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# Outlook 2020 Teleconference: Washington, D.C. Updates and Insights on Life Sciences and Health Care

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**Al:** Hello, and thank you for joining our teleconference today. I am Al Cacozza, partner in the Washington, DC office of Ropes & Gray and member of the firm's life sciences regulatory compliance group. This teleconference is part of our ongoing Capital Insights series, where we are capturing our latest thinking on developments from the federal government that might affect our clients— in this case, the outlook for regulatory and compliance issues in 2020 of particular interest to life sciences and health care companies.

Our Capital Insights page at www.ropesgray.com includes alerts, analyses and podcasts, and we invite you to continue to visit that page throughout 2020.

Joining me today are several of my colleagues from the DC office: Tom Bulleit, from our health care group, Kellie Combs, Beth Weinman, and Greg Levine, from our life sciences regulatory compliance group, and Samantha Barrett Badlam, with our litigation and enforcement group.

Over the next hour, we will discuss specific issues within three broad categories: healthcare policy topics, FDA drug and device regulatory issues, and compliance and enforcement trends that could impact health care and life sciences companies in 2020. We plan to save time at the end of the teleconference to address questions from our listeners.

If you have questions during the teleconference, please email them to rgevents@ropesgray.com. That's rgevents@ropesgray.com, and we will try to get to as many as we can. One further note, we are offering CLE credit for this teleconference. I will provide you with the necessary information to receive such credit at the end of the teleconference. Additional supplementary materials for content mentioned today can also be found in your confirmation email.

## Prescription Drug Pricing

**Al:** So now, let's begin with Tom Bulleit from our health care group. Tom, last January at this teleconference, we discussed how neither of us had ever seen so much attention on the subject of prescription drug pricing. If anything, the noise around this issue has only grown louder. Can you catch us up on what happened on this issue in 2019?

**Tom:** Thanks, Al. Yes, once again, drug prices were in the crosshairs of both the Trump administration and Congress. I just published an article in Law360 analyzing what happened over the past year, and the short story is that despite the flurry of proposals out there, few measures of any consequence took effect in 2019. The administration did finalize modest reforms to expand transparency and encourage utilization controls like step therapy in Medicare, but several of their more consequential proposals were defeated. The administration abandoned proposals to weaken the Medicare Part D protected classes, and to reform anti-kickback statute regulatory safe harbors to redirect manufacturer drug rebates from Medicare and Medicaid plans and PBMs to beneficiaries at the point of sale. CMS's rule requiring list prices in television advertisements also was struck down by the courts and is currently on appeal.

**Al:** Tom, is there anything likely to happen on pricing in 2020?

**Tom:** In two words, not much. HHS has teed up two proposals that could be finalized in 2020. First, the administration has proposed allowing states to import certain drugs from Canada. This is a major reversal in policy for FDA; but, even if it's implemented, it's unlikely to have much of an impact: Canada is a small country and gets a proportionately small number of drugs, manufacturers are likely to discourage their distributors from increasing the number, and the Canadian government is likely to take measures to make sure the Canadian supply doesn't run short. And Beth, I wonder if there's any issue here with FDA's regulatory authority?

**Beth:** I think there is, actually. I think that's a serious question. The statute requires that the HHS Secretary certify, if one wants to implement a program like this, that the program not only poses no additional risk to public health and safety, but also that it's going to result in a significant reduction in cost to consumers. The second part of this certification is really, I think, the root of the problem here. The agency notes several times in the proposed rule that it doesn't know anything about the cost impact here, and that the Secretary is going to make the required certification upon issuance of the final rule. Tom, if you and other commentators are right, that the importation rule is not going to have much of an impact on cost, I just don't see it. I don't see how FDA can meet the legal requirement for implementation of the program under the current statute.

**Tom:** Thanks, Beth. And then the second thing that might have some impact this year is that HHS also could move forward with the demonstration project proposed back in October 2018 to use an international pricing index to pay for certain drugs under Medicare Part B. Now, if you've been watching the news, the current rumor is that the administration may release, before next week's State of the Union, that rule, so the President can claim a victory. If so, it would face significant legal challenges as being beyond CMS demonstration authority and inconsistent with current law. So, whatever happens, it's unlikely to take effect this year.

**Al:** So, let's turn from the executive branch to what's going to happen in Congress.

**Tom:** Again, not much. Last year, Congress enacted only a few drug pricing measures: two non-controversial tweaks to the Medicaid Drug Rebate Program, plus the CREATES Act, which will help companies obtain samples of brand-name drugs to develop generics. Senator Grassley's bipartisan bill stands the best chance of enactment, and its limits on inflationary rebates for price increases that exceed the rate of inflation would certainly have some impact, and the President has endorsed that bill. We'll see if that is enough to get Senator McConnell to give it a vote. And if it is successful in the Senate, if the House will compromise on something less than Speaker Pelosi's bill, which is a much stronger measure that would allow the government to negotiate prices, but stands no chance of actually passing.

## Surprise Billing

**Al:** Let's turn from drug pricing to another issue called surprise billing. Tom, can you explain what that is, and where things stand?

**Tom**: Sure. Surprise billing is where consumers receive unexpected, often high medical bills for out-of-network care, even though they did not intend to see an out-of-network provider, like a patient visits an in-network hospital, but a physician, like an anesthesiologist, radiologist, or laboratory to which samples are sent, is out-of-network. Ironically, there is agreement that something should be done, and the argument in Congress is over whether to get to the rate by arbitration (which the providers generally favor) or benchmark rates (which insurers and employers favor). With that being the only difference, it seems that there could be a

compromise on that this year when lawmakers revisit expiration of must-pass healthcare funding in May; again, that would still likely face legal challenges.

### Provider Pricing Transparency

**Al:** Let's talk about another topic. Tom, how about pricing transparency, but not just for drugs; what's happening there?

**Tom:** Well, in December, some of the nation's largest hospital groups and three individual hospitals and health systems sued the Trump administration over a new federal rule that requires hospitals to disclose, publicly, the discounted prices that they provide for insurers for various procedures. The hospitals argue that the administration exceeded its statutory authority under the Obamacare requirement which requires posting "standard charges" for items and services. They further argue that requiring hospitals to disclose their private negotiations would violate their First Amendment speech rights. CMS Administrator Seema Verma was widely-quoted this week scolding hospitals for standing in the way of consumer welfare. This is one, again, that will be stuck in litigation for a while.

### Affordable Care Act

**Al:** You just mentioned that the authority for these transparency proposals comes from the Affordable Care Act. Let's turn to that Act. I understand there is a good chance that the law will come before the Supreme Court, once again, now for the third time. Can you tell us more about where the challenges stand?

**Tom:** This is great political theater, and since the Supreme Court recently decided that the issue won't be decided until after the election, it's going to remain that way for all of 2020. The case is about Congress's zeroing out of the tax penalty for violating the individual mandate, and a group of Republican attorneys general, joined by the Trump administration, sued to have the Act declared unconstitutional, since the Supreme Court had upheld the mandate as an exercise of Congress's taxing power. Without getting into the weeds on the procedures, the case is back at the trial court, which now has to justify why, if the mandate is unconstitutional, the rest of the law, much of which, like the FDA pathway for biosimilar approval and the Centers for Medicare and Medicaid Innovation, seems to have nothing to do with the mandate. It's unlikely this will get back to the Supreme Court before the election, so the ACA will stay in effect this year.

**Al:** Anything else happening with the ACA? What about taxes that were repealed?

**Tom:** Yeah, in December, President Trump signed into law a spending bill that repealed three of the major taxes that were supposed to fund the ACA, although none of them had ever been implemented or were suspended at the time of their repeal. They were the excise tax on high-cost, employer-sponsored health plans, called the "Cadillac tax," the health insurance tax on health plans, and the excise tax on medical devices. Though a win for industry and employers, the repeal of the taxes is estimated to increase the federal deficit by $373 billion over the next decade.

### Value-Based Healthcare

**Al:** Let's turn to our last policy topic in this area, and that's value-based healthcare. Can you summarize anything noteworthy that happened on that front in 2019?

**Tom:** Sure. Both HHS and the private sector continue to pursue value-based health care. As a refresher, this means paying for quality of outcomes rather than the quantity of procedures. The most significant development

in 2019 came from OIG and CMS, which released long-awaited proposed rules amending regulations under the Stark Law and the Anti-Kickback Law to protect value-based arrangements, and again, without getting into the weeds, in general for contracts with referral sources that could otherwise present Stark and AKS issues, the more downside risk assumed by the referral source, the more freedom to share upside would be allowed. Perhaps of most interest here is who would benefit. As currently proposed, the providers, doctors and hospitals would be able to use these, but clinical labs, pharma manufacturers, and DMEPOS suppliers wouldn't. Other medical device manufacturers seem to have survived the first cut, but there are suspicions that the final rules will not be as generous to device makers, especially those making physician preference items, like implantables. And aside from the proposed rules on Stark and Kickback, the main value-based proposal is CMS's Primary Cares Initiative, which offers primary care doctors the chance to enter into contracts that will make their pay more performance-based. It's a voluntary program, so its impact is uncertain. Applications are still being accepted for some of the models, and those would begin in January of next year.

**Al:** Tom, thanks for that very detailed discussion of those healthcare policy issues. Now we are going to turn to our next broad category, which is FDA regulation in the drug and device sectors. I first turn to my colleague, Greg Levine, to talk about the new FDA commissioner. Greg, Dr. Steven Hahn recently was confirmed by the Senate as the new FDA commissioner, following Dr. Scott Gottlieb's resignation last March. In the interim we have had two acting Commissioners. Can you tell us what you know about Dr. Hahn and what impact we should expect his confirmation to have?

## New FDA Commissioner

**Greg:** Thanks, Al. Well, first I'd say, compared to other past Commissioners, we know less about what to expect from Dr. Hahn. We know he was a prominent clinician, we know he was an administrator– a healthcare administrator– until December, he was the chief medical executive of The University of Texas MD Anderson Cancer Center, a very prominent institution in Houston. And before that, he had been in other roles, both at MD Anderson and also at the University of Pennsylvania, both as an administrator and as a clinician. He has a bachelor's degree from Rice University, a medical degree from Temple, and he's board-certified in medical oncology and radiation oncology. He's a cancer doctor. He's also been a clinical researcher, specializing in lung cancer and sarcoma. He's authored more than 200 peer-reviewed research articles, journal articles. So, undoubtedly, he has a fair amount of exposure to FDA, at least in the clinical trial area and drug development, but he hasn't worked for the FDA or in state public health agencies as a regulator.

**Al:** MD Anderson Cancer Center is a very large place that has 21,000 employees and annual revenues of $5 billion, so obviously he is an experienced clinician and a seasoned executive, at least in the hospital sector. That does not seem like a typical resume for an FDA commissioner, now does it?

**Greg:** That's right, if we look at the commissioners over the last thirty years anyway, compared to that, he doesn't have the kind of government experience you typically see, whether it's at the federal level or at state or local levels. We have commissioners with those kinds of backgrounds more typically. He worked at NCI, National Cancer Institute, in the late '80s and early '90s, but he was a researcher doing clinical trials, he wasn't in a regulatory position, so it is atypical. I think the challenge there that will be interesting to see is how he

handles the job, because it's a very highly public position and, as we know, they're often in the political crosshairs there.

**Al:** Is it your sense that lack of Government experience had any impact on the confirmation process that he went through in the Senate?

**Greg:** There was some criticism, some concern about that, but he got through pretty easily actually. If we look at the vote, his confirmation vote in the Senate was on December 12; it was 72 in favor and 18 against. If we go back to Dr. Gottlieb in May of 2017, that was 57 to 42. A lot less concern with Dr. Hahn.

**Al:** Any thoughts on why the vote totals were so different?

**Greg:** I think primarily it's because in Dr. Gottlieb's case, the Democrats, there was a lot of concern about the nominee's longstanding ties to industry, he had previously been in the government, he had gone out, he worked for a venture capital firm for a lot of years and so there was concern that he may be too biased towards industry and would not make his decisions based on science and the law. And Dr. Hahn just didn't have that degree of ties to the industry.

**Al:** And as you noted, 18 senators voted against his confirmation. What concerns did those senators have about Dr. Hahn?

**Greg:** Mostly whether he would put science and data above partisanship and ideology. So, whether he would show independence from the White House. The most prominent Democrat speaking out on this was Senator Patty Murray from Washington State, she's the ranking member on the committee that held the confirmation hearing. Among other things, she tried to get Dr. Hahn to commit, at that hearing, to a ban that the administration had previously announced it was going to implement on all flavored e-cigarettes, other than tobacco flavor. All non-tobacco-flavored e-cigarettes, including menthol flavor. She found his answers evasive. Ultimately she said she was going to vote against him. She has a number of concerns, she did mention the lack of government experience, he didn't have a public record on FDA policy issues to judge him against. His experience was in leading a hospital, but he didn't have experience leading an organization as large or complex as the FDA. But she did say that the big red flag for her was that he wouldn't commit to this total ban on the flavored e-cigarettes. And that the Trump administration had reversed course on it after it "heard from the tobacco industry" on it, so it was being politically driven.

**Al:** What other issues came up at his confirmation hearing?

**Greg:** He got a taste of a lot of the hard issues, there were a lot of questions on the vaping and e-cigarettes, also issues like drug shortages, drug pricing, opioids, antimicrobial resistance, rare disease, CBD, OTC monograph reform. A pretty wide range.

**Al:** Do you think we learned anything from his answers to those questions?

**Greg:** Not much, he stuck to his talking points, he said he'd put the interests of the American people first, be guided by science, data, and the laws, you know, the right answers. He also mentioned he had a deep respect for Congress. So, Senator Romney did question his judgment on that one.

**Al:** Now he has only been on the job for a few weeks, so any thoughts on his short tenure?

**Greg:** It's hard to say so far, it's pretty early. He does seem to be trying to match his predecessor on use of social media, so he's tweeting frequently, daily, sometimes multiple times a day. We'll see if he can keep up that pace like Commissioner Gottlieb did. Probably not a big surprise that one of his first tweets was in favor of the administration's enforcement policy on flavored e-cigarettes, so he came out in favor, he said he thought it struck the right balance, but they did exempt menthol from the flavor ban and also exempted these "open tank," so if it's not in a cartridge, it's exempt. So about five minutes later Senator Murray sends him a letter basically excoriating him, actually her headline in a press release says she was "slamming" the FDA's policy, asking him to abandon it as inconsistent with the available science.

**Al:** So, he has a lot of challenges ahead of him. Which of those many issues facing him do you expect to be following most closely?

**Greg:** There's a lot of things, as we've said, but two that I have on my radar screen are this issue about the globalized manufacturing supply chain and also, some issues about initiatives the FDA has had in the works about the medical device area.

## Globalized Manufacturing Supply Chain

**Al:** So what do you see on the manufacturing issue, which I think is a very important issue?

**Greg:** Yeah, and it's not a new one, it's been around for years now. It just continues to increase in prominence. Potential risk posed on our reliance on foreign manufacturing is increasingly a concern; some of the recent data shows that only 28% of API used in drugs sold in the U.S. is manufactured domestically, for example. The concerns are kind of on two different planes: one is quality and safety, and the other is there is now some concern being expressed on national security-type grounds. On the quality side, there's been a number of issues with ingredients coming from China and elsewhere, particularly API– active pharmaceutical ingredients. We had a wide-scale recall of the blood pressure medications that were caused by contamination in API from Chinese suppliers. Actually right now, today, there were reports of some surveys of manufacturers in China saying they think the emergence of the Coronavirus could actually lead to shortages. So, we'll have to see. Some of the manufacturers over there are saying "No. it won't," so we're kind of in the fog of war on that, but we'll see where that goes. National security-wise, there have been some concerns expressed that on one hand, we could be unprepared for an emergency; secondly that the Chinese government or other governments, but China in particular, could "weaponize" the drug supply, as they could threaten to choke the drug supply. There's no evidence that that could actually could happen. But they've done it with other things, like they've threatened Japan with rare earth minerals, that they would reduce the supply of that. So, that's a concern. The things I'm looking at here, FDA has been focusing on the need for manufacturers to have mature quality systems along the lines of aerospace, automotive, and electronics industries. And they're talking about creating a rating system for quality so that purchasers could compare potential suppliers based on quality and not just price. I'd expect to see some developments on that front. And then also, the FDA is encouraging manufacturers to invest in advanced manufacturing technologies and maybe get into totally new types of technology, like "continuous manufacturing" rather than traditional "batch manufacturing." So, we'll see where that goes. I think there's actually legislation already on the Hill relating to that. And then also this issue that FDA pre-announces foreign inspections, that's the one that continues to be a concern.

## Device Safety Initiatives

**Al:** The other major issue you mentioned was the device safety initiatives. Can you give us a little context there?

**Greg:** Yeah, I'm just going to give you one specific on it. The broad issue is that from around spring of 2018 to the end of the spring of 2019, Commissioner Gottlieb became personally involved in issuing a set of policies and defending a set of proposals relating to devices, in particular, device safety measures. The one that I'll mention is the FDA put out–floated, I would put it as– an idea that they would move away from the current 510(k) system in that now you can compare your device to any predicate device, any legally marketed device, no matter how old it is. And the FDA said, Well, we want to encourage more innovation, so, if a device is on the market today, having to be compared to a device that's more than ten years old, they're going to put it on a list with the idea that manufacturers would try to move away from those older predicates and try to modernize. They got lots of pushback on that, lots of controversy. And then Commissioner Gottlieb has been gone and he was the one who was really defending that policy. So, with the interim commissioners we haven't heard anything more about it. So, what I'm interested to see is if that policy– that's one example, and there are probably ten others in this area– is the new commissioner going to become a big champion in this area, is this going to be a big issue for him, or is his attention going to be elsewhere.

## Biosimilars

**Al:** Thanks, Greg. I am now going to turn to my colleague Kellie Combs, to discuss a number of other FDA policy issues that I think are going to be significant in 2020. Let's first of all turn to the current landscape for biosimilars, Kellie. Are there any significant regulatory developments for biosimilars in store for 2020?

**Kellie:** Last year, FDA approved 10 biosimilars, making 26 approved in total. Only 14 are currently marketed in the U.S., though, because so many of the biosimilar manufacturers continue to be tied up in patent disputes or have delayed launches due to patent settlements. As we think about 2020, we should keep in mind that Commissioner Hahn, like his predecessors, has expressed support for faster approval of biosimilars to increase competition in the market, and presumably, to lower prices. Sarah Yim, who was just named the permanent director of the Office of Therapeutic Biologics and Biosimilars, or OTBB, has expressed a similar sentiment and said just yesterday in *The Pink Sheet* that she's hoping for a market in ten years where the biosimilars "looks like Europe's," with a "30% reduction in costs." With enhanced competition as a key driver, we're expecting a couple of important changes this year. First, the so-called "transition provisions" will take effect on March 23. On that date, the approved New Drug Applications for insulin and certain other protein products—more than 80 in total—will be "deemed to have a "Biologic License Application" or a "BLA" approval and will accordingly be regulated as biologics by CBER. This has huge implications for the industry. Most notably, once a biologic, any transitioned product could ultimately be subject to biosimilar competition; also, with the exception of any unexpired orphan or pediatric exclusivity, the transitioned product is actually going to "lose" other types of exclusivity, once the transition date occurs. And, even though reference biological products are ordinarily entitled to 12 years of exclusivity, FDA has determined that the transitioned products will not be eligible for that 12 years (presumably because the agency believes that these manufacturers have already had their bite at the exclusivity apple at the time of NDA approval). All of these changes will likely result in a lot more biosimilar and interchangeable applications, an outcome viewed as favorable by Director Yim at OTBB, though she's also concerned it may be a drain on resources. The second big development that I think we'll see is potentially the first interchangeable biosimilar approved this year or maybe next year. FDA issued two guidance documents in 2019 in which the agency reversed prior policy positions on interchangeability. In the

first, finalized in May of 2019, FDA stated that sponsors could use reference products NOT licensed in the US in their clinical switching studies to support interchangeability status; this was a change from the draft version of the guidance. In the second guidance, published in draft in November and relating specifically to the development of biosimilar or interchangeable insulin products, relevant to the transition I was just discussing, FDA reversed a prior position to proclaim that in general, developers of biosimilar or interchangeable insulin products would not have to conduct comparative clinical switching studies. These policy changes, which FDA has expressly said were intended to facilitate the approval of interchangeable biosimilars, could significantly speed the process and lead to approvals as soon as this year.

## Real-World Evidence

**Al:** In recent years, and most notably since the passage of the 21st Century Cures Act in 2016, there has been a flurry of activity related to the generation and use of "real-world evidence," ("RWE"). What do you think is on the horizon in 2020 on this topic, and in particular, do you think we are moving toward a model where real-world evidence carries the same weight as controlled clinical trials?

**Kellie:** So, there's obviously been a substantial increase in the availability of real-world data and real-world evidence and significant progress in the evolution of technology and the ability to mine big data. We have electronic health records, mobile devices, wearables—all of which contribute to more data collected in the real-world setting. Since 2016, FDA has been incrementally developing policy and soliciting views from industry and other stakeholders. That said, there remains a lack of clarity from the Agency, particularly with respect to when real-world evidence can be used to support regulatory decisions. For example, in December of 2018, FDA published a real-world evidence framework, but that only discusses, at a very high-level, the agency's approach for assessing real-world evidence for safety and effectiveness. It does not provide details on use of specific study designs, it doesn't provide details on how the Agency will interpret the "substantial evidence" statutory standard for drug approval as it relates to RWE, and it doesn't tell us how we should be thinking about the traditional notion of replicating study findings in the RWE context. Additionally, while there are a handful of examples where FDA has accepted RWE in some form, for example, using it for a safety signal evaluation, or as a synthetic control in a single-arm clinical trial, FDA has made clear in some cases that regulatory decisions have been made primarily on the basis of traditional randomized controlled clinical trials. So, essentially downplaying the role of RWE as compared to other data sources, the FDA has expressed outright skepticism in many other cases, specifically calling out the "selection bias" that can exist with observational data in particular. In terms of what's to come, the Agency has committed to issuing guidance in the near term, although I can't say for sure that it will be 2020, on a number of important RWE topics, including use of specific designs incorporating RWE to support a regulatory finding of effectiveness, topics like FDA's assessment of the reliability of RWE and specific types (such as from electronic health records), and how sponsors should address "gaps" or "missing data" in RWE data sources. We also don't know yet how to think about selection of safety or efficacy endpoints in the RWE context; we don't know how regulatory requirements like record maintenance and reporting should be interpreted and enforced when sponsors may not technically "own" the data set for the RWE that they're relying on, or how expectations, standards, and approaches to RWE could shake out across different countries and regulators. Those topics are hugely important, and the lack of guidance there really underscores that we still have a long way to go. I think that certainly in the short term, what we're likely to see is real-world evidence being used as a complement to evidence generated through randomized controlled clinical studies, rather than it being an actual replacement.

## Big Data and Digital Health

**Al:** Thanks again, Kellie. As you mentioned, the use of real-world evidence has been made possible in part by "big data" and the digital tools that allow health care professionals and their patients to track and record health care data in real time. FDA has implemented a number of initiatives related to digital health innovation. What recent efforts stand out to you, and what should we be watching for in 2020 in this large topic?

**Kellie:** Let's start with the Pre-Certification program. Since 2017, the Center for Devices and Radiological Health, or CDRH, has been working with nine manufacturers in a pilot for the Pre-Cert program. At a high level, the Pre-Cert program is intended to allow certain manufacturers of software-based devices to get products to market faster; the program involves what's know as an "Excellence Appraisal" where FDA will evaluate a company's commitment to patient safety, product quality, clinical responsibility, cybersecurity, and proactive culture. If a company passes FDA's Excellence Appraisal, then they would be entitled to a streamlined review. In 2019, the program moved from the pilot development phase into the testing phase, which is really intended to demonstrate that the Pre-Cert program doesn't compromise safety or effectiveness of the devices going through the program. The testing phase is still in process, and the only update we've seen from FDA so far doesn't yet speak to the impact of the streamlined review process on safety or effectiveness—really, what will be the most critical output of this pilot program. In 2020, we're likely to see some continued pressure from Capitol Hill, as Senators Warren, Murray, and Smith have reiterated questions about FDA's legal authority to run the program and have also expressed concern that the Excellence Appraisal is too amorphous and doesn't adequately protect the public health. Given that we don't see anything in CDRH's guidance agenda for 2020 related to the Pre-Cert program, and because the Commissioner's Office hasn't been really out front to express support for the program, it remains to be seen what the future holds.

Switching gears a bit, in April 2019, FDA released a discussion paper about Modifications to Artificial Intelligence based Software, which proposed a novel regulatory framework for evaluating modifications to AI-based medical devices. In its discussion paper, FDA recognized that its current approach to the regulation of medical devices is ill-suited for AI algorithms, because many changes to the algorithm or to the output could technically trigger premarket review. The discussion paper contemplates a number of changes whereby the manufacturers could describe to FDA in advance what modifications to performance, inputs, or intended use are anticipated and also describe the algorithm change control, so that the manufacturer would not have to go back to FDA every time a change occurs. While industry is generally supportive of the approach FDA laid out, there are a lot of unanswered questions. FDA is committed to releasing guidance based on the framework and industry feedback, but it's not clear that guidance is coming in 2020, or whether the agency will address these questions in the near future. Otherwise, with respect to digital health, CDRH has issued a complicated patchwork of guidance documents on discrete issues rather than putting forth any kind of cohesive approach to regulation. It looks like that will continue in 2020, as FDA intends to finalize three different guidance documents including one on Clinical Decision Support Software, and also plans to publish in draft form a guidance on the Content of Premarket Submissions for Cybersecurity.

## FDA Key Areas of Enforcement

**Al:** Thank you, Kellie. We are now going to turn from these important policy topics to move to discussion of enforcement and compliance trends that could impact this sector. Let me turn to my colleague Beth Weinman.

First, Beth, what can you tell us about FDA's key areas of enforcement this past year, and are there any trends that you expect to continue in 2020?

**Beth:** Sure. Look, there's no doubt that the attention-grabbing headlines have been on opioids and the huge increase in youth vaping this year–that's undoubted– and on questions around youth vaping and when vapes, as Greg mentioned, are going to be banned, if they're going to be banned, when enforcement is going to start, what that's going to look like. Those are all sort of critical questions. They're in the spotlight. That is for sure going to continue in the coming year, but that being said, FDA is plugging along, doing its traditional enforcement, keeping drug, device, biologics companies busy responding to 483s, warning letters, dealing with safety alerts and recalls, trying to be responsive to DOJ on the criminal enforcement front. Manufacturing practices, compliance with reporting obligations, transparency in dealing with FDA, data integrity–all of these issues were front and center this year, and they're going to be continuing to be at the forefront. It's FDA's bread and butter.

**Al:** Let's focus, then, a little bit more on drug enforcement and compliance. How do you see 2019 comparing with past years, and what are the most notable trends that jump out at you?

**Beth:** Sure. On the warning-letter front, the total number of drug warning letters has gone up this year. It jumped from 176 letters in calendar year 2018 to 200 this year. Not surprisingly, manufacturing practices made up 60% of those letters. That's typical. I will note, as a trend, or the breaking of a trend, for the first time since I think before 2015, there were more warning letters issued this year to domestic drug manufacturers than to foreign manufacturers. This is interesting with all of the attention, as Greg mentioned, to our reliance on foreign manufacturing. That being said, and as Greg noted, there was a big issue this year with respect to the undetected nitrosamines in API, and that was really a foreign issue. Products that were widely used, brand and generics, of Valsartan, and then Zantac. There were warning letters and recalls, both foreign and domestic facilities. No doubt that investigations into the processes facilitating the formation of these impurities and others are going to continue in the coming year. There were many letters that went to OTC drug manufacturers, and I think some of the violations cited there will sort of shock more mature pharmaceutical companies, including wholesale failure to test incoming components, failure to conduct finished products testing, lack of quality-control units. Those issues were front and center in a lot of letters. Again, data integrity was a big issue last year, and it will be a big issue this year. That was cited by agency officials in addition to DOJ, when enforcement priorities are discussed. The trade press covered, pretty widely, FDA's public shaming of a big company this year with respect to potential data manipulation in a submitted BLA. The FDA stood by the product's approval but expressed its significant displeasure that the manipulation was disclosed after the product was approved and threatened the possibility of future action. We haven't seen that yet, but it's important to mention that even outside of the formal enforcement context, FDA can and will use its public perch to bring attention to issues that it's really concerned about. One last trend to mention on the drug side is that warning letters to compounding and outsourcing facilities are way down, and that's been an ongoing trend, but even while that's happening, these entities are still under scrutiny by DOJ. There was a big criminal action this year against Pharmacon, a compounding pharmacy, against their former CEO and director of compliance. There was a conviction, there was a plea in connection with distribution of sub-potent and super-potent drugs. And while this year there were no injunctions against traditional drug manufacturers, there were four against outsourcers and compounders.

**Al:** I noticed you did not talk about drug promotion in that summary of enforcement trends. Did the agency send any messages this year through letters regarding promotion?

**Beth:** Maybe. Though there isn't a lot to say. There were ten letters this year, as opposed to seven last year. Three were warning letters. Seven were untitled letters. There was only one letter that involved a boxed warning drug. Last year all of the letters involving approved products were boxed warning products. So I guess one message you could take is Hey, you're not safe if your product isn't a boxed warning product, but I think people probably know that. The most common citation this year among the OPDP letters was omission of risk information and other material facts. Two letters this year cited sort of broadening of the indication messages, not off-label promotion, but there was attention to the approved indication. The letters were styled in the form of failure to disclose material facts, failure to disclose the full indication, failure to disclose a relevant limitation of use. It would have been useful this year to get some guidance from OPDP on when companies are going too far in talking about studies that are consistent with labeling, but are not in the labeling, but we didn't hear anything about that this year. Maybe that's something we will see in the coming year.

**Al:** What can you tell us about device and biologics enforcement?

**Beth:** Well, on the device side, there were two letters that were squarely, clearly off-label promotion letters. You know, they didn't come from headquarters, they came from ORA. One was to a device maker of facial implant devices, for a non-approved indication, another to a manufacturer of sterilization trays. Those were off-label promotion letters where the off-label promotion message wasn't hidden in other types of citations. There was I think one more device letter than last year, but still mostly QSR issues. There were seven letters about unapproved devices for failure to comply with post-approval studies. One was a GLP citation, and one letter cited a company for failure to submit adverse event information related to serious injuries or death. That was to a manufacturer of wheelchairs, interestingly enough. I don't think the type of conduct we see cited in these letters will change much in the coming year. On the biologics front, twelve of fourteen letters went to makers of human cellular tissue and cellular and tissue-based products. That continues to be a big focus. Half of those were about the distribution of unapproved products, half were for significant regulatory violations. I think this this attention to HCTP products will continue. I think as we see the gene therapy area starting to get more attention, we saw that with the dropping of several guidances this week. I think as products start to be commercialized, we're going to see enforcement in that space as well.

**Al:** From your perspective, what are the most important or interesting criminal or civil cases this year? And what do they tell us about enforcement in the coming year?

**Beth:** I think I would pick the ACell device case as an interesting and notable case. It's a reminder that regulatory requirements really do matter and that DOJ will seek criminal enforcement when it believes patients are being put at risk. This is a case involving the alleged silent recall of a device. It involved a wound dressing powder that was allegedly contaminated with endotoxins, and the company removed the product from the market without reporting it to the FDA or to providers. There were off-label allegations, actually, in connection with this joint criminal/civil federal case, but only on the False Claims Act side. It's interesting because the product was allegedly promoted for internal use, but it was only cleared for topical use. That increases the risk, obviously. But those off-label allegations were only discussed in the False Claims Act context. I think we're seeing a lot of core FDA-regulated conduct is being enforced through the False Claims Act. We saw that in the Avanir case, there were some off-label allegations also on the False Claims Act side, but not on the criminal side, which focused on anti-kickback violations. We saw that in Avalign, a case about the alleged distribution

of unapproved devices. So I think we'll continue to see that in the future, though the Granston Memo and Escobar's materiality standards should help in weeding out cases that lack merit or threaten FDA policy priorities.

**Al:** Are there any particular big cases we should be keeping our eye on in 2020?

**Beth:** I think we should be looking at the US Stem Cell Clinic injunction case that's on appeal now in the 11th Circuit. It's almost fully briefed. I talked about this a little bit last year and have written about this a little bit, but what I think is really interesting about this case is that it involves an arguably ambiguous regulation about whether or not the same surgical procedure exception applies to the entity at issue. In this case, the U.S. District Court deferred to FDA's interpretation of the regulation based on Auer deference. And the case came out three weeks before *Kisor v. Wilkie*, and as I'm sure everybody knows, the *Kisor v. Wilkie* case really looked at Auer deference and upheld the doctrine, as was a surprise to some, but sort of changed the analysis slightly and we haven't yet seen *Kisor v. Wilkie* applied in the context of an FDA interpretation of an FDA regulation. So, I think that's one reason to be on the lookout for this case. And the other reason to look out for this case is FDA really wants to be taking enforcement action against these stem cell clinics that are popping up all over the country, and that the agency views as posing threats. The outcome of this case will determine whether or not it's able to do that in the future.

## DOJ Enforcement Update

**Al:** Thank you, Beth. Let's broaden our enforcement lens. Let me turn to our litigation colleague, Samantha Barrett Badlam. To start off, Samantha, what are the major trends and concerns for healthcare and life sciences companies with regard to DOJ enforcement going into 2020?

**Samantha:** Well, this should come as a surprise to no one on the phone, but healthcare fraud continues to be a source of large, monetary recoveries for the federal government. In 2019, the DOJ recovered over $3 billion in settlements and judgments in civil cases involving fraud and false claims against the government. That totaled $2.6 billion related to matters that involve life sciences and healthcare companies. As Beth was touching upon, the false claims act really continues to be the primary vehicle for which the government is bringing these enforcement actions and the payment of these large settlements. And in 2019, in particular what I expect to see in 2020, is a continued focus on the Anti-Kickback Statute. Beth was talking about some of the other enforcement areas, but the Anti-Kickback Statute is just a big focus right now. Part of this is because of high drug prices, kind of what Tom was touching upon earlier. So I think as we move into 2020, we should continue to expect to see enforcement of the AKS.

## Anti-Kickback Statue

**Al:** Given that enforcement environment, what type of specific conduct is the government pursuing under the Anti-Kickback Statute?

**Samantha:** I think we're all familiar with the independent charity care and assistance program cases, and this has been a large focus of the government in the past couple of years. And they're really at their tail end, I would say at this point. In total, the government has collected, I think it's more than $870 million for nine pharmaceutical companies to resolve allegations that they use these third-party foundations as instruments for kickbacks. The overarching theory in these cases is that manufacturers used independent charity programs to channel money to patients in order to pay their co-pays for medicines, reimbursed by healthcare programs. I

think it's important to note that OIG has sanctioned manufacturer donations to these charities and has specific guidance on this topic, which I'm sure many of the people on this phone are intimately familiar with. And you must basically as a manufacturer follow this guidance, according to DOJ's perspective, to ensure that you're not running afoul of the AKS. Now, violating the guidance doesn't equal a violation of the AKS, but what it's used as is evidence of intent to knowingly violate the AKS. So, in June of 2019, the government filed a complaint under the false claims act against Mallinckrodt, arguing that it violated the False Claims Act, by using one of the foundations as a conduit. And the court just recently issued an opinion last week denying Mallinckrodt's motion to dismiss. And Mallinckrodt had some very compelling and excellent arguments about the guidance being ambiguous at best and whether it had in fact complied with the guidance and therefore had not knowingly violated the AKS. But the court, it's an interesting opinion, out of Eastern District of Pennsylvania, the court held that the complaint successfully pled non-compliant with the regulatory guidance and therefore had successfully pled that the company knowingly violated the AKS, at least at the motion to dismiss stage. It's a notable opinion, and I think it brings up the question of whether this will really embolden the government in its pursuit of AKS violations, because there really has been a lot of debate around what it means to not follow OIG guidance, and I think what this opinion really shows is that it can be used as evidence of intent at the pleading stage, to overcome a motion to dismiss. Another thing to note about these cases that's really interesting is that it's the patient who is the recipient of the kickback, so in the quid pro quo relationship, it's the patient, not the doctor, the provider, which is a novel approach that has really yet to be tested. It will be interesting to see what happens with this in 2020, and as I mentioned, I think we can expect to see continued active enforcement of the AKS in this space, even more broadly than the ICPAP cases, the Independent Charity Patient Assistance Programs cases. I think companies really need to be thinking hard, which I'm sure they all are, on the programs that they have in place to help patients afford and access medicine, and the entities that they're using and the relationships they're using: specialty pharmacies, PBMs, payers, any other entities or programs that are helping with cost-sharing obligations for patients.

### Qui tam Patient Support Programs and Patient Assistance Lawsuits

**Al:** Thanks, Samantha. Beyond the DOJ's role as an enforcer, can you speak to the recent changes in DOJ's response to qui tam patient support programs and patient assistance lawsuits?

**Samantha:** Let me just touch on this quickly, because it's interesting, while DOJ is actively enforcing the AKS in a patient assistance space, at the same time it actually was on the side of life sciences and healthcare companies in an array of recent qui tam suits alleging that manufacturers that violate the False Claims Act by offering free patient support programs to prescribers and patients in violation of the AKS. And these programs involved nursing services adherence programs, assistance with insurance verifications, prior authorizations and other reimbursements. There were eleven of these False Claims Act cases that were brought by "shell company," backed by the NHCA Group, and these were brought in 2016 and 2017. But at the end of 2018, DOJ filed dismissal motions against all ten of the active FCA suits and nine at this point have been dismissed. There is one that is outstanding that's going to be dealt with. So this is new. This intervention is new, and historically, DOJ has rarely sought dismissal of non-intervened qui tam cases. This new approach was encouraged by the "Granston memo," which Beth mentioned, which was in January 2018. It encouraged DOJ to seek dismissal of meritless qui tam actions. Now, in response to DOJ's approach, what we saw was a letter that was issued in September of last year from Senator Charles Grassley to AG Barr expressing concern about DOJ's efforts to seek dismissal, and DOJ basically said, listen, this is only going to happen in limited circumstances, so don't worry. So I think in 2020 I wouldn't expect to see this happening very often. I think it was great that they did this, and I think these cases merited this happening, but I think in 2020 we're not going

to see a lot of this, and I think the fact is in the last two years, only four percent of cases have been dismissed in this manner.

**Al:** Beside the patient assistance programs, are there any other areas that you believe DOJ will focus on in 2020 when it comes to anti-kickback statute enforcement?

**Samantha**: It seems that we've seen a resurgence in enforcement in speaker programs. So of course, patient assistance and patient support remain the focus, because there's a couple of cases that have come down recently in S.D.N.Y., Novartis and Teva. Teva's a non-intervened private relator case that was just settled, Novartis is still out there. It is a DOJ-intervened case. But basically the allegations are that the vast majority of speakers were nominated by sales reps to conduct sham educational programs at high-end restaurants, and were really intended to entertain doctors to induce them to prescribe the drugs. I'll also mention the Insys case that settled in 2019 also had a speaker program component around this idea of sham speaker programs. I do think these cases, I urge companies to pay attention to these cases, because I think our focus has shifted, but we still need to make sure that we're addressing concerns around speaker programs, because I can see the government continuing to pursue these cases with more of a traditional kickback approach as opposed to some of the patient support approaches.

## FCPA

**Al:** What about current trends in enforcement of the Foreign Corrupt Practices Act in the life sciences space?

**Samantha**: Just as a quick refresher, the Foreign Corrupt Practices Act is a law that is broadly applicable to U.S. companies, as well as foreign companies or persons that have a nexus to the United States, and their affiliates. It's pretty simple, what it's focused on. It's focused on preventing bribery and corruption involving foreign government officials, and requiring companies to keep accurate corporate books and records so that bribes, if they are given, cannot be hidden. So the FCPA is being actively enforced in the life sciences industry. I think historically there was a big resurgence in FCPA enforcement in life sciences and I would expect it to continue in 2020. A big case was Fresenius. In March of 2019, a $231 million settlement. Fresenius was a German-based provider of medical products. The allegations with Fresenius involved bribes being paid to publicly employed health and government officials to obtain business in Angola and Saudi Arabia, and then it also had some books and records components to it as well. Also, recently, it was publicly announced in May of last year that the FBI, the DOJ, the SEC were coordinating with Brazilian authorities to investigate a number of medical supply manufacturers for allegations involving supposed bribes that are being paid as part of a scheme involving medical equipment sales in Brazil. And this really is being led by the Brazilian prosecutors, but what we're seeing ever since Operation Car Wash, not this industry, another industry. But what we've seen is a lot of coordination between international regulators, specifically in Brazil and the U.S. authorities. And this is a good example of that coordination. I do think that in 2020 the government will continue to take FCPA enforcement very seriously, pursuing both companies and individuals, and it's more important than ever for life sciences and healthcare companies to have robust compliance programs, including internal controls and well-maintained books and records.

## Q&A's

### Reach of Grassley/Wyden Prescription Drug Pricing Act

**Al**: Thank you, Samantha. We have a minute or two left, and we are open to questions. If you have questions, please submit them to rgevents@ropesgray.com, and we actually have a question. I think this one is directed to Tom Bulleit. The question is, "As currently written, does Senator Grassley's proposal to restrict drug price increases to inflation/CPI, is this per individual drug (each drug would be limited to inflation), and also, would this limitation be applicable only to CMS purchases, or is it all government purchases?"

**Tom**: Sure, Al. So this is the prescription drug price reduction act, which is a bipartisan bill from Senator Grassley and Senator Biden. It currently has not passed the Senate, but the White House has said yes to it. The answer to the question is that it applies to individual drugs. They're called rebatable drugs, so if they're covered under Medicare Part B, it would be price increases above the rate of inflation for the average sale price, and for Medicare Part D, increases of the list price above the rate of inflation. It does not apply to other government purchases, only Medicare. That's the same as the Trump rule, which has yet to be released. The difference, principally, between what Trump has been proposing or may propose and what Grassley-Biden is proposing, is that because Grassley-Biden is legislation, there's no question about Congress' authority to do this for the Medicare program. There is a significant question about whether it can be done by administrative rule.

### Impact of Insys Corporate Integrity Agreement

**Al**: Thank you, Tom. We have a second question. This one I think is directed to Samantha. "The Insys CIA included a number of novel provisions. Have you seen, or do you expect to see, similar provisions in CIAs going forward, or were those provisions unique to the facts of the Insys case?

**Samantha**: I think OIG usually tries to tailor the CIA to the specific facts of a particular case. What you end up seeing is that the CIAs in particular issues start to mirror each other, because when companies are negotiating their CIAs, they refer to the other CIAs in their negotiations. So I do think with Insys, it was unique and those provisions are designed to be tailored to specific facts. There are a lot of CIAs out there, and there are people on the phones that are under CIAs right now, but they do start to mirror each other, so I think it's a bit of both.

### Increasing International 483 Warnings

**Al**: And one last question, I think this is directed to Greg or Beth, whoever wants to jump on it. "Considering that the percentage of 483 warnings from FDA are dramatically increasing for international sites, especially in China and India, along with Congressional calls for the military to become independent on sourcing API for national strategic reasons, given repeated problems in data integrity matters, especially in China, what do you see happening, especially with tariffs and trade wars likely to intensify after the election as a second trade deal is unlikely to be reached?" That's a very easy question.

**Greg**: I think that the level of concern about reliance on foreign API and even foreign finished dosage form manufacture, I didn't mention that before, but only 47% of the registered facilities for finished dosage forms are in the United States as well. So I think that the interest in the level of concern in Congress is going to intensify. There was a hearing towards the end of last year in the Health Subcommittee in Energy and Commerce in the House, where FDA testified about this issue but also they had someone from— I'm sorry I

don't have the name of the China-US something council in front of me right now– but I've never heard so much focus on the national security concern that the trade wars could play into all this, and so on. So I think the consequence is more interest in this issue. From the agency side, I think they're going to continue to push some of the initiatives that they're working on, like advanced manufacturing technologies and continuous manufacturing, to see if possibly that could have the consequence of moving some of the manufacturing back to the U.S. There are others who have more radical proposals, such as about building government-run manufacturing in the U.S., and so on.

**Al**: Thank you. I think that is all the time we have for questions right now. I would like to thank everyone for joining us today. As I mentioned at the outset, we are offering CLE credit for this conference. For those seeking CLE credit, you need to fill out the attorney information form that is included in the registration confirmation email you received yesterday. The CLE confirmation code for this program is 4552. Please email the completed time to professionaldevelopment@ropesgray.com or fax it to 617-235-9606 within 48 hours. We will continue to provide additional news and analysis about regulatory enforcement issues emerging from the federal government throughout 2020. Once again, you can access that information by accessing the Capital Insights page at www.ropesgray.com. Thank you all for your attention, and I wish you a good day.