5bn debt maturity owed in 2020. * * Wright Medical to be acquired by Stryker*

Source: Jefferies, FactSet

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TytoCare Raises $50M Amid Rising Demand To Remotely Monitor COVID-19 Patients

Executive Summary
TytoCare will use the $50m it raised in a funding round to expand the reach of its telehealth solutions.

TytoCare Ltd. has raised $50m in its latest funding round, which will help it meet the surging demand for its telehealth solutions used by doctors to remotely examine COVID-19 patients in hospitals and at home, the company announced on 8 April.

Tyto Care markets a handheld device to health care professionals and consumers that comes with a series of adapters for the remote examination of ears and throat and for listening to the heartbeat and lungs.

"This new funding comes at a pivotal moment in the evolution of telehealth and will enable us to continue to transform the global health care industry with the best virtual care solutions," said Dedi Gilad, co-founder and CEO of Tyto Care. "We look forward to further expanding the reach of telehealth and introducing new solutions as demand for remote care continues to soar."

The funding round was co-led by Insight Partners, Olive Tree Ventures and Qualcomm Ventures LLC with participation from previous investors, bringing the company's total funding to $105m.

The funding will allow the company to continue its commercialization efforts in the US, Europe and Asia and introduce new product capabilities such as machine learning-based home diagnostics solutions.

Tyto Care saw a three-fold growth in 2019 and works with hundreds of hospitals and more than 100 health organizations, primarily in North America, Europe and Israel.

The firm has reported double-digit adoption of telehealth in the wake of the pandemic.

Tyto Care ranks among the telehealth companies that have benefitted from loosened regulatory restrictions on the telehealth industry in recent weeks to help health professionals connect remotely with patients during this pandemic. The Centers for Medicare and Medicaid Services expanded coverage of telehealth for Medicare beneficiaries, allowing them to use online tools such as FaceTime and Skype to visit with doctors by phone or videoconferencing at no cost. (Also see "Start-Up Spotlight: Tyto Care Brings Medical Exams To Homes " - Medtech Insight, 24 Dec, 2019.)

David Bardan, vice president of provider solutions for Tyto Care, told Medtech Insight in March that the loosening restrictions on phone use has been a huge plus, because it allows telehealth companies such as Tyto Care to leverage asynchronous visits where a patient can collect health data and then forward it to the physician for review later.

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COVID-19: Medtronic Shares Ventilator Specs Amid Multi-Industry Efforts To Increase Ventilator Production

Executive Summary
Medtronic shares an open-source design for its ventilator to help mitigate the nation's ventilator shortage for COVID-19 patients.

Medtronic PLC is publicly sharing design specifications for its PB 560 ventilator to help the global multi-industry effort to devise options for rapid ventilator manufacturing.

The medtech giant shared on 30 March all the schematics and software for its portable Puritan Bennett 560 ventilator, which was introduced in 2010 and is sold in 35 countries around the world.

This comes after the US Food and Drug Administration temporarily waived its enforcement and inspection requirements to allow companies that are not ventilator manufacturers to begin making much-needed parts for ventilators and other respiratory accessories to help tackle diminishing supplies in US hospitals as they treat the rising number of COVID-19 patients.

"It's a good thing for manufacturers to release a comprehensive set of documentation that would allow other capable groups to build ventilators that have a proven design," said Julian Goldman, an anesthesiologist and the director of Massachusetts General Hospital's Medical Device Interoperability and Cybersecurity program. He's also the hospital's medical director of biomedical engineering.

"One of the more difficult things to do is building a new ventilator and design it safely, and consider all of the hazards and all of the clinical needs. If it's an older design that is less capable than a state-of-the art modern ventilator, it would still be a lifesaving device," Goldman added.

"By openly sharing the PB 560 design information, we hope to increase global production of ventilator solutions for the fight against COVID-19," said Bob White, executive VP and president of the Minimally Invasive Therapies Group at Medtronic.

Medtronic CEO Omar Ishrak said in an interview with CNBC on 25 March that his company had already ramped up production of ventilators by 40%, making 250 ventilators a week, and is on track to double its capacity by working 24/7.

In the discussion, Ishrak also said Medtronic partnered with automaker Tesla Inc., which converted a New York production plant used to produce solar power cells, to make ventilators instead.

"One of our ventilators will be made by [Tesla] and they're fast on track to try to make that as well," Ishrak said. He also alluded during the discussion that Medtronic would open-source one of its lower-end ventilators used for less acute situations for others to make, noting that "this product is a little more generic in form and can be made more easily than the one we make."

Auto Makers Turn To Ventilator Production

Two weeks ago, auto giant General Motors Co. said it had teamed up with Seattle-based Ventec Life Systems to help meet the demand for ventilators. (Also see "GM Partners With Ventec Life Systems To Make Ventilators" - Medtech Insight, 21 Mar, 2020.)

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And Ford Motor Co. announced a few days later that it joined GE Healthcare and 3M Health Care Ltd. to make ventilators and respirators. (Also see "Ford Races To The Rescue: US Auto Maker Partners With GE, 3M To Make Ventilators, Respirators During COVID-19 Crisis" - Medtech Insight, 24 Mar, 2020.)

Meanwhile, 3D companies such as HP Inc., FormLabs and Prisma Health are also mobilizing their efforts to produce key components for ventilators, as well as personal protective equipment such as face masks and respirators, to help mitigate shortages in medical supplies. (Also see "COVID-19: FDA Offers Cautionary FAQs On 3D Printing Of Key Medical Supplies" - Medtech Insight, 27 Mar, 2020.)

Indeed, "there are many, many efforts to build and work together, and new teams are forming and they are gathering and they are sharing information," said Goldman, whose own "call to action" on LinkedIn for clinical and engineering experts to join forces was heard by many.

"We have over 40 members of that [LinkedIn] group that stood up within a week, in which groups of experts in simulation and modeling are working together to develop tools, so that clinicians could look at better deploying that ventilation approach if it's needed in an absolute emergency," Goldman said.

Some hospitals, fearing that they may be faced with a ventilator shortage, meanwhile, are repurposing devices and equipment into makeshift breathing devices. At Northwell hospital in New York, doctors are repurposing devices normally used to treat sleep apnea patients into ventilators, according to published reports.

And San Diego-based ResMed Inc., which develops and sells equipment for sleep-related breathing disorders, is working with governments, health authorities, hospitals, physicians and patients to assess the need for ventilation therapy to treat COVID-19 patients.

"We are looking to double or triple the output of ventilators, and scale up ventilation mask production more than tenfold," ResMed CEO Mick Farrell said. (Also see "Exec Chat: ResMed's CEO Mick Farrell Outlines 2025 Strategy For 250 Million Users" - Medtech Insight, 10 Sep, 2019.)

Meanwhile, in other parts of the world, manufacturing groups are also coordinating efforts to meet the rising demand for ventilators. In the UK, a group of manufacturers, received a government order to build 10,000 ventilators to help treated COVID-19 patients. The devices are being supplied by the Ventilator Challenge UK consortium, a group of 14 firms including non-health care groups such as Siemens AG, Rolls-Royce and Airbus. (Also see "Smiths Medical Ramps Up ParaPAC Ventilator Production For UK Order Of 10,000 Units" - Medtech Insight, 31 Mar, 2020.)

Goldman foresees rapid innovation.

"I think what we may see is ultrafast ventilators and rapidly developed ultra-simple ventilators that can be deployed over the next few weeks and then somewhat more sophisticated designs coming together over the next few months."

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Belgium Bans COVID-19 Antibody Self-Tests But UK Goes Ahead

Executive Summary
While the UK is moving forward quickly to provide COVID-19 antibody self-testing, the Belgian government considers the tests not sufficiently accurate to be used in the pandemic.

Belgium has banned self-tests for the presence of antibodies to SARS-COV-2, the virus that causes COVID19 until 17 September. Meanwhile, Public Health England (PHE) could be just days away from approving a first government-approved COVID-19 antibody self-test for distribution via Amazon.

COVID-19 self-tests will be in high demand as they would enable people, in theory at least, to make lifestyle choices about, for example, returning to work and supporting family and others.

In a decree published in the Moniteur Belge, however, the Federal agency for medicines and healthcare products warns that a patient could still be a carrier of SARS-CoV-2 despite a negative result because there may not be sufficient antibodies in the sample at the time of testing. It adds that immunoglobulin M (IgM) tests are susceptible to giving false positives.

The agency warns, also, that self-testers could equally misinterpret the result due to a lack of scientific understanding. The risks are incompatible with the current situation, it says.

Tests that fall under the Belgian ban, for example are IgG, IgM and IgA antibody tests.

UK Risk-Taking?

In the UK, meanwhile, officials from PHE said last week that COVID-19 self-tests could soon be available to buy in the UK and elsewhere, through Amazon or pharmacies.

The UK has even ordered 3.5 million 15-minute home test kits for SARS-CoV-2 antibodies from an unnamed company (Also see "UK Govt Buys 3.5M 15-Minute COVID-19 Antibody Home Tests From Mystery Manufacturer" - Medtech Insight, 26 Mar, 2020.) But news is still awaited of these test kits proving sufficiently accurate. They were being assessed by PHE.

The UK government's chief medical officer, Chris Whitty, has been more cautious than PHE. He said on 25 March at a press briefing: "The key thing for us to do is evaluate if these tests accurate enough to be used by the general public … If they are incredibly accurate, we will work out the quickest way to release them. If they are not accurate, we will not release any of them."

There are many other self-tests in development. More information on UK self-tests has been covered in Medtech Insight (Also see "COVID-19 Fact File: Global Diagnostic Test Pipeline" - Medtech Insight, 18 Mar, 2020.) and in its sister publication, HBW Insight (Also see "The Race Is On To Launch COVID-19 Antibody Home-Test In The UK" - HBW Insight, 31 Mar, 2020.).

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UK Publishes COVID-19 Self-Test Specifications

Executive Summary
The UK's MHRA is looking for manufacturers to submit COVID-19 self-tests that meet minimum and desired criteria for evaluation, after finding its recently purchased 3.5 million self-tests failed to meet these standards.

The UK's Medicines and Healthcare products Regulatory Agency (MHRA) has published specifications for at-home COVID-19 tests, following disappointing results so far from its self-test trials.

After none of the self-tests acquired by the UK government met the standard required – including 3.5 million from an unnamed in-vitro diagnostics company – the MHRA has made public its minimum and desired requirements from such devices. (Also see "UK Govt Buys 3.5M 15-Minute COVID-19 Antibody Home Tests From Mystery Manufacturer" - Medtech Insight, 26 Mar, 2020.)

Published yesterday, the MHRA's "Specification criteria for serology point of care tests and self-tests" sets out the "minimally (and some preferred options) clinically acceptable specifications for point of care and self-tests to be made and used in the UK during the current COVID-19 pandemic caused by SARS-CoV-2 virus."

With the government eager to "scale up" its coronavirus testing strategy, the MHRA is inviting applications from manufacturers whose self-test meet these specifications.

As for self-tests already on the market – both for home use and for use in pharmacies – the regulator warned that the "use of these products is not advised."

"We can confirm that there are no CE-marked tests for home use, and it is illegal to supply such products," it clarified.

No Knowledge Or Training Required

According to the MHRA's specification criteria for serology/antibody self-tests, use of the device must require "no knowledge of self-testing technology" or training. There should also be no need for an "operator" to assist with either the testing procedure or the interpretation of the results. The minimum level of accuracy for a COVID-19 self-test – which the MHRA defined as an "in vitro diagnostic medical device intended to be used by a lay person on a home environment" – must be "greater than 98% (within 95% confidence intervals) for the immunoglobulin G (IgG) antibody between 14 and 20 days from appearance of first symptoms, the agency insisted. Preferably containing no more than two tests per pack, the CE-marked tests should be simple to use, requiring only three or four steps: extract blood from finger using a lancet, apply the blood to the testing stick, read the results. These results should take between five and 20 minutes to appear on the testing stick, the MHRA recommended. While these specifications were based on the MHRA's best available information, the agency noted that the science was "rapidly evolving." "These specifications are subject to review and may need to be updated at short notice," the authority warned.

Approved Self-Tests 'At Least A Month Away'

Despite the UK government's hope that self-tests would already be available to buy from Amazon and high-street pharmacies, none of the COVID-19 self-tests evaluated so far by Public Health England have met these specifications. "This is not a good result for test suppliers or for us," commented UK government adviser and Oxford

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University Regius Professor of Medicine, Sir John Bell. “Sadly, the tests we have looked at to date have not performed well,” he explained. “We see many false negatives – tests where no antibody is detected despite the fact we know it is there – and we also see false positives.”

“We clearly want to avoid telling people they are immune when they are not, and we want all people who are immune to know accurately so they can get back to work,” he continued. “We will of course continue to look for a test that meets the criteria of an acceptable test,” Professor Bell said. “The government will be working with suppliers both new and old to try and deliver this result, so we can scale up antibody testing for the British public. This will take at least a month.”

A Problem Shared

The UK was not the only country struggling to find a reliable COVID-19 self-test, Prof Bell noted. “The Spanish apparently returned test kits that were not working, and the Germans who are developing their own sensitive kits believe they are three months away from getting these available and validated,” he reported. “No test has been acclaimed by health authorities as having the necessary characteristics for screening people accurately for protective immunity,” he added. Belgium recently banned COVID-19 self-tests until 17 September, including IgG, IgM and IgA antibody tests. (Also see “Belgium Bans COVID-19 Antibody Self-Tests But UK Goes Ahead” - Medtech Insight, 31 Mar, 2020.) In a decree published in the Moniteur Belge, the Federal agency for medicines and healthcare products warned that a patient could still be a carrier of COVID-19 despite a negative result because there may not be sufficient antibodies in the sample at the time of testing. The agency also warned that self-testers could equally misinterpret the result due to a lack of scientific understanding. The risks were incompatible with the current situation, it said.

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Telemedicine Is Riding High, Hopes For More Provisions In 'Phase Three' COVID-19 Stimulus Package

Executive Summary
The nation's leading telehealth advocate group expects CMS will provide additional support for telemedicine to help curb the spread of COVID-19.

The American Telemedicine Association (ATA) told members in a 24 March webinar it expects the Centers for Medicare and Medicaid Services (CMS) to tear down even more barriers to US telehealth services as part of the global effort to curb the spread of COVID-19.

The telehealth industry has seen explosive demand in recent weeks, driven in large part by CMS' decision, announced on 17 March, to lift multiple restrictions on telehealth services for Medicare beneficiaries. Among them are relaxed reimbursement regulations for treating Medicare patients via telehealth, including coverage for out-of-state clinicians to provide telehealth services, and permitting patients to use online tools such as FaceTime and Skype to visit with doctors.

The ATA hopes that the "phase three" bill, also called the CARES ("Coronavirus Aid, Relief, and Economic Security") Act, a roughly $2tn stimulus package, will provide funding and policy change for telehealth. The stimulus package is expected to inject $100bn into hospitals and the nation's health system and billions more into providing personal and protective equipment for health care workers as well as fund small businesses, other industry, the unemployed, direct payments, payroll taxes and state and local governments. Today, after marathon negotiations, the White House and Senate struck a deal to pass the historic relief package with full details being released later.

In a webinar focusing on telehealth reimbursement, hosted by the ATA on 24 March, Kevin Harper, the organization's director of public policy, outlined several provisions that the group has been actively advocating.

"I think there is a good chance we'll see a good portion of this list make it across the finish line," Harper said.

- Rural Areas – Lift telehealth reimbursement restrictions and allow rural health clinics and rural health care programs to serve as distant sites for the provision of telehealth during the COVID-19 emergency.
- Health Plans – Allow high-deductible health plans with a health savings account to cover telehealth services prior to a patient reaching the deductible.
- Medicare Waive 'Qualified Provider' Fix – Address the three-year pre-existing patient-provider relationship requirement from the first coronavirus supplemental.
- Home Dialysis – Temporary waive the requirement for face-to-face visits between home dialysis patients and physicians.
- Hospice Care – Allow hospice providers to use telehealth to conduct a face-to-face encounter required for recertification of eligibility.
- HRSA TRC Grants – Reauthorization of telehealth network and telehealth resource centers grant programs.
- Infrastructure – Prioritize federal funding to support telehealth access and infrastructure for providers.

Harper said, "the situation is fluid and negotiations are ongoing. We will have to wait and see what makes it into the final package

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Robert Jarrin, a strategic advisor for digital health companies, told the webinar listeners that CMS Administrator Seema Verma told health providers that "CMS would be issuing guidance in the next couple of days that would further expand on telehealth."

Jarrin noted that Verma, who addressed providers in a previous conference call, didn't offer specifics or specifically discuss remote monitoring, "but I feel that if there is an opportunity for clarification to come from CMS, it would most likely be in whatever guidance gets put out," he said. He added he is eager to see what the guidance will offer in terms of clarifying remote monitoring codes for reimbursement during this pandemic.

One listener asked how long the expanded Medicare coverage for telehealth will be in place.

The CMS Fact Sheet notes that the expansion is being done under a "temporary and emergency basis" and under the president's 1135 waiver authority and Coronavirus Preparedness and Response Supplemental Appropriations Act.

However, Harper echoed the views of others in the telehealth industry who said the rapid expansion of telehealth under Medicare will not just disappear once the public health emergency is over.

"There is probably going to have to be some sort of transition period," Harper said. "The goal here is to be able to collect as much data and understand the value that telehealth and virtual care provided during the pandemic so we can really come back and make permanent changes to the law."

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Compliance Corner: How To Survive An FDA 'Desk Audit' During The COVID-19 Crisis

Executive Summary
A former US FDA investigations branch director explains how a paper-based "desk audit" would be performed by the agency in lieu of an on-site quality systems inspection. Last month the FDA hit the pause button on in-person inspections as the coronavirus pandemic rolls on.

Last month the US Food and Drug Administration hit the pause button on on-site quality systems inspections as the COVID-19 pandemic rolls on. One tool the agency has in its compliance arsenal, however, are so-called "desk audits" that it can conduct in lieu of an in-person inspection.

Below, Ricki Chase – compliance practice director for Lachman Consultant Services and a former FDA investigations branch director – explains how a desk audit would unfold.

Chase became a consultant in 2016 after spending 16 years at the FDA, where she was also an investigator, medical device specialist and supervisory investigator. Her conversation with Medtech Insight was lightly edited for clarity.

Q: Medtech Insight: The FDA, as you know, has suspended quality systems inspections domestically and abroad. But the agency can still conduct paper-based desk audits. What advice do you have for firms that might have to undergo such an audit?

A: Ricki Chase: Before I give out tips, I think it's important to note that the only companies that would be subject to that kind of experience would be lower risk. I can't imagine a world where if you're up for a PMA inspection on a class III device, that the FDA is going to desk audit you. I also can't imagine that a firm would have a desk audit if it was previously violative and/or is trying to clear a warning letter, or something like that.

Having said that, the point of a desk audit is to see if you have the basic elements of the quality system in place. So I would say, if you're subject to a desk audit, first off, make sure you clearly understand what you're being asked for. And if the FDA isn't clear on what's being asked for, ask them to refine the question, because the question could be very broad – "Send me a list of all your complaints for the last two years, or send me a list of all your complaints." Make sure that the FDA narrows the scope so you don't overprovide information.

Second, be cautious, because there can be a lag time. This isn't being done via a Zoom meeting. So firms need to be really careful that they're not making adjustments to their documents before they turn them over to FDA. It will give a very, very bad impression if firms make document changes or they suddenly have a brand-new revision of an SOP [standard operating procedure] a day after the FDA announces they need them to send in documentation. So they need to be very careful to resist the urge to correct or change records before sending them in.

Third, companies need to make sure they ask the agency for feedback in real time, and they need to make sure they're having a conversation with the FDA up front to say, "If you're seeing things, given that you'll be reviewing them without being at the firm, will we have an opportunity to discuss any observations you might have before you would

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issue an FDA-483 [inspectional observation form]?" In the normal course of action, you have a face-to-face interaction opportunity to explain and discuss. But when it's a desk audit, you don't.

So firms need to determine what the rules of engagement are going to be from the very beginning. For example, will they meet just at the end of the review? Will they meet halfway through the review? What will be the situation? And they should also ask if the desk audit will be considered their formal inspection. Will they be receiving a notice of inspection through email or other media, to make it official under the same scope and rules that a notice would normally be issued?

Fourth, manufacturers need to be very conscious of how the FDA wants them to communicate. I have seen companies communicate via email back and forth to the FDA all of the time. And that is a real slippery slope because it's not an official communication. So how does the FDA really want them to communicate? Does the agency want firms to collate the documents and mail them overnight to the FDA for review? Does the FDA want them uploaded to a secure server or downloaded onto a thumb drive? How does the agency want to receive that information? Because normally firms do not release original documentation – they release copies, photocopies. And companies should make sure that if they're transmitting their documents electronically that their data's secure.

Q: What kind of documents should manufacturers have on hand? The same documents they would have ready if the investigator was actually coming on-site? And will the FDA tell them in advance what kind of documents they want?

A: Chase: If they're going to do a desk audit, then the FDA will send the firm a list of what they want them to provide. But there are key things that they should have ready for a desk audit, including making sure they have their quality manual up-to-date and that they're ready to provide the quality manual, because it gives a top level of review of the organization. They should also make sure they have their metrics up-to-date and ready to provide – that's your complaint trending, your nonconformance trending, how many CAPAs [corrective and preventive actions] you have open, and what your CAPAs look like.

Also, have you reported any MDRs [Medical Device Reports]? Have you had any field actions? Have you made any changes – or what's the most recent change to your device – particularly if it's a class II or class III. Those are very common things, and that's usually where the FDA starts. And then once they take a look at those things as good indicators of where you are, then they'll usually ask for specifics.

Another thing I really recommend is that manufacturers take a look at what's in their most recent history. So, for instance, if they've filed a bunch of MDRs this year, if they've had a recall this year, and if they got a new 510(k) in the last two years, those are areas where the FDA will typically look and ask questions. So firms should make sure they're ready with answers to those types of things, and they're prepared ahead of time with an explanation of what happened, why those things are occurring and what they've done to correct them.

Q: How long do desk audits typically take? About the same amount of time as an on-site visit?

A: Chase: Well, first of all, it is a rare, rare, rare instance that the FDA ever does a desk audit. I mean—

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Q: Can you think of the last time—

A: Chase: I can't. I can't even think of the last time. I literally cannot think of a time in probably 16 years that I've known them to do this as a routine course of business. Of course, we've not been in a pandemic like this as a routine course of business in the last 16 years. So I can't say that it's off the table, and it's not novel thinking.

If I were still at the agency, if I were still a director there, here's what I would do: I'd try to knock out as many desk audits for lower-risk companies that will count toward my work plan obligation, so that when we do come back to work, I only have to focus my resources on those highest-priority, highest-risk inspections that haven't been done. I'm obviously not going to perform a desk audit for my highest-risk firms because that's dangerous.

So I would imagine that that's what the FDA is going to do, that they're going to go for the lowest risk, biggest bite out of their work plan, and get them done as quickly as possible. I could imagine that if a firm has an established quality system, and it provides the documentation, that the FDA could get through a review of that documentation in two or three days.

Q: What are some pitfalls for manufacturers that undergo a desk audit?

A: Chase: Not having current data, and then therefore not being able to hand over the documents in the timeframe in which the FDA establishes. Particularly, if they're subjecting you to a desk audit, you do not want to ask for an extension. You do not want to delay. The impression that gives is terrible. Also, don't get nervous, because this is a new process, and when people get nervous, they tend to like to talk. Don't get nervous, and don't start bombarding your investigator with emails and telephone calls. Just let them do their process. And when they're ready to talk to you, they'll talk to you. Don't bombard them with communication. Let them do their job.

And don't get defensive, because you have to remember that they're doing a review in a vacuum. They don't have the ability to converse with you while they're doing it. If they come back at you with a concern or an observation, try to take a calm approach to discussing it, particularly if you feel like they don't have the entire picture because it is a desk audit. And try to talk through those in a calm, collected way, and not let the situation and the newness of the situation put you on edge. That won't be perceived well, either.

Q: How would the FDA give out a 483, if it had to?

A: Chase: Well, the FDA has mailed 483s before, so I would hope that if there were going to be a 483 observation, that they would at least have a conference call, talk through the 483 observation, and give the company the opportunity to respond to those observations as they would in any other case. And then the agency, if necessary, would send the 483 to the firm for it to sign, and then it would be sent back.

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‘Have Some Level Of Fear’: How Scrapped FDA Inspections, Hastily Made Ventilators Could Portend Product Problems

In the haze of COVID-19, deadly ventilator failures could go undetected, ex-agency official warns

Executive Summary

Two former US FDA officials tell Medtech Insight they’re concerned about product problems down the line as automobile manufacturers make critically needed medical ventilators amid the COVID-19 crisis, and as device makers quickly scale up manufacturing on items like masks and gowns. Compounding problems is the agency’s decision to stop conducting quality systems inspections domestically and abroad.

Kwame Ulmer is troubled about makers of automobiles contract manufacturing complex medical ventilators as the world struggles with the COVID-19 pandemic.

“It worries me. I can’t lie,” the former US Food and Drug Administration official told Medtech Insight.

General Motors Co. has partnered with Seattle-based Ventec Life Systems to manufacture ventilators, and Ford Motor Co. is working with GE Healthcare to do the same. Even Tesla Inc. has gotten in on the action by ramping up production of the devices with Medtronic PLC.

GM says its goal is to make more than 10,000 ventilators a month, while Ford claims it will manufacture 50,000 of the machines within the next hundred days. (Tesla hasn’t said how many of the devices it will make.)

“In a normal world, qualifying and adoption of a contract manufacturer, and doing pilot manufacturing runs, et cetera, would take weeks,” Ulmer said.

“This timeline [to make ventilators] appears to be compressed, and while GM will likely follow good manufacturing practices, it is a new set of procedures and approach to processes like CAPA [corrective and preventive action], complaint handling and Medical Device Reporting that GM has to learn,” he said.

And in a March 20 LinkedIn post on the topic, Ulmer said “the general public does not have a good sense of the complexity involved in making ventilators.” He even added a hashtag: #Ventilatorsarenothubcaps.

Ulmer would know. For five years – 2009 to 2014 – he helped regulate ventilators as deputy director for the FDA’s (now defunct) Division of Anesthesia, General Hospital, Respiratory, Infection Control, and Dental Devices (DAGRID).

“I think the devil will be in the details,” said Ulmer, who is principal consultant at his own firm, Ulmer Ventures. “If these auto companies are playing to their strengths of logistics or quickly sourcing suppliers so the supply chain can be robust, that’s one thing. But it’s worrisome if they’re a contract manufacturer.”

Ulmer isn’t the only ex-FDA official who’s concerned.

“If somebody tells me they don’t have any fear of a company like Tesla or Ford making a ventilator, I question where they’re coming from. You should have some level of fear,” said Ricki Chase, a former FDA investigations branch director.

“Now, the answer isn’t necessarily saying, ‘Heck

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no, don't let them make vents' – but you should have some healthy level of fear," she said in an interview.

Chase became a consultant to the life sciences industry in 2016 after spending 16 years at the FDA, where she was also an investigator, medical device specialist and supervisory investigator.

Many 'Reasons To Be Worried'

Chase said there are "a lot of reasons to be worried" about an auto company manufacturing a high-risk, life-supporting, life-sustaining medical device.

"But that's not because they don't have the engineering capabilities. They certainly have the engineering capabilities. They certainly have the money to put behind it," she said. "But manufacturing a vehicle or even parts of a vehicle is very different from manufacturing a ventilator, or even a BiPAP or a CPAP."

The FDA is allowing the use of continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) devices on COVID-19 patients, it said in a 22 March enforcement policy guidance. (Also see "FDA Allowing Modifications To Ventilator Equipment To Bolster Supplies During COVID-19 Crisis" - Medtech Insight, 23 Mar, 2020.)

"So, let's consider the best-case scenario. A ventilator manufacturer hands an auto company its design for a ventilator. Well, the car company still has to source the materials. It still has to have qualified people put it together properly. And it still has to be able to validate the process," Chase said. "All of those activities look very different in the medical device world than it does in the automobile manufacturing world.

"And a lot of [the auto makers] will say, 'We're certified by ISO [the International Organization for Standardization].' But it doesn't matter. That's completely irrelevant," she added.

Chase is also worried that the auto companies will cut corners on quality in an effort to get the ventilators to market faster.

"I'm concerned that they'll not make the best choices in grade of material, and not understand that something that is a plastic is not a plastic when it's operating in that type of device. So I'm concerned about the sourcing and materials being of medical grade," she said.

Ventilator Failures Could Go Undetected

Another concern for Chase is the car makers' ability to detect problems with finished ventilators in the postmarket space.

"GM, Ford and Tesla aren't set up to be a medical device company. So how are they going to manage feedback from the field?" she asked.

"That feedback isn't going to come from the patient, the end user. Rather, it's going to come from the clinician or the hospital," Chase said. "But how are they going to do that? Do you actually think that the clinicians in the hospital are going to be taking time to report back to one of those auto companies that there's something wrong with their vent? No – not until there's been a lot of incidents."

And unless a ventilator obviously malfunctions, health care workers might believe it was the coronavirus that killed a patient, when in fact the death could've come as a result of a faulty vent.

That means that malfunctioning device – which led to a patient's death – could be used again and again, with its deadly problems going undetected.

"So what killed the patient? The device or the disease? It's going to be really hard to tell," Chase said – although with many life-sustaining devices

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it can often be difficult to detect a failure and determine if the products contributed to a death.

"I could imagine a situation where a vent is reading that it's putting out a certain max flow, or it's creating a certain pressure in the pulmonary space, but it's not giving a true measure and the patient desats and dies," she said. "It would be very easy to think that the patient desatted and died because of the disease, and not because the vent is showing one value of pressure and flow when it's really delivering something different."

She noted that a ventilator would have to suffer a "fatal failure" for most health care workers to know that it's not working correctly.

"It would have to be a situation where the vent doesn't turn on or the vent suddenly turns off – or it blows up and catches on fire. An obvious flaw," Chase said.

"I'm definitely concerned about the hidden, less detectable fault."

The Pitfalls Of Quickly Scaling Up

More broadly, the COVID-19 crisis could be the catalyst for troubles in other product types.

"There are medical device manufacturers that are ramping up production on things like masks, gowns and other personal protective equipment. They're talking about doing 50% higher production in a month, doubling production in two months, and even tripling production in three months," Chase said.

"Any time you scale up production that rapidly, the margin for error when it comes to deviation, nonconformance, material, cutting corners on material acceptability, testing, et cetera, is small," she said.

"Even if you're a skilled medical device manufacturer, if you ramp up production like that, you're at risk of seeing more complaints and more MDRs, and you're putting yourself potentially in a recall situation, because you don't have the skill to manage that type of capacity."

'When The Cat's Away, The Mouse Plays'

Compounding problems is the FDA's decision last month to put the kibosh on conducting quality systems inspections at manufacturing facilities in the US and abroad. (Also see "COVID-19: US FDA's Hahn Slams The Brakes On Domestic Inspections 'For The Health And Well-Being Of Our Staff'" - Medtech Insight, 19 Mar, 2020.) and (Also see "COVID-19: FDA Expands Overseas Inspections Freeze Through April" - Medtech Insight, 14 Mar, 2020.)

The agency had stopped inspections of Chinese plants in February. (Also see "Coronavirus: All FDA Inspections Of Chinese Manufacturing Facilities Come To Screeching Halt" - Medtech Insight, 15 Feb, 2020.)

"I'm always concerned when FDA delays an inspection," said Chase, who managed a team of investigators when she worked at the FDA.

She said manufacturers can become lackadaisical if they know they won't be seeing an agency investigator at their facility anytime soon.

"When the cat's away, the mouse plays," Chase said. "And that's just something that industry has typically done, even when we saw the H1N1 crisis and swine flu, when FDA slowed down inspections.

"So, yeah, I'm definitely worried about that."

Stephen Sunderland, a partner in the Shanghai office of consulting firm L.E.K. Consulting, told Medtech Insight that he, too, is concerned about the trickle-down effects of suspended FDA

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inspections, but he believes the impact will be minimal.

"The shutdown of FDA's inspection program in China is expected to be relatively short term. And a manufacturer might only get an inspection once or twice a year anyway. So if we're just delaying that by a couple of weeks, then maybe that's OK," Sunderland said.

But "ultimately, if companies aren't producing, then there's not much to inspect," he added. Investigators "can go over records and things, but clearly, actually seeing the day-to-day practices of an operating facility is an important part of how to get a sense of whether that facility is safe or not in producing product. And those facilities are shut down due to COVID-19 and won't be producing anything.

"So FDA wouldn't see anything even if it did the inspections."

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CMS Doubles Up On Test Reimbursements, Will Pay Labs $100 Per Test For COVID-19 Clinical Diagnostic Assays

Compensation nearly double the current $51-per-test rate

Executive Summary

The US Medicare agency said on 15 April it will double its reimbursement rate for certain COVID-19 lab tests.

The US Centers for Medicare and Medicaid Services (CMS) announced on 15 April that it will pay nearly twice what it usually does for certain laboratory assays using high-throughput technologies to rapidly diagnose the COVID-19 virus.

The agency's reimbursement for the tests will increase from $51 per test to $100, retroactive to 14 April and run through the duration of the coronavirus national emergency, CMS ruling CMS-2020-01-R says.

The objective of the hike in reimbursements for COVID-19 assays is to get as many people – particularly the Medicare population in nursing homes – tested as quickly as possible, according to CMS administrator Seema Verma. She called the move "an absolute game-changer for nursing homes."

Medicare will compensate laboratory companies and clinical labs at the higher payment rate for use of high-throughput technologies that allow for increased testing capacity, faster results and more effective means of combating the spread of the virus.

High-throughput lab tests can process more than 200 specimens a day using highly sophisticated equipment that requires specially trained technicians and more time-intensive processes to assure quality.

"CMS has made a critical move to ensure adequate reimbursement for advanced technology that can process a large volume of COVID-19 tests rapidly," Verma said.

For other lab tests, local Medicare Administrative Contractors (MACs) remain responsible for developing the payment rate in their respective jurisdictions, with the going rate currently set at $51 per test. As with other lab tests, there is generally no beneficiary cost-sharing under original Medicare plans.

Lab Group ACLA Applauds The Change

The American Clinical Laboratory Association praised the Medicare agency's action.

"In an acknowledgement of the considerable strain that has been placed on clinical laboratories supporting our nation's response to the COVID-19 pandemic, the administration today took decisive action to expand the availability of testing for patients nationwide," ACLA president Julie Khani said in a statement.

"As we've said from the beginning, this crisis demands the full force of the clinical laboratory industry – private, public, academic and hospital laboratories are all in this together," she added. (Also see "US Clinical Labs To Lose Money On COVID-19 Testing Without $5Bn Set Aside In Third $1Tn Aid Bill" - Medtech Insight, 20 Mar, 2020.)

Khani noted that the lack of predictable reimbursement for tests performed "has been a

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barrier to entry for some laboratories, and today's decision will help encourage all laboratories with the appropriate expertise to come to the table and perform COVID-19 testing. We also hope that other payers will follow CMS' strong example."

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Weathering The 'Cytokine Storm': US FDA Gives EUA To Blood Purification Machine

Executive Summary
US regulators have given emergency use authorization to a blood purification system that can remove excess cytokines to help patients recover from the novel coronavirus. Recent studies on COVID-19 indicate some patients may be dying from the body producing excess amounts of the proteins that direct the immune system's response.

The US Food and Drug Administration has given emergency use authorization (EUA) to a blood purification system to help patients filter out excess proteins known as cytokines. Physicians have reported "cytokine storms" in response to COVID-19 that could account for why some patients relapse and die from organ failure after initially showing symptoms of improving.

The agency on 9 April sent a letter to Terumo Corp. giving the company EUA for the its Spectra Optia Apheresis System with the Depuro D2000 Adsorption Cartridge. The system, also known as an extracorporeal blood purification (EBP) device, is intended to clear the blood of inflammation-causing cytokines. The EBP is only intended for adults confirmed to have COVID-19 who have been admitted into the intensive care unit (ICU) or are at risk of imminent respiratory failure. The agency also stipulates the device can only be used up to four hours a day. [I'll put letter in SD]

Denise Hinton, the FDA's chief scientist, said several tests and clinical case series have found that the Spectra system may effectively separate plasma from whole blood, and the Depuro cartridge may remove various pro-inflammatory cytokines from that plasma before returning the blood to the patient.

"FDA believes based on the totality of scientific evidence available, that the removal of pro-inflammatory cytokines may ameliorate cytokine storm due to the overabundance of proinflammatory cytokines and, in turn, provide clinical benefit," Hinton wrote.

Cytokines are released by the patient's immune system in response to an infection to help coordinate its ability to fight a disease, which under typical circumstances is a good thing. However, physicians have reported that patients with COVID-19 seem to produce an overabundance of cytokines – called a cytokine storm – which may mean the body's immune system ends up attacking its own organs instead of just the disease. This overreaction from the immune system could explain why patients initially recover from COVID-19 only to get sicker and eventually die.

Cytokine storms became a focus of attention after the 2005 H5N1 bird flu outbreak when patients were reported to have died, not necessarily form the virus, but from the body's immune system overreacting because of an overabundance of the proteins. The storms are also associated with other respiratory diseases such as the flu, SARS and MERS, as well as certain rheumatic diseases.

Until now the only option physicians had to reduce the effects of cytokine storms were anti-inflammatory drugs, but the FDA hopes the EUA will help their ability to reduce cytokines in patients and as a result the body's potential overreaction to the disease.

"With today's authorization of a blood purification

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device, we are expediting the availability of a treatment option for patients in the ICU to help reduce the severity of the disease," FDA commissioner Stephen Hahn said in a 9 April statement. "Our staff will continue our around-the-clock review of all medical products to expedite the availability of treatments to help fight this devastating disease."

Hinton explained that the Depuro cartridge contains absorption materials that have shown to be effective in removing significant proportions of cytokines such as IL-3, IFN-gamma, IL10, IL-1B, IL-6, IL-8, MCP-1 and TNF-alpha.

"The adsorbents attract solutes through a variety of forces, including hydrophobic interactions, ionic (or electrostatic) attraction, hydrogen bonding and van der Waals interactions," Hinton said. "Management of the cytokine storm and cascade associated with COVID-19 whilst treating the underlying pathogenesis may decrease patient morbidity."

However, she cautioned that "the reduction of cytokines must be done in a discrete, controlled fashion to balance the patient's immune response to the infection with the removal of the excess inflammatory cascade. Therefore, therapy with the [Depuro cartridge] will be administered for up to four hours per day."

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FDA Relaxes Regs For COVID-19 Mental Health Apps

Executive Summary
With the increasing concern for people's mental health as they cope with the COVID-19 crisis, the US agency has relaxed regulations for apps that are intended to treat disorders such as anxiety, depression and insomnia. Certain digital health products would not require a 510(k) clearance during the crisis to enter the market under an immediately-in-effect 15 April guidance document.

Much of the focus during the ongoing novel coronavirus pandemic has been on diagnosing and treating the COVID-19 disease, but health officials are also growing increasingly concerned about the psychological toll it's having on society. As a direct response, US regulators have published a an immediately-in-effect guidance document that relaxes regulations to allow patients to have more access to digital mental-health products.

The US Food and Drug Administration on 15 April published "Enforcement Policy for Digital Health Devices For Treating Psychiatric Disorders During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency." The guidance allows some mental health apps to skip the traditional product approval pathways in order to help patients cope with a slew of potential psychiatric disorders during the pandemic.

The temporary emergency guidance will be revoked when the national public health emergency is over.

"FDA believes the policy set forth in this guidance will help address these urgent public health concerns by helping to expand the availability of digital health therapeutic devices for psychiatric conditions," the agency said. "Device availability may increase patient access to digital therapeutics while individuals are following 'stay at home' orders or practicing social distancing, without the need for in-clinic visits during the COVID-19 public health emergency. Furthermore, increased utilization of digital therapeutic devices may ease burdens on hospitals and other healthcare facilities and reduce the risk of exposure to SARS-CoV-2 for patients and health care providers."

The products that would be allowed through this new guidance could be used to treat symptoms and disorders including depression, alcohol use disorder, anxiety, insomnia, suicidality, autism, attention deficit hyperactivity disorder, obsessive compulsive disorder, and post-traumatic stress disorder.

In a recent article in the Journal of the American Medical Association, researchers warned that the current crisis will have long-term psychological effects that societally we should prepare for.

"In the context of the COVID-19 pandemic, it appears likely that there will be substantial increases in anxiety and depression, substance use, loneliness and domestic violence; and with schools closed, there is a very real possibility of an epidemic of child abuse," the authors wrote.

"This difficult moment in time nonetheless offers the opportunity to advance our understanding of how to provide prevention-focused, population-level, and indeed national-level psychological first aid and mental health care, and to emerge from this pandemic with new ways of doing so," they opined. "The worldwide COVID-19 pandemic, and efforts to contain it, represent a unique threat, and we must recognize the pandemic that will quickly follow it – that of mental and behavioral

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illness – and implement the steps needed to mitigate it."

Increasing Access To New Apps

The FDA seems to agree with that assessment and finds it important to relax regulations so more tools are available to health care providers and patients to mitigate such mental health risks. Digital therapies covered under the guidance are intended to provide patients with access to therapy tools used during treatment sessions to improve recognized treatment outcomes.

The agency says certain computerized behavioral therapy devices and other digital health therapeutic devices for psychiatric disorders will not be required to have a 510(k) clearance. But their makers must report corrections and removals, include a Unique Device Identifier on the product, and follow registration and listing requirements or institute special controls as long as they don't create undue risks. The guidance, however, does not apply to previously cleared class II products, or those intended to be solely or primarily used by health care providers and patients to make a clinical diagnosis or treatment decision.

To prevent any undue burdens the FDA says the manufacturer needs to ensure there has been software has been verified and validated, and has undergone a hazard analysis that shows the product works as intended. The product also needs to have appropriate cybersecurity protections in place and follow labeling guidelines that include measures such as telling patients to talk to a physician before using the device, even if the device is marketed directly to the consumer.

"An example of a circumstance where FDA currently believes devices would create such an undue risk includes treatment claims for specific psychiatric conditions where the underlying psychiatric condition may require an urgent or immediate clinical intervention and the delay of the intervention may pose significant harm to the patient, such as treatment of suicidality," the FDA added.

General Wellness Products Get A Pass

The agency also reiterated that it won't regulate low-risk general wellness devices .

"In light of the public health emergency, FDA is providing clarity on our policy, set forth in the General Wellness and Software Functions and Mobile Medical Applications guidance documents, for low-risk general wellness and digital health products for mental health or psychiatric conditions, arising due to situations created by the COVID-19 public health emergency, such as isolation, quarantining and social distancing, to help foster the continued availability of these products, particularly without the need for in-clinic visits," the agency said.

Specifically, the agency says there are four categories of wellness products that it will refrain from regulating, including those for promoting relaxation, mindfulness, meditation and sleep. General wellness software products specifically related to the COVID-19 pandemic, such as those giving motivational tips via text or other modes to improve mental outlook, are also included as products that promote social distancing practices.

The new guidance seems to be in line with the FDA's overall thinking on digital health products in general. The agency has been working on developing a new pathway for digital health products through its precertification pilot program; it recently cleared Pear Therapeutics' Somryst insomnia treatment tool via that pathway. (Also see "FDA OK's Insomnia Treatment Through Software Pre-Cert Program" - Medtech Insight, 2 Apr, 2020.)

The program allows the agency to clear digital

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health products based on the level of trust they have in a company to produce safe and effective products, but also gives the companies flexibility to update their products faster.

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COVID-19: String Of FDA Guidance Docs Lay Bare Enforcement Policies For Infusion Pumps, ECMO Devices, Thermometers, And More

Executive Summary

In three separate immediately-in-effect guidance documents, the US agency says makers of infusion pumps and accessories, extracorporeal membrane oxygenation (ECMO) and cardiopulmonary bypass devices, and remote ophthalmic assessment and monitoring devices can make "limited modifications" to those products so they can be used during the ongoing novel coronavirus crisis, without the need for firms to seek out a new 510(k). A fourth guidance says clinical electronic thermometers that aren't yet 510(k)-cleared by the FDA can be distributed for use.

The US Food and Drug Administration has released a quartet of guidance documents that lay out enforcement policies for infusion pumps, ECMO and cardiopulmonary bypass devices, ophthalmic devices, and electronic thermometers.

The immediately-in-effect guidances were issued in response to the ongoing COVID-19 crisis in the US; they will be revoked when the national public health emergency is over.

Infusion Pumps And Accessories

The FDA's guidance for infusion pumps and accessories, dated 4 April, says manufacturers can make "limited modifications" to those devices without having to deal with the red tape of applying for a new 510(k) from the agency.

"FDA does not intend to object to limited modifications to the indications, functionality, hardware, software, design or materials of FDA-cleared devices used to support patients who require continuous infusion therapy … for the duration of the public health emergency," the document says.

Pumps covered by the guidance include large volume parenteral (LVP) infusion pumps, syringe infusion pumps, patient-controlled analgesia (PCA) infusion pumps and ambulatory infusion pumps; the document includes a detailed listing of eligible devices.

The guidance says the policy will give device makers the flexibility to make changes to address "manufacturing limitations or supply shortages."

The FDA's doc offers as an example a company that makes changes to its infusion pump motor so it can use an alternate supplier and still meet the pump's design specs.

"We believe this approach will help manufacturers that want to add production lines or manufacture at alternative sites which may have different manufacturing equipment to increase manufacturing capacity and supply, and reduce supply chain interruptions and manufacturing bottlenecks," the guidance says.

The agency makes clear in its doc that any changes must not create an undue risk. The guidance offers examples of modifications that do and don't create such risk.

Further, the FDA says it won't object to manufacturers making modifications to their pumps that allow for increased remote monitoring, including the use of wireless and/or Bluetooth capabilities.

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For those types of changes, "manufacturers should develop and implement appropriate cybersecurity controls," the guidance says.

And pump accessories such as tubing, filters and manifolds can be used beyond their expiration date as long as it doesn't create any undue risks. Again, the guidance offers examples of what would and wouldn't create such risk.

The agency's document also includes a listing of international standards and other FDA guidances designed to aid companies "in designing, evaluating and validating modifications made under this policy."

Firms that modify their pumps should make sure that the labeling clearly explains to users the changes that were made, the guidance says.

The FDA also says it wants to "interact" with "manufacturers of infusion devices that are not currently legally marketed in the US."

The guidance urges such companies to provide information about their unapproved pumps so the agency can determine whether to grant emergency use authorizations (EUAs) for them.

Finally, the document says the FDA wants to talk to firms that "have not previously been engaged in medical device manufacturing with capabilities to increase supply" of the pumps.

"This may include US manufacturers in other manufacturing sectors," the guidance says. "FDA intends to work collaboratively with these manufacturers through its EUA process."

ECMO And Cardiopulmonary Bypass Devices

Meanwhile, a 6 April enforcement policy guidance from the FDA targets devices used for extracorporeal membrane oxygenation (ECMO) therapy, as well as cardiopulmonary bypass devices.

The guidance says makers of those devices can also make "limited modifications" to the products without seeking out a new 510(k), as long as the changes don't create undue risks.

And just like the infusion pump guidance, this document also includes examples of changes that do and don't create such risk, as well as recommendations for what manufacturers should include in the modified devices' labeling.

The guidance also offers a listing of international standards that firms should use as they make device changes.

"Manufacturers must document changes to their device in their device master record and change control records, and make this information available to FDA, if requested," the document says.

The guidance applies to devices that pump or oxygenate blood by:

- Moving the blood to a component that pumps/oxygenates the blood;
- Controlling pump speed;
- Controlling or monitoring gas flow for the circuit; or
- Controlling the temperature of the blood.

It doesn't apply, however, "to devices intended only for extracorporeal carbon dioxide removal, because such devices may not oxygenate the blood at clinically meaningful levels."

Nevertheless, the agency says makers of those types of devices can request an EUA, as can "manufacturers of ECMO devices, or manufacturers of cardiopulmonary bypass

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devices seeking indications greater than six-hour use to be used for ECMO, that are not currently legally marketed in the US."

Remote Ophthalmic Assessment And Monitoring Devices

A third enforcement policy guidance, this one also dated 6 April, says makers of remote ophthalmic assessment and monitoring devices can make "limited modifications" to their products so they can be used remotely.

Such devices include visual acuity charts, visual field devices and general-use ophthalmic cameras – all products that are exempt from 510(k) requirements.

Tonometers, which do require 510(k) clearance, also fall under the scope of the guidance.

The ophthalmic devices "have the potential to be connected to a wireless network through Bluetooth, wi-fi or cellular connection to transmit a patient's ophthalmic parameters directly to their eye care provider or other monitoring entity," the guidance notes.

It goes on: "Modified use of these devices may facilitate patient management by health care providers while reducing the need for in-person treatment during the COVID-19 public health emergency, and may help reduce the risk of exposure for patients and health care providers."

Once again, any changes to the devices should not create undue risks, and the document offers examples. A listing of international standards that companies should use is also provided.

Further, labels for the modified devices should include information for users detailing the changes that were made.

Clinical Electronic Thermometers

Finally, a fourth enforcement policy guidance from the FDA dated 4 April allows makers of clinical electronic thermometers that aren't 510(k)-cleared to distribute the devices for use, as long as they don't create undue risks.

The agency "believes such devices will not create such an undue risk" as long as the company making them follows regulatory requirements found in the agency's Quality System Regulation or international quality systems standard ISO 13485.

The thermometer also should have marketing authorization from another country or conform to international standards, a listing of which is provided in the guidance.

The document adds that the thermometer's labeling should include "a clear description of the available data on the device's indications or functions," including:

- Device performance;
- Method of determining temperature;
- Potential risks; and
- Cleaning and reprocessing instructions.

The labeling should also note that the thermometer isn't FDA approved or cleared.

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