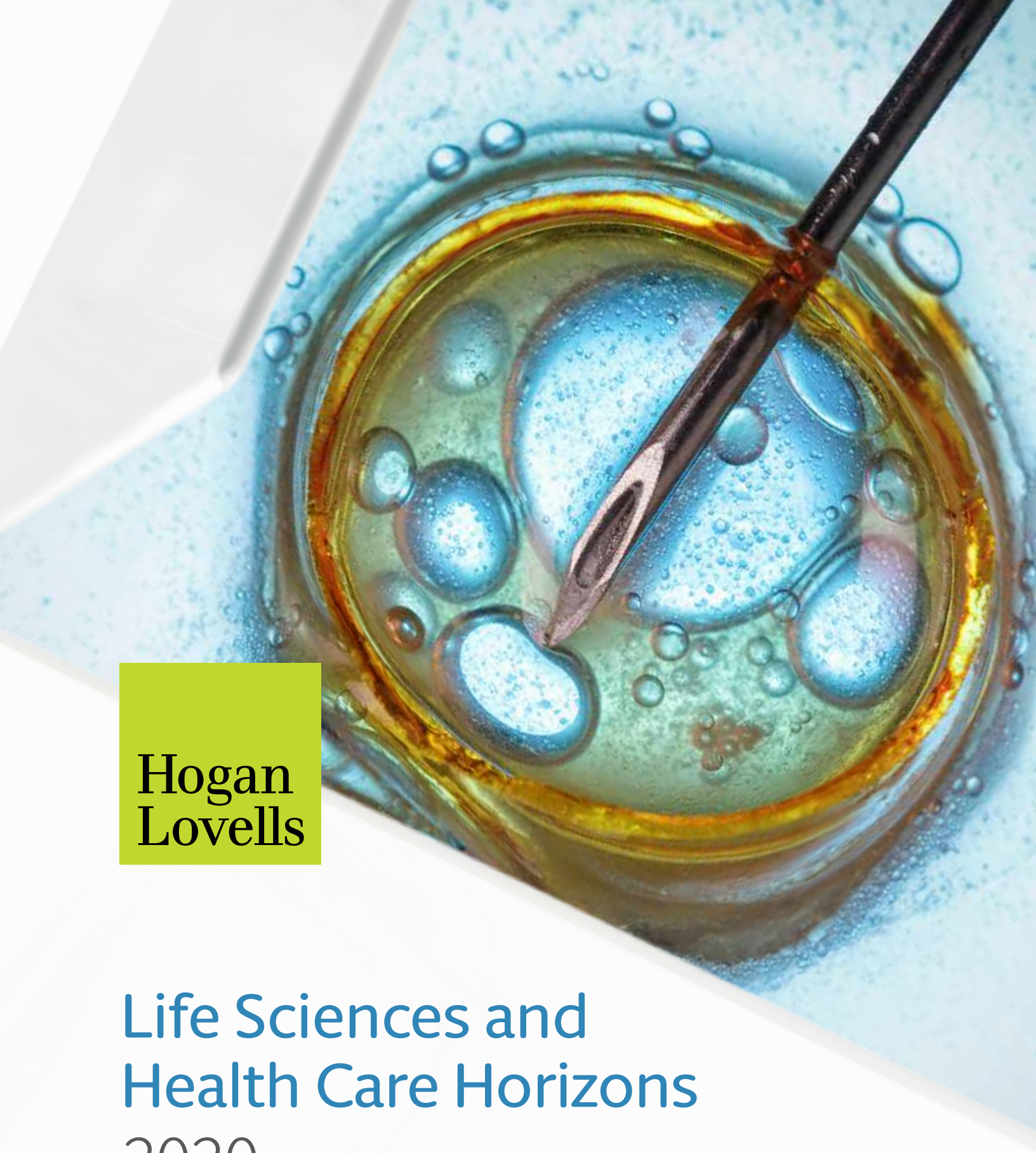

Hogan Lovells

Life Sciences and Health Care Horizons 2020

Welcome

We are pleased to provide you with the third annual installment of our Life Sciences and Health Care Horizons guide. For each of these guides, we have asked our industry thought leaders throughout the world to write about trends and compelling legal issues within industry and within their particular region that are both of interest to them and that they believe will impact our clients in the near future.

Interestingly, many members of our team chose to highlight the emergence of digital technologies and the convergence of those technologies with patient care, and with more traditional pharmaceutical, biological products, and medical devices. These articles have been provided by our colleagues in Asia, Europe, Mexico, and the United States, and reflect global trends and forces for the future in areas of cybersecurity, artificial intelligence, and monitoring and drug dosing optimization, among others.

We also highlight concerns over the increasing cost of pharmaceutical products, and the attempts by governments to lower those costs, while still encouraging innovation. Maybe contrary to conventional opinion, increasing drug costs are not a problem exclusive to the United States. Our Tokyo-based partner, Frederick Ch'en, notes that the high-cost of biologics is a problem that the Japanese government is trying to address.

Now that Brexit has become a reality, our London-based partner, Jane Summerfield, foreshadows the challenges that life sciences companies will need to address when the UK's split from the EU is finalized by the end of 2020.

In a first article of its kind for Hogan Lovells, London-based senior scientist, Dr. Marion Palmer, highlights some potential impacts of climate change on the Life Sciences and Health Care industry. Her thought provoking essay scratches the surface of unfortunate new health challenges the industry is likely to face as a result of increasing global temperatures.

We hope you find our view of the horizon for life sciences and health care intriguing as you think about your businesses for 2020 and beyond.

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Asia

Biologics and biosimilars in Japan

Japan is the world's third largest pharmaceutical market, and commentators currently expect it to reach a value of US$105 billion by 2021 (and US$109 billion by 2026). With an average life expectancy of 85 years, the rapidly aging nation is experiencing a health care cost pressure that is pushing the increasing use of biosimilars, both through domestic development and increased investment by international companies.

Beginning with the approval of Sandoz's growth hormone treatment Somatropin BS in June 2009, the Japanese regulator has approved 25 biosimilars of 12 originator products, including granulocyte colony-stimulating factor, erythtropoesis stimulating agent, and insulin and tumour necrosis factor-inhibitor.

In September 2019, three biosimilars of darbepoetin alfa for the treatment of anaemia were approved in Japan (products of JCR Pharmaceuticals/Kissei Pharmaceuticals, and the South Korean companies Chong Kun Dang and Dong-A ST, respectively); in the same month, Mochida Pharmaceutical obtained approval for its Teriparatide BS treatment for osteoporosis.

Historically, Japanese pharmaceutical companies have focused their R&D efforts on small chemical molecules, but due to increased government pressure, attention is now shifting towards various diversified models, including gene therapies, oligonucleotides, digital health and more biosimilars.

Recent press reports suggest that in addition to partnering with international companies, Japanese biosimilars manufacturers are also seeking to acquire relevant secondary patents. This strategy may help strengthen Japanese companies' negotiation position — especially with respect to potential cross-licensing arrangements — and enable them to be more nimble when entering the fast-growing biologics market.

As the push for increased biosimilar availability in Japan continues, more competition, collaboration and challenges are expected to follow.

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Digital transformation opportunities in China

As a result of new technologies, revolutionary digital health tools that measure, monitor, and support the diagnosis and treatment of diseases in the health care industry, such as web platforms, software, and mobile applications, are gaining traction in the Chinese market.

Despite the attractions of the market, those seeking to gain exposure (including both traditional medical device, pharmaceutical and health care companies and high-tech firms) to this heavily-regulated sector face a variety of regulatory hurdles and requirements to overcome when launching their digital products in China. These include the following:

The classification of the tools and NMPA market authorization

Digital health tools that target clinicians and patients with one or more medical functions are typically classified as medical devices, and hence subject to the marketing authorization by the National Medical Products Administration (NMPA) before their commercialization. The registration of these normally takes years, depending on the risk level associated with the medical devices.

Cybersecurity supervision

Chinese regulators are intensely focused on cybersecurity issues at present. As most digital health tools function over the internet, they will very likely be subject to China's extensive and fast-evolving cybersecurity-related rules and regulations. Where digital health tools are designated as medical devices, a thorough cybersecurity risk analysis report is required to be submitted to the NMPA when applying for the product marketing authorization in order to prove the confidentiality, integrity, and availability of data in the products.

Privacy protection requirements

Digital health tools normally hold large volumes of personal information, including, for example, sensitive personal health data. The owners/operators of digital health care products must demonstrate strong personal data protection capabilities and comply with Chinese data privacy regulations and standards when collecting, processing, using, storing, and transferring such personal data and to protect personal data from cyber attacks, data breaches, and other unauthorized disclosures during the entire data processing life cycle. Where personal data needs to flow from China to another jurisdiction, China's still evolving data cross-border transfer regime (which remains in draft form at the time of writing) comes into play.

Telecommunication regulations

Digital health tools may also be subject to Chinese telecommunication licensing requirements. For example, engaging in the provision of profit-making (operational) internet information services using the server of a web platform/digital portal located in China requires the service provider to obtain an internet information provider (ICP) telecoms business operating permit, a sector in which foreign investment is capped at 50% at the moment and we do not expect that such restriction will be lifted any time soon.

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Navigating China's expanding and evolving drug market

2019 continued to be a milestone year for China's drug regulatory and health care reform. Starting from 1 December 2019, the new Drug Administration Law (DAL) took effect. The DAL codified many of the reforms that had already been implemented, with the main objective of developing a modern and more welcoming regulatory environment for new drugs. For global pharmaceutical companies, the most encouraging change under the new DAL is the more streamlined drug registration process with NMPA. For example, a clinical trial in China no longer requires explicit approval, and sponsors can proceed after 60 working days of notification to NMPA unless they receive objections from NMPA (Article 19 of the DAL). NMPA will grant priority review for pediatric drugs, shortage drugs for urgent clinical needs, new drugs for severe infectious diseases and rare diseases. These changes would greatly shorten the drug review time. Other notable encouraging developments include the potential for expanded access to certain unapproved drugs during the clinical investigation stage (Article 23 of the DAL) and leniency for importing a small amount of drugs approved outside of China but unapproved in China (Article 124 of the DAL).

Consistent with the initiative, the Center for Food and Drug Inspection or CFDI, the inspection arm of NMPA, has been strengthening its overseas inspection program, under which, NMPA will not only target facilities outside of China for drugs that are already marketed in China, but also drugs that are pending NMPA's approval. In the event of inspection violations identified by NMPA during these inspections, NMPA can request the manufacturer to attend a regulatory meeting, impose timelines for corrective actions, issue warning letters, suspend drug importation, or suspend sale and use. For the most serious cGMP violations, NMPA can even ask the manufacturer to conduct product recalls or event revoke the product's approvals. The inspection findings published by NMPA so far show that many overseas manufacturers are unfamiliar with the Chinese laws and regulations. For example, it is required that all drugs sold in China must comply with the specifications of the 2015 Chinese Pharmacopeia (ChP), which can be different from prevailing international standards such as USP or EP.

With the opportunity for global pharmaceutical companies to gain new access to the Chinese innovative drug market presenting itself like never before, generic drug manufacturers are facing fierce pricing pressure in China. The pilot centralized drug procurement program (the 4+7 city centralized procurement program) has already been rolled out nationwide. For the third round of centralized drug procurement, which likely will take place in early 2020, 35 generic drugs are involved. Based on the bidding results from the previous rounds, we expect their prices to be reduced by at least 50%, which hopefully will be in exchange for 70% of the market share in China. Stay tuned!

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Digital health

Overview

Technology is rapidly changing the way the health care industry operates, introducing unique solutions for longstanding challenges and creating enormous business potential. Standalone software that analyzes consumer health data to help detect disease, wearable sensors used for enhancing fitness or facilitating collection of patient data in clinical trials, artificial-intelligence-based machine-learning algorithms used in health care facilities to triage medical images or diagnose particular cancers, and advanced digital therapeutics — on their own or in combination with a drug therapy — are just a few examples of these developments. Partnerships between technology and pharma/biotech promise to yield transformative improvements in R&D efficiency, the nature of therapeutic solutions, and the delivery of health care, but there is still much to be figured out.

After some failed attempts to apply laws and regulations designed for more "traditional" technology to this sector, the legal and regulatory landscapes have begun to evolve iteratively to address it in a more tailored manner. Thus companies innovating or leveraging digital health technologies must simultaneously understand and comply with the existing requirements and expectations while working actively to anticipate new developments. Likewise, regulators need to consider their regulatory models to avoid stifling the potential that is inherent in the industry before it has a chance to bloom.

The coming year promises more developments – some through exciting partnership in AI, robotics, telehealth, and new types of technologies to address chronic diseases, mental health, therapy adherence, and support for aging adults. At the same time, business models for digital health have not been firmly established and digital health companies face tremendous pressure to demonstrate their commercial viability. On the other hand, some countries seek to foster the digital health environment by support through public initiatives or first attempts of reimbursement for digital health applications.

In the months and years ahead, success in developing and leveraging new digital health products and services will require a deep understanding of numerous forces at work and a nimbleness in shifting focus as needed to keep pace with the continued rapid evolution of both technology and regulation. Effective advocacy before the relevant regulators and the other players in the ecosystem, when appropriate, is also key. Our practice groups are well-versed in the increasingly complex global privacy regulations, novel reimbursement models, and evolving paradigms for demonstrating the safety and effectiveness of digital health solutions to regulators, as well as the unique liability and intellectual property questions that arise with digital health products. We help clients daily to navigate strategically so that they can achieve the promise of these endeavors.

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Artificial intelligence: hype or happening?

In recent years, commentators have been speculating on the impact of artificial intelligence (AI) on the pharmaceutical industry. With 2019 seeing yet further developments in the use of AI in drug discovery, the industry is considering how to respond if the promised advances in AI and innovation are more than just hype.

In drug discovery, AI is promising to cut the time and costs of generating a hit to candidate, from around five years to one or less. In particular, AI is being used to identify and plan the synthesis of new molecules or known molecules for new uses, by analyzing vast amounts of public and proprietary data. The use of AI in drug discovery is already having a tangible effect on the industry. Last year, we saw further partnerships between pharmaceutical companies and external companies dedicated to AI. Pharmaceutical companies continued to boost their internal resources around the technology. There was also a continuation of investments in AI startups.

In response to developments in AI, regulatory bodies have been required to make decisions concerning the regulation of AI-derived innovation. In 2019, a number of patents supposedly invented by an AI were filed at patent offices around the world. The UK Intellectual Property Office and European Patent Office have been the first to reject these filings on the basis that an inventor cannot be an AI. While these outcomes are perhaps not surprising, what is interesting is that regulators have not altogether turned their back on the topic. In August 2019, the U.S. Patent and Trademark Office published a request for comments on whether or not AI entities should be allowed to own a patent. Most recently the World Intellectual Property Organization has called for comments on intellectual property issues and AI. With regulatory bodies giving serious thought as to whether or not regulatory changes need to be made to deal with the increased use of AI in innovation, this suggests that the impact of AI on industry is more than just hype.

For the pharmaceutical industry, AI could have consequences on traditional models for protecting innovation. Apart from the question of whether or not an AI will one day be able to be listed as the inventor, or owner of a patent, if AI cuts the time and costs of innovation, the coming years could see a rapid churn of patent filings. This could add momentum to development in newer areas of treatment, such as personalized medicine.

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Cyberattacks and data breaches

With the media regularly reporting on cyberattacks and data breach investigations, and calls for increased regulation growing louder, the existence of cyber threats to digital health businesses cannot be ignored. Legislators and regulators around the world are enacting data breach notification laws and the trend toward imposing industry-specific cybersecurity standards is expected to continue. The EU General Data Protection Regulation (GDPR) and California Consumer Privacy Act (CCPA), for example, both include key provisions requiring data breach reporting and imposing security obligations. And a number of jurisdictions are considering additional health-specific reporting and cybersecurity requirements this year.

Hackers view health systems and devices as high value targets. Liability for class action and shareholder suits, regulatory penalties from enforcement actions, and reputational damage associated with health cyber events continues to grow. Threats to health information include increasingly sophisticated ransomware and phishing attacks, insider threats, disruption/destruction attacks (e.g. denial-of-service, wiper), and lost/stolen equipment and data. Increasingly larger data sets also raise heightened risks. Digital health organizations must account for the unique and heightened risks associated with health information, and implement programs for ongoing cyber risk identification, management, and protection that go beyond "check-the-box" compliance efforts.

Every digital health organization should have an Incident Response Plan (IRP) ready and rehearsed. It may be advisable to maintain playbooks for different stakeholders as well as addressing particular scenarios (such as ransomware and coordinated vulnerability disclosure). Effective preparation for managing a cyber event helps ensure a swift and coordinated response that can minimize harm to patients and consumers, as well as reduce reputational impact and potential legal liability. As the threat of cyberattacks continues, nearly every digital health organization will be faced with a cyber event. Organizations that have plans in place to mitigate the risks will be better positioned to survive and thrive.

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Securing medical devices from increasing cyber threats

Medical device manufacturers have a critical role in health care organizations' sensitive infrastructures, given the increase in sophisticated cyber threats and manufacturers increasingly handle larger amounts of health data, through connected devices and partnerships with other health sector stakeholders. Cyber threats have expanded from seeking health data to taking control or disrupting the function of the devices themselves.

Device cybersecurity is a high priority issue for regulators worldwide, and various competent authorities and agencies are bringing together stakeholders and providing additional guidance so that entities involved in securing medical devices have detailed information to help prevent and manage cyber risks. Regulators worldwide have recognized that device cybersecurity is a shared responsibility among manufacturers, health care providers, service providers, suppliers, patients, and regulators — with stakeholders each having a role in secure device deployment, operation, and management.

The FDA has been busy defining and addressing potential vulnerabilities in medical devices; newly developed or already deployed. One FDA focus area is providing additional clarity about when to interact with the FDA, what information would be useful in submissions, and what level of documentation is expected. Additionally, the FDA and the Health Sector Coordinating Council (HSCC) have been working to get stakeholders to work holistically and coordinate to fortify cybersecurity practices. Meanwhile the European Commission and Medical Device Coordination Group (MDCG) recently published device cybersecurity guidance in support of the new Medical Devices Regulation (MDR) and In Vitro Diagnostic Medical Devices Regulation (IVDR) coming into force in 2020 and 2022, respectively.

The guidance covers both pre- and post-market cyber considerations, while recognizing the importance of other European privacy/cybersecurity requirements (including GDPR and NIS Directives).

Protecting devices and their associated infrastructure will require vigilance and in-depth understanding of the environments in which they operate and the unique challenges presented by decades of device innovation. When confronted with crises, understanding the issues, the risks they present and how best to mitigate them without disrupting the entire ecosystem, coupled with effective advocacy before relevant regulators and other players in the ecosystem, when appropriate, will be key.

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Combination products and digital enhancement of therapeutics

We are students of drug-device combination products, and have been side-by-side with our pioneer clients on charting pathways for novel drug delivery systems, light activated drugs, and drug eluting and coated devices. Immediately ahead, we will be working with our clients as enforcement of the FDA's new rules for reporting of adverse events for combination products goes into effect in July 2020.

On the manufacturing side, our clients are already experiencing the effect of the FDA widening its enforcement lens for combination products, including preloaded syringes and IV bags, transdermal systems, and drugs delivered in pumps, inhalers and other active delivery systems. FDA is inspecting both drug and device standards and noting in 483 observations failure to include design history files, among other device quality system concepts. This has been jarring for companies with GMP compliance cultures who may be less fluent in device quality standards.

The exciting area of emerging interest is the direct integration of digital technology into the dosage form of drug and biological products. In late 2018, we saw approval of the first digitally enabled asthma rescue inhalers, with embedded sensors to detect and communicate usage and air flow data to a patient-level app. Similarly, we saw the introduction of the first digitally enabled syringe products that record injection date and time, speed of delivery, and depth of needle penetration. When paired with a proprietary app, patient information can be organized, tracked and shared with health care providers. The third category are "digital pills" with embedded ingestible sensors to record medication use through a wearable patch, for tracking of patient compliance.

In addition to bringing more information to the patient and provider experience, digital integration may draw patients and providers into a specific digital ecosystem. The impact that digital integration will have on patient switching, care delivery, and pharmacy substitution, are key issues on the horizon. For example, will patients be willing to move away from a digital platform that holds their historical data and feels comfortable and familiar? Another issue is Orange Book patents based on the digitally enabled dosage form, and whether FDA will take steps to limit listing of "device-only" patents. While FDA has appropriately signaled that it would be reluctant to allow digital tools to limit or delay entry of generic alternatives, the potential issues are manifold, including patient preference and the potential for these tools to become elemental to the safety, effectiveness, or functionality of digitally integrated therapeutics.

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Digitization of the supply chain

The digital revolution is poised to create sweeping changes for life sciences companies — helping them better understand patients, but also transforming their manufacturing and supply chain operations.

Machine-learning and autonomous machines will also change views on regulatory responsibility and liability in contracts. While, for instance, the U.S. Food and Drug Administration has issued first guidance documents on the design of AI-based medical device software, there is still no guidance documents from European or national authorities.

Digitization of the supply chain holds enormous potential in helping companies cope with the challenges that life sciences companies face. Integrated digital supply chains will allow companies to improve planning accuracy, manufacturing efficiency, productivity, inventory levels, and service levels.

Sharing digital data throughout the entire supply chain (starting with the patient and ending with the supplier) may allow continuous manufacturing instead of “siloed” batch manufacturing. Access to real-world patient data and to machine data will be of major importance but also a big hurdle for competitors, likely leading to disputes.

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Telehealth: the challenges ahead

Health care providers increasingly reach across borders using technology to provide medical services directly to patients and physicians. Telecommunication technology (such as e-mail, audio, video conferencing, and mobile apps) may facilitate diagnosis, consultation, treatment, and remote monitoring. Remote second opinions — whereby a health care provider is asked by either a clinician or a patient to verify a diagnosis or treatment from a distance — has surged in the international medical sector.

Although the practice of medicine is regulated across the globe, the practice of telemedicine does not always fit within the traditional areas of law and regulation applicable to the medical profession. Where countries do regulate telemedicine, such laws do not necessarily address the circumstances in which a foreign physician sitting outside the country may render remote services into the country.

Telehealth solutions raise myriad complex topics:

- Practice of medicine: physicians and institutions that are considered "engaged" in the practice of medicine in a particular country may have licensure/registration requirements or face limitations on the precise services that can be rendered lawfully from a remote location.
- Privacy and data protection: regulation of patient medical information and data varies significantly from country to country, and use of genetic information is restricted in some jurisdictions. Processing health data must rely on a solid legal ground which will often be the patient's consent.
- Billing and reimbursement: whether, and under what circumstances, telehealth services can be billed and reimbursed by government and other third party payers varies. Health care providers that receive reimbursement for services provided in a country may then be subject to various regulatory requirements imposed by that country.
- Telehealth devices: telehealth services are made possible thanks to software and connected devices. Such software may classify as a medical device. For example, as of 26 May 2020, the new European Regulations for medical devices (MDR) and in vitro diagnostic devices (IVDR) will apply, introducing new classification rules for medical devices software and creating new obligations for the economic operators. The design of the solution must include from the outset the constraints resulting from medical device regulations.

Other challenging issues include liability and malpractice, e-commerce regulation, advertising constraints, intellectual property protection, and tax compliance.

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The potential of adaptive medical devices

Artificial intelligence (AI) holds great promise for all facets of health care, from speeding the drug discovery process, facilitating clinical evaluation of investigational products, driving faster and more personalized diagnosis, management and treatment of patients, and enabling smarter, more efficient workflows for health care providers. The pace of innovation in the medical device sector shows no signs of slowing, with a wave of medical devices incorporating AI or machine learning (ML) algorithms already entering the U.S. market. The devices that have been cleared and approved by the U.S. Food and Drug Administration (FDA) have, to date, largely employed AI/ML in development and training, with the final algorithms "frozen" for validation, FDA premarket review and commercialization. In light of this, while these technologies have raised unique issues requiring the agency to develop data requirements and preferred study designs to demonstrate performance of these algorithms, the existing regulatory framework has been able to accommodate these devices.

This will not be the case for future waves of AI medical devices – those that are truly intelligent, capable of continually learning, and adapting in the field based on real-word clinical use. The FDA regulatory framework is not designed for regulating the safety and efficacy of devices that are continually changing in the field. Recognizing this disconnect, the agency issued a proposed framework in April 2019 as the first step in the process of innovating the regulatory paradigm for adaptive devices. Change will come slowly, however, with additional statutory authority likely needed. In the meantime, adaptive AI medical device firms must work within a regulatory framework that is ill-equipped and evolving. For the small start-up innovators with limited capital – which represents a sizable segment of the medical device industry – this environment will prove particularly challenging. Unpredictability in regulatory processes and requirements can quickly deplete resources and lead to significant delays to market – hurdles that small AI medical device innovators will need to be prepared to face.

The FDA appears to appreciate the need for changes to the regulatory framework to properly regulate the next generation of AI medical devices, and is currently reaching out to industry for feedback through public meetings, pre-certification programs, and on a device specific basis through the pre-submission process. Importantly, these activities offer invaluable opportunities for industry players to educate regulatory stakeholders on current and future innovation in this space, and help to shape how the regulatory construct is ultimately modernized. In the meantime, companies looking to bring truly intelligent and adaptive devices to the U.S. market in the near term will need to be strategic, creative and flexible when engaging with the FDA to successfully weather an evolving and unpredictable process in the absence of a formalized framework.

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Regulatory outlook

Pricing and reimbursement in the U.S.

The cost of pharmaceuticals and issues of patient access will remain at the forefront of the policy landscape. Two legislative measures introduced in 2019 will remain relevant in 2020, and while wholesale adoption appears unlikely, individual provisions with a significant impact on manufacturers could be enacted as part of other legislation:

- The "Elijah E. Cummings Lower Drug Costs Now Act," H.R. 3, would require manufacturers to negotiate drug prices with the U.S. federal government, subject to a price cap based on international drug prices.
- The "Prescription Drug Price Reduction Act of 2019," S. 2543, would retain the current paradigm where drug prices are established in the free market and communicated to the federal programs through price reporting, but would heighten and expand existing manufacturer compliance and rebate obligations.

Two regulatory initiatives remain ongoing but may be impacted by the outcome of the election:

- The Centers for Medicare & Medicaid Services (CMS) has announced plans to issue a proposed rule that, through a demonstration project, would set Medicare Part B reimbursement rates by reference to a so-called international pricing index.
- The FDA issued a proposed rule and draft guidance for industry that would permit importing (presumably lower-priced) drugs into the U.S. States are seeking to pressure manufacturers to offer more substantial rebates when drugs are reimbursed by state Medicaid programs, and certain states are considering regulatory approaches that would establish limits on payments for certain categories of therapies in state-funded programs, including Medicaid. With court challenges to California and Oregon drug pricing transparency laws underway — and with drug price transparency bills expected in numerous states — states show no sign of slowing their legislative efforts related to drug prices.

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OTC drugs

After years of delay, we expect a breakthrough in 2020 in the way over-the-counter (OTC) drugs are regulated by the U.S. Food and Drug Administration (FDA). The regulatory scheme that governs the marketing of OTC drugs is widely recognized as outdated and inadequate. Last year, Congress came very close to passing legislation that would have overhauled the 45-year old OTC drug monograph system. In fact, the Senate passed the bill in December 2019, and the House has passed a very similar bill at least twice before. We believe that this legislation is likely to finally be enacted in 2020.

The FDA has complained publicly that the monograph system is cumbersome and impedes prompt agency action on safety issues. The draft legislation is designed to expedite agency action on evolving science and safety issues and to create new incentives for innovation, including a new exclusivity provision. The new system is expected to result in opportunities for marketing OTC drugs with new ingredients and dosage forms, including some that were previously only available overseas or by prescription.

The FDA is also developing a regulation, expected to be issued as a proposed rule in 2020, to expand the types of drug products that may be considered OTC. The proposed rule is expected to suggest companies employ OTC conditions of safe use, such as consultation with a pharmacist, the use of a self-selection algorithm in the retail pharmacy setting, or even a mobile medical app with the sale of their products. Using these new technologies and other conditions, certain products now available only by prescription will become more widely available as OTC drugs.

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Right to try

In May 2018, the U.S. federal Right to Try Act was signed into law. This was the culmination of a multi-year effort by Right to Try advocates to enact this legislation at the federal level. Key elements of the Right to Try (RTT) Act include the following:

- Companies can make unapproved drugs available to patients with life-threatening diseases without the FDA's authorization.
- Drugs must only complete one Phase I trial before becoming eligible for RTT use.
- As a general rule, the FDA may not use clinical outcomes from "right to try" patients during the new drug review processes.
- Manufacturers cannot be held liable for making their drugs available on a RTT basis.
- Companies may be able to charge patients for certain costs of drugs provided under RTT.

For patients seeking access to unapproved drugs, the provisions of the RTT Act established a new and distinct pathway that co-exists with the FDA's existing Expanded Access regulations. And for drug companies willing to consider compassionate use requests, these competing laws put them in the position of having to determine if they will make their drugs available under RTT, Expanded Access, or both.

Although the passage of the RTT Act was somewhat controversial, its enactment seems to have had little impact to date. Over a year and a half since its enactment, we are only aware of two publicly reported cases where investigational drugs were made available to patients under RTT. In stark contrast, according to a June 2019 statement from FDA, it had authorized more than 11,000 applications (or 99% of overall applicants) to use investigational products under its Expanded Access program.

Some RTT advocates continue to push for greater patient access to unapproved drugs. For example, there is an ongoing initiative to expand FDA's so-called "Parallel Track" program. The FDA established Parallel Track in the 1990s in an effort to combat the nation's HIV/AIDS epidemic. The Parallel Track program significantly expedited the access to novel drugs for treating HIV/AIDS, that were still in Phase II and III clinical trials.

Many RTT proponents are now pressing FDA to make renewed use of its Parallel Track for new drugs intended to treat other terminal diseases. For example, in May 2019, Senator Ted Cruz spearheaded a letter signed-off by three additional Republican legislators, asking FDA to broaden its Parallel Track program beyond HIV/AIDS drug applications. A letter signed by ten other members of congress argued that the drug approval process is "outdated" and the "one innovative solution that the FDA has at its disposal" would be to extend the Parallel Track program to other diseases.

For now, drug companies will need to carefully consider whether they should make their investigational therapies more widely available under the RTT Act. Doing so could pose significant risks (such as undermining their relationships with FDA), but may also lead to substantial benefits (including obtaining broader patient experience outside of the framework of clinical trials).

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U.S. federal funding for cutting edge research

Policymakers are increasingly focused on leveraging a combination of government and private resources to accelerate innovation and improve health outcomes. In the last few years, several high profile public-private initiatives have emerged.

- The National Institute of Health (NIH) HEAL Initiative — an "all hands on deck" approach to the opioid crisis, to accelerate research and address the public health emergency from all angles. More than US$900 million was awarded in 2019.
- The NIH BRAIN Initiative — a US$500 million per year investment in neuroscience research.
- The Precision Medicine Initiative and the Cancer Moonshot — both featuring dozens of collaborations across industry and academia.

While the government encourages industry participation in these programs, regulatory complexities abound in federally-funded research projects. For example, protection of intellectual property and valuable data may be in tension with the principles of transparency and openness in federally-sponsored research.

Pressures on corporate budgets and perceptions of value have companies paying increased attention to opportunities to partake in federally-funded initiatives. University-industry compacts also are on the rise, and the government has shown willingness to support them through federal grants and cooperative agreements. Companies that receive federal funds as recipients, sub-recipients, or contractors have important obligations; some of these obligations extend to participation in federal projects even without receipt of federal funds.

Strict requirements apply to recipients and subrecipients of federal funds, and to the contribution of private funds as "cost share" to a federal project. The government's regulation of intellectual property, data sharing, and conflicts of interest may differ from how companies traditionally approach these areas. Federal interest in foreign influence in scientific research also is a factor as international research collaborations surge.

Alliances between government and industry are imperative in the modern research environment. To the government's credit, myriad programs are helping to nourish and expand these interactions but the government has limited regulatory flexibility in these projects, and companies must be attentive to the downstream implications.

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Medical products with military application

In 2018, the U.S. Food and Drug Administration (FDA) launched a program to expedite development and review of certain products designed to address unmet medical needs. The program — which expanded upon legislation enacted in 2017 that helps accelerate availability of medical products for the U.S. military — follows earlier enactment of a new priority review voucher for material threat medical countermeasures.

Starting with blood products designated as high priority by Department of Defense (DOD), the program has increased collaboration between FDA and DOD. We expect that the program will expand to include other DOD priorities, including vaccines, regenerative medicine, and other medical products. The program includes involvement of senior FDA leadership, enhanced communication with FDA, and extensive manufacturing and clinical advice — all aimed to encourage the FDA to treat DOD priority products at least as favorably as "breakthrough" therapies.

In late 2018, the FDA approved a sublingual opioid drug product that the DOD had designated as a battlefield medicine priority. In addition, in August 2019, the FDA granted a variance for cold-stored platelets when conventional platelet products are not available, and in December 2019, the FDA finalized guidance to assist in the development of dried plasma products intended for transfusion.

We anticipate that the FDA will issue further guidance in 2020 and gradually expand this program beyond its current military context. Based on the FDA's initial work plan, the FDA aims to expand the program beyond the battlefield to include other products for "austere environments" and other "front-line conditions" that may provide benefits for military personnel, and in turn, the general population.

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The politics of health technology

Many countries use health technology assessment programs (HTAs) to evaluate the cost effectiveness of medicines as a basis for national pricing decisions. HTAs can also have a wider impact as one country may use the results of a HTA carried out in another country as a reference point for its own pricing decisions.

While HTAs are ostensibly technical processes for determining whether a new medicine is good value for money, such appraisals and their recommendations have an inherently political context as they are used by governments to manage health expenditure, an inevitably political issue. As a result, HTAs have often been thrust into public and political attention, particularly in relation to rare diseases.

For example, in England, the National Institute for Health and Care Excellence (NICE), the body that carries out HTAs, has a separate process for assessing very rare disease treatments, known as the Highly Specialised Technology (HST) process. The most important difference between the HST and the standard appraisal route is their differing threshold for cost effectiveness. This recognises that, because of a range of factors including paucity of available data and comparators and that they may be lifelong treatments, medicines for very rare diseases will almost certainly not be cost-effective at standard thresholds.

However, eligibility criteria for the HST process are very narrow and many new medicines treat rare conditions that are not rare enough to qualify for the HST route. These treatments are much more likely to receive negative NICE appraisals under the standard process, adding to the tension between making medicines available to patients with rare diseases, recovering development costs and managing health expenditure.

Balancing these tensions is and will continue to be highly charged and highly political. Consequently, it is becoming increasingly vital for manufacturers to navigate not only the regulatory and procedural aspects of HTAs but the associated political environment as well.

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MDR and IVDR

The Medical Devices Regulation (MDR) will come into effect on May 26, 2020 and the In Vitro Diagnostics Regulation (IVDR) in May 2022. Manufacturers are already feeling the impact of the upcoming changes, including their interactions with "notified bodies," an independent certification organization that is "notified" by a European Member State's Competent Authority to determine if a product or system meets applicable requirements for CE marking.

A number of notified bodies have decided either not to seek designation to the MDR and IVDR or to limit the scope of these designations. As a result, these notified bodies will either cease to exist or have a reduced capacity to issue CE Certificates of Conformity when the Regulations enter into application. Thus far, only nine notified bodies have been designated to the MDR and three to the IVDR. Although a number of other notified bodies anticipate designation before the MDR enters into effect, there is likely to be a substantial disparity between the available notified bodies and the manufacturers in need of their services, at least in the short to medium term. As a result, manufacturers are facing the risk of losing their notified body and the CE Certificates of Conformity that are essential to marketing of their medical devices in the EU and facing challenges in engaging alternate notified bodies.

The European Commission has prepared a number of guidance documents to address a variety of issues. These include clinical evaluation, classification of software and guidance on cybersecurity for medical devices, the role and activities of the notified bodies, and the validity of CE Certificates of Conformity during the transition period. Further g uidance is anticipated in the coming months. The changes that the regulations will introduce, including those related to interactions between manufacturers and other economic operators and the need to establish related procedures and to conclude related agreements or revise existing agreements, should however, be addressed before the regulations enter into application.

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"The team has a very good understanding of the pharmaceutical business, quickly grasps subject areas, and processes them with a high level of quality and in a very practical way."

Client, Life Sciences, Chambers Europe-wide, 2019

Regulatory exclusivities in the EU

Regulatory exclusivity rights in the EU were originally developed to incentivize the industry to continue development of innovative medicinal products, including for the treatment of rare diseases and for use by children. In an effort to further promote development of these innovative treatments, the European Commission continues to consider the legal environment and its effects on innovation, as well as, now, pricing.

In the EU, innovative medicinal products can be protected by several regulatory exclusivities including regulatory data protections that safeguard data contained within marketing authorization dossiers and market exclusivity protections for orphan drugs. Pediatric extension of SPCs or of orphan exclusivity is also available in return for conducting pediatric studies.

With continued emphasis on innovative drugs, governments in the EU have been considering to what extent the legal framework for regulatory exclusivities is successful and how regulatory exclusivities relate to pricing and affordability of medicinal products.

The European Commission has recently launched several projects to evaluate the legislation on regulatory exclusivities and is currently finalizing its evaluation of the EU Orphan and Paediatric Regulations. In 2020, the European Commission is expected to publish a working document on how to improve the legislation on medicines for children and rare diseases. Amongst others, the report is expected to provide insight into how the various regulatory incentives have been used and what financial consequences this has had.

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Government enforcement

Patient support programs

As health care systems around the world have gotten more complex and treatments more costly, navigating access to treatment has become a major challenge for patients. Pharmaceutical, biotech and device manufacturers increasingly have stepped into the breach with a variety of Patient Support Programs (PSPs) aimed at helping patients better understand their treatment options, secure insurance coverage, and afford the out-of-pocket costs of treatment. More advanced PSPs provide nurse education and adherence monitoring services to maximize the benefits of advanced therapies. It's no exaggeration to say manufacturer-sponsored PSPs have improved and saved the lives of millions of patients.

PSPs that involve direct interactions with patients and/or health care professionals are impacted by a variety of regulations, and recent digital tools enhancing these programs have brought their share of new legal developments. Data privacy requirements are triggered when collecting patients' information and advertising law restrictions may apply when communicating on a specific medicinal product. Telemedicine and medical device regulations set boundaries on how PSPs operate, how the tools used are to be legally classified and whether they require regulatory approval. Direct engagement with patients also brings increased product liability risks. And the participation of health care professionals is key to PSPs, but related incentives need to be carefully assessed in terms of compliance with applicable conflict of interest, disclosure and anti-kickback laws. Deploying global PSP policies and programs require a holistic approach on these topics and awareness of local differences in regulatory treatments of PSPs, notably in the U.S. and the EU.

In the U.S. in particular, manufacturer PSPs have been the subject of intense government scrutiny in recent years. After a period of uncertainty, federal officials have reaffirmed the benefits of patient access to basic product support services, such as insurance authorization assistance and nurse educator services. At the same time, new developments in personalized medicine and the emergence of complex immunotherapies and gene therapies have expanded the scope of manufacturer PSPs into new areas, including diagnostic testing and travel support. As PSPs expand and become more important than ever, it remains the case that they involve significant legal risk.

Life sciences companies must legally anticipate, address, and mitigate these legal risks when launching PSPs to prevent any subsequent liability claims, as well as regulatory and reputational risk exposure. PSPs have the indisputable potential to improve clinical, adherence, and cost outcomes, but it's essential that they be carefully structured to comply with the myriad laws and regulations that govern their operation.

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U.S. procurement of drugs, biologics, and medical devices

Driving down costs for pharmaceuticals and medical devices will continue to be a high priority for the U.S. government in 2020, and manufacturers that position themselves to take advantage of opportunities created by government contracting initiatives stand to benefit greatly.

Apart from efforts targeting government spend in U.S. Health Programs, including the overarching Medicaid and Medicare programs, legislators and policymakers are taking a hard look at the budgets for the federal government's substantial "in house" health programs. These are the Veterans Health Benefit, which is managed by the U.S. Department of Veterans Affairs (VA), and the Department of Defense (DoD) TRICARE program, which covers active duty service members, their dependents, and military retirees.

Pharmaceutical and medical device manufacturers can anticipate increased efforts at standardization and consolidation of requirements to meet savings goals for the VA and DoD programs.

- In terms of pharmaceuticals, VA and DoD in recent years have sought to leverage their extensive purchasing power to extract deep discounts for multisource drugs. We can expect the agencies to conduct formulary-based procurements with increasing frequency in 2020. We can also expect the agencies to take additional steps to curb non-competed "open market" purchases.
- As for medical devices, in 2020 we can expect the programs to continue to work toward meaningful standardization and to increase collaboration in their procurement efforts, in particular with the DoD opening up VA access to certain DoD contracts. For its part, VA is launching a revamped Medical Surgical Prime Vendor contracting program that collapses its requirements into competed product categories.

It is worth noting that these efforts can have impact well beyond the U.S. federal market. In recent years, a number of state governments have considered proposals to leverage federal contract drug pricing for their programs. Other countries also are focusing on U.S. government contract pricing as "reference" pricing for their health programs.

Finally, in 2020 we can expect wider application of Buy American and country of origin-based restrictions that may restrict procurement of products made outside the U.S.

More than ever, pharmaceutical and medical device manufacturers will be well-served by keeping abreast of U.S. procurement developments.

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IWCF developments in life sciences

The Department of Justice's (DOJ) still gives opioids its highest enforcement priority. In 2019, fentanyl manufacturer Insys Pharmaceuticals resolved criminal and civil liability for US$225 million. DOJ then successfully tried to verdict a RICO case against the founder and three other executives, whose sentences range from 30-66 months. Expect more novel uses of the health care and wire fraud statutes against manufacturers and distributors.

State and local governments are in a pitched battle with the opioids industry. Purdue Pharma has reportedly agreed to pay US$3 billion over seven years to county and municipal governments to settled claims in a multidistrict litigation case (MDL) in the Northern District of Ohio. Other states are trying cases against manufacturers under state consumer protection laws. Some manufacturers are engaged in settlement discussions for the release of the consumer protection claims. For example, TEVA reportedly offered state Attorneys General US$250 million and US$23 billion of free opioid treatment products. Distributors report offering Attorneys General cash and free distribution services.

DOJ is investigating the electronic medical records software certified by the U.S. Health and Human Services (HHS) Office of National Coordinator (ONC), exploring the bona fides of certifications on product functionality and the relationships developers have with labs and drug manufacturers. In January, a developer entered the first criminal resolution, by a deferred prosecution agreement, settling for US$145 million criminal and civil False Claims Act allegations that it accepted kickbacks from opioid manufacturers in exchange for utilizing features of its software to "recommend" prescribing opioid products and that it misrepresented its software capabilities. Two other health software developers entered civil settlements for US$57.2 million in 2019 and US$155 million in 2018 of allegations that they misrepresented the capabilities of their electronic health records products as to clinical terminology and clinical data calculations. DOJ alleged physicians received incentive payments to which they were not otherwise entitled as a result. Both settlements also resolved claims that physicians received remunerations to induce them to recommend other doctors adopt their software. The HHS Office of Inspector General (HHS-OIG) is entering Corporate Integrity Agreements with software developers on its compliance requirements. We expect more scrutiny in this arena by DOJ, HHS-OIG, and the ONC.

The DOJ industry-focused investigation into allegations that pharmaceutical companies violated the False Claims Act by paying kickbacks to Medicare patients through charitable foundation disease funds continues. In 2019, settlements with six manufacturing companies totaled approximately US$265 million. Moreover, disclosures by other pharmaceutical companies suggest that additional resolutions are likely.

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Precision medicine

Gene therapies

The U.S. Food and Drug Administration (FDA) approved the first gene therapies in 2017, marking a new era in precision medicine. Gene therapies are beginning to deliver on their promise of eradicating the underlying causes of diseases, and we anticipate continued progress throughout the coming year. In 2018, the FDA received over 150 gene therapy Investigational New Drug Applications (INDs), bringing the total number of active INDs to over 800, and the number still appears to be growing.

The FDA has approved Luxturna, a treatment for a rare, blindness-causing genetic mutation; Yescarta and Kymriah, two gene-based blood-cancer treatments which are CAR-T immunotherapies; and Zolgensma, which cures the progressive muscle wasting disease, Spinal Muscular Atrophy. Gene therapy is also being developed for more prevalent diseases, such as hemophilia, Parkinson's disease, Huntington's disease, and cystic fibrosis; and potential treatments utilizing CRISPR gene editing technology have entered clinical trials.

Despite this remarkable progress, challenges remain. Thoughtful clinical trial design continues to be a critical component. Small patient populations and serious and progressive symptoms in diseases targeted by gene therapies create barriers to generating the robust clinical evidence needed for both FDA approval and reimbursement decisions by payers.

There is also uncertainty and concern about long-term outcome durability, immunogenicity reactions and unique manufacturing challenges. Government policy and payers' views continue to evolve on key issues of coverage and reimbursement, which will be a critical determinant of patients' access to these treatments.

Gene therapies undoubtedly will play a growing role in medicine in this new decade, but the market and regulatory landscape are still fluid, and substantial challenges will need to be addressed to realize their full potential.

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Personalized medicine

Personalized medicine seeks to precisely target therapies to the specific characteristics of individual patients. Rapid advancements in genetic and molecular testing have improved the ability to select the right therapy at the right dose for the right patient. Other forms of personalized medicine, such as 3D printing of individually matched implants, also promise to improve targeted treatments. While initial developments in companion diagnostics and personalized devices have proven promising, these technologies are only at the very beginning of their opportunity.

Given these developments, personalized medicine is also changing the way therapies are developed. Collaboration between pharmaceutical and diagnostic companies allows for the design and use of companion diagnostic assays early in the development of novel therapies. This approach allows therapeutic manufacturers to better target optimal patient populations, potentially increasing efficacy and reducing side effects.

While these medical approaches are revolutionizing certain areas of medicine, they also require adjustment of traditional legal and regulatory frameworks. Companion diagnostics and their associated pharmaceutical products must be approved by the U.S. Food and Drug Administration in parallel, requiring close collaboration between companies.

Similarly, a complex framework of reimbursement is slowly developing and traditional models of laboratory regulation are melding with diagnostic product regulatory requirements. Given these novel regulatory and reimbursement issues, agreements governing the relationships between pharmaceutical and diagnostic companies must establish a framework for the companies to cooperate and share data as they pursue regulatory and reimbursement approvals, and address contingencies such as clinical holds, approval delays and protracted reimbursement negotiations.

As these technologies grow in prevalence, questions surrounding the legal issues – and the strategies for addressing them in the collaboration context – will continue to evolve as well.

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Regenerative medicine

Regenerative medicine — which includes breakthroughs like stem-cell-regenerated organs and personalized gene therapies — has been recognized by the U.S. Food and Drug Administration (FDA) Commissioner as one of the "most promising fields of science."

To support innovation, the FDA has issued four guidance documents outlining its regulatory framework for these therapies. This framework includes the Regenerative Medicine Advance Therapy (RMAT) designation program, which offers sponsors more active involvement and guidance from the FDA during product development.

These guidelines also attempt to clarify which human cellular and tissue products (HCT/Ps) may continue to be marketed without prior FDA approval. The FDA announced that it will not enforce its stricter interpretations until November 2020, and urged companies to approach the agency for product-specific input. To encourage such approaches, the FDA issued an extension until March 31, 2020 for its Tissue Reference Group (TRG) Rapid Inquiry Program (TRIP), which is intended to provide non-binding HCT/Ps classifications within a week. The FDA also recently issued numerous "It has come to our attention" letters that identify categories of products, such as amniotic fluid and exosomes, that generally require the FDA pre-approval before marketing, in the agency's current view.

For regenerative medicines that will require FDA pre-approval, the FDA may consider innovative approaches adapted to the revolutionary nature of these products. The FDA outlined some of these approaches in six draft guidance documents on gene therapies in July 2018, and has promised more.

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M&A

Pharma and biotech M&A

2019 was a strong year for life sciences M&A, led by two very large transactions – BMS/Celgene and Abbvie/Allergan, each announced in the first half of the year. However, a careful look behind the headlines yields more mixed results. The aggregate value of announced deals fell significantly in the second half of the year as a result of the absence of additional "mega" mergers during this period. Further, there was a noticeable downturn in year-end M&A volume after activity peaked in Q3. Even the recently completed JPMorgan Healthcare Conference didn't seem to prompt the same volume of M&A as in years past.

In early 2020, many of the key deal drivers in the sector continue to be in play. Large biopharmas have cash on the balance sheet and are strongly motivated to add new products and technologies to their platforms. We would expect that cell and gene therapies will continue to drive deals. Another area of significant industry focus is the development of AI, digital health and other health care technologies, which is generating joint ventures, collaborations and other tie-ups between biopharma and tech, which we would expect to continue.

However, a number of factors are causing near-term uncertainties, never a good thing for transactions. These include the U.S. presidential election, continued focus on drug pricing reform in the U.S., the transactional regulatory environment (antitrust, CFIUS etc), the potential for an economic downturn at some point and, of course, geopolitical uncertainties. Another variable is whether the IPO market continues to be a reliable alternative to M&A as an exit for venture-backed biotechs.

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Transfer pricing

As the life sciences sector continues to evolve, adopt new technologies, and seek new growth opportunities, Transfer Pricing (TP), tax, and supply chain planning will continue to play a very important role in 2020.

The use of technology and the fragmentation of IP make it increasingly difficult to determine where value creation is. What's more, an increase TP focus on the location of people involved in the development, enhancement, maintenance, protection, and exploitation of IP, means that companies are not able to operate in many jurisdictions without people on the ground.

Tax authorities are becoming more aggressive, and businesses should expect new legislation on IP and an increased number of TP audits.

M&A, joint ventures, and collaborations are often common in life sciences as a way to grow product lines, market products, or divest from mature markets and products to focus on new opportunities. Assessing risk and identifying opportunities through supply chain planning can generate significant financial benefits for businesses in this sector and mitigate tax and TP risk.

If carefully planned and aligned with commercial strategy, TP can enable businesses to achieve their strategic goals and become more efficient. If ignored, it can result in significant cost and reputational damage.

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Europe

Wide class actions on the horizon

Class and collective actions in Europe are becoming more and more challenging for businesses. The EU Commission's proposal for a directive on representative actions for the protection of the collective interests of consumers, one of the latest initiatives in this area, is about to set an EU-wide standard creating an action that will have impact across all EU member states. Several key provisions of EU consumer law are within the scope of this action, including, amongst others, laws on products liability, product information and labelling, E-Health, and commercial practices, as well as the General Data Protection Regulation.

Towards the end of 2019, representatives of the EU member states agreed on a mutual position regarding the Commission's proposal. The project is now set for "swift adoption" as there is agreement on the concept between Commission, Parliament and Council. Adoption is expected in the first half of 2020, whereas dates for compulsory implementation are still under discussion.

One of the key features of the envisaged action is the motion for redress measures, enabling a ruling that obliges traders to provide consumers with remedy. Such remedies can be compensation, repair, replacement, price reduction, contract termination or reimbursement of the price. As the proposal goes beyond some of the actions and procedural systems currently established in EU member states, you can expect a larger impact on practice and on legislation. Another noteworthy item is the cross-border effect of rulings. In a case involving multiple EU member states a final ruling in one of the member states will have impact on the others.

It is fair to say that an EU-wide class action is at the horizon. The EU is about to add another layer to litigation in Europe, where the aggregate of collective and individual actions in the various jurisdictions often are a challenge burden for business and require sophisticated defense strategies.

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Inspection of marketing authorization documents

Biotechnological innovators own many valuable process patents, specifically regarding the manufacture for biological products, but rarely are these actually subject of litigation. One reason for this is the lack of evidence the patentee suffers from. Evidence showing that the protected process used is not readily available or even obtainable in situations where the use of the protected process cannot be established by analysis of the marketed product. There are possibilities, though.

In the U.S., the Biologics Price Competition and Innovation Act (BPCIA), 42 U.S.C. § 262(l) requires the manufacturer of a biosimilar to disclose information from his abbreviated Biologic License Application (aBLA) to the manufacturer of the reference product and the UK procedure offers possibilities of discovery with the exception of the French *saisie contrefaçon* that has a long-standing tradition. Evidence gathering proceedings in non-common law countries in the EU are still not usual, despite the fact that Art.icle 6 and 7 of the EU Enforcement Directive (2004/48/EC) require member states to provide these.

Under German law, Section 140c, The German Patent Act provides the possibility to inspect the production process at the premises of a purported infringer or the inspection of documents. Specifically in the heavily regulated field of biologic drugs and small molecule pharmaceuticals, inspection of the aBLA/ dossier can be a powerful tool in the hands of the patentee to gather the required evidence for showing infringement. The actual procedure of the inspection is based on case-law and may differ significantly between the various courts. In order to protect know-how and business secrets of the respondent, courts often have the respondent provide the documents to an independent court appointed expert who will then determine the facts relevant for the assessment of infringement.

Considering the complexity of biopharmaceutical production, we will likely see more of these inspection proceedings in the future, specifically given that under European law, the use of a process in another country may serve as a basis for an injunction against distribution of a product on the domestic market (Article 64 (2) EPC).

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Excessive pricing in the pharmaceutical sector

Competition authorities have historically been reluctant to investigate cases of excessive pricing in the context of antitrust enforcement. These cases traditionally presented "formidable difficulties" and authorities were concerned about appearing to assume the role of price regulator. However, developments over the past few years, at both the EU and the national level, suggest that the tide is turning, particularly in the pharmaceutical sector.

Excessive pricing can constitute a breach of competition law under certain circumstances. Under Article 102 of the Treaty of the Functioning of the European Union (TFEU) dominant firms are prohibited from "directly or indirectly imposing unfair purchase or selling prices or other unfair trading conditions."

In recent years, national competition authorities in EU Member States have vigorously pursued cases against pharmaceutical companies. Recent examples include the Aspen case (September 2016) in Italy and the CD Pharma case (January 2018) in Denmark. In addition, several excessive pricing investigations are currently underway in the pharmaceutical sector, initiated by the UK Competition and Markets Authority (CMA) (Actavis, 2016 / Concordia, 2017) and the European Commission (Aspen, 2017). The Dutch Competition Authority also launched an excessive pricing investigation (November 2018) into CDCA, Leadiant's treatment for a rare genetic disease. Similar proceedings were also launched by the Belgian (April 2019) and Italian (October 2019) Competition Authorities.

However, some recent court cases may have cast a shadow over these successes. In France, the Paris Court of Appeal overturned a fine of €199,000 imposed on Sanicorse, the only company able to dispose medical waste in Corsica during a four year period, for price increases ranging between 135% and 194% (19 November). The Court found that the French Competition Authority had not established that Sanicorse's end prices were excessive and explained that it was insufficient to demonstrate that the price increases were unjustified.

In *Pfizer/Flynn Pharma* (June 2018), the UK Competition Appeal Tribunal (CAT) held that the CMA had misapplied the legal test for excessive pricing when it fined Pfizer and Flynn Pharma over GBP£89 million for charging unfair prices for an anti-epilepsy drug. The CAT's judgment is damning. It states that "cases of pure unfair pricing are rare in competition law" and that such cases should only be brought where they are "soundly based on proper evidence and analysis." The CAT also warns that competition authorities should be "wary of casting themselves in the role of price regulators." Both the CMA and Flynn appealed the CAT's decision to the Court of Appeal. The appeal was heard in November 2019 and the decision is expected this year.

It is unclear whether the Pfizer/Flynn Pharma decision will deter competition authorities from bringing excessive pricing cases in the future. The CMA has already announced that its ongoing investigations in this area are likely to be "severely delayed" as a result of the CAT's decision and until the appeal process is concluded. However, the excessive pricing landscape is likely to continue to evolve in 2020 as competition authorities grapple with the difficult task of balancing, on the one hand, the need to crack down on the abusive charging of high prices by dominant companies, and, on the other hand, the recognition that high prices are necessary to reward the investment and innovation of such companies. The pharmaceutical sector is likely to remain at the centre of this debate.

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Brexit

The UK formally left the EU on 31 January 2020, after 40 years of membership. The UK's relationship with the EU is now no longer governed by the EU Treaties but instead by the terms of the "Withdrawal Agreement" between the UK and the EU. Under the Withdrawal Agreement, a "transition" period is now in place during which the UK will be treated for almost all intents and purposes as if it remains an EU Member State. From a business perspective, it will feel as if the UK has not left, providing short term certainty.

The transition period is due to end on 31 December 2020. The UK and EU intend to negotiate a new free trade agreement to come into effect on 1 January 2021. The details of that agreement, and whether it can be agreed in under a year, are not yet known. If not and no extension of the transition period is agreed, the transition period will end and the UK and EU will have no international agreement governing their ongoing relationship.

The life sciences industry in both the EU and UK are agreed on the need for close cooperation and alignment of the future UK and EU regulatory and customs regimes for medicines and devices under any new trade agreement — and the overarching need to ensure patient safety and supply continuity.

Life sciences companies across the world with operations, third party manufacturers, suppliers, customers, or clinical trials in the UK need to monitor the UK-EU trade agreement negotiations closely. The legal and business impacts of both possible outcomes, being a new UK-EU free trade agreement or no agreement, should be assessed and planned for to ensure that companies can continue to develop, manufacture, and supply products after the end of the transition period.

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R&D in the EU

The promotion of R&D in the EU is aimed at ensuring the continuous development of treatment methods, as well as the appropriateness, affordability, and accessibility of medicinal products.

Certain steps have been taken at the EU level, for example:

- Innovative Medicines Initiative: a public-private partnership between the European Commission and the pharmaceutical industry offering grants for innovative research.
- Horizon Europe (in 2021-2027): the new European Innovation Council will fund fast-moving, high-risk innovations.
- InnovFin Infectious Diseases: the European Investment Bank supports projects related to innovative vaccines, drugs, medical and diagnostic devices, and novel research infrastructures for combatting infectious diseases.

Individual countries are also taking action, for example:

- IP Box: a preferential tax rate for revenues generated by IP rights covering innovations. This has been introduced in several EU countries, for instance, in the UK (a reduced rate of 10%), Luxembourg (80% of revenues exempted from taxation), Poland (a reduced of 5%).
- Medical research entities: supporting innovations and sponsoring medical research, especially those that do not generate an easy profit. These include the Medical Research Council in the UK, the Danish Medicines Agency, and Inserm in France. In Poland a Medical Research Agency was created.
- Preferential reimbursement procedure: Poland declares the will to continue to work on an innovative procedure for development which would provide companies that manufacture or invest locally in R&D preferential treatment in reimbursement proceedings (e.g. partial or total exemption from fees, or a shortening of procedures).

However, since many patients and countries cannot cover the costs of innovative treatment, various countries have started negotiating reimbursement deals in groups, such as BeNeLuxA, Valetta, and V4 Plus Fair and Affordable Pricing. Another project was launched in the end of October 2019 – the International Horizon Scanning Initiative. For now, it involves nine European countries, but Canada and South Korea are interested to join. The aim of this new project is to highlight life sciences innovations before they reach the market in order to gain their better understanding which is supposed to influence price negotiations and arrangements with the industry.

The overall trend is observed towards the stimulation of innovation and competitiveness. The EU searches for new long-term solutions and more initiatives on the national-level can be expected.

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Ranked Band 1

for Life Sciences – Europe-wide

Chambers Europe-wide, 2019

Latin America

Health care innovation and new Public Policies

Transnational companies from the sector will continue to view Latin America and its emerging markets as attractive for expanding their activities and businesses. Among the factors key to Latin America's appeal include:

- Increasing growth and expansion of health infrastructure and services aimed to better cover the population's needs.
- Innovative but not yet fully explored business and regulatory models aimed to improve access to innovative technologies, therapies, and products.
- Regulatory frameworks which in some jurisdictions aim to simplify the launch of drugs and devices.
- Adoption of specific recognition agreements between certain Latin American countries aim to expedite regulatory processes.
- Developing of new technologies including innovative artificial intelligence devices and techniques that contribute to the diagnosis and treatment of diseases, generating of Big Data, handling of medical records, etc.

New regulations, public policies and trends related to regulatory enforcement, competition, compliance, public procurement, data privacy, consumer protection and health regulation (which includes innovative therapies, digital health, and clinical trials) are and will still be relevant aspects in several Latin American territories. Strategic investments and divestitures adopted globally are still delineating new business models for the further expansion of the life science industry sector throughout the region.

Mexico

Mexican Health Law has recently been amended to adopt new public policies regarding (i) rendering of public medical services, (ii) fighting against obesity and diabetes, and (iii) for the prescription of drugs. These amendments have a direct and immediate impact for both Mexican and multinational companies engaged in the health care and food and beverages sectors.

The Federal government of Mexico has adopted new public policies and models concerning the procurement of drugs, and for the rendering of medical services for people not covered by the IMSS and ISSSTE traditional social security systems. The National Institute of Health for Well-Being, which started operating on January 1st 2020, will now provide medical services to more than 70 million Mexicans without insurance.

Current administration is working in the discussions and amendments to the existing framework governing labeling of food and beverages as part of its public policy strategy adopted for fighting against obesity and diabetes. Important impacts for both health care and food and beverages industry are foreseen.

Telemedicine and other novel health care delivery models are being explored within the Mexican health care sector. Amendments to the Mexican Health Law and its regulations governing the provision of medical services now contemplate the possibility for prescribing through electronic means and by graduated nurses.

Through an amendment to the Health Law Mexico has set the grounds for the adoption a new framework concerning the legalization of activities and products involving cannabis. Mexico's Supreme Court has ordered to the Ministry of Health to enact the required Regulations for making effective the amendments made to Mexican Health Law concerning cannabis for medicinal use and other authorized activities and products.

Also, new anticorruption system and public procurement schemes have been adopted, which has significantly impacted the way in which the supply of drugs and devices and performance of certain activities are carried out within the public sector.

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On the horizon

Effects of climate change

The last year has been notable for its illustrations of the effects of climate change from rising sea levels to the fires ravaging Australia.

Life sciences companies are going to be at the forefront of efforts to tackle both the causes of climate change and to rapidly develop techniques and products to allow the mitigation of, and adaptation to, the effects of increased global temperatures.

Many pharmaceutical companies are already involved in developing treatments for hitherto localised diseases, such as Zika and malaria, carried by mosquitoes which will be able to flourish in the warmer temperatures in previously temperate parts of the world. Respiratory distress resulting from poor air quality and conditions arising from heat exhaustion and water-borne illnesses associated with flooding are all expected to rise. Other issues relevant to the life sciences industry include problems with food security such as that highlighted by a recent paper predicting significant harvest failures in 'breadbasket' regions. Biotechnological adaptation and development of food crops will be amongst the measures necessary to compensate for these changes.

However, many of these scenarios are based on the ability to limit the global average temperature to rise to 1.50C which, according to the IPCC 2018 report, will only likely be possible if we achieve net zero global carbon emissions by 2050 or before.

Efforts to do this will rely on all companies to expand and access renewable sources of energy in addition to strenuous efforts to improve energy efficiency. However, this alone will not be sufficient to reach Net Zero by 2050 and intense research is ongoing into methods for absorbing greenhouse gases directly from the atmosphere. Recent successes in this work include yeast engineered to use CO_2 as a carbon source, and the genetic enhancement of microalgae in addition to growth optimisation and utilisation strategies of other biofuels

An additional consideration for all organizations relates to questions over potential responsibility for past emissions and the potential loss of reputation, or legal action for unsubstantiated sustainability claims. Science-based targets, accurate emissions accounting and appropriate disclosure is likely to be of ever-increasing importance to an organization's demonstration of climate commitments.

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3D printing

3D printing is quickly taking hold in the medical devices market and poised to change how we think about health products, manufacturers, and the legal issues they create. While medical devices like implants, prostheses, and even bones are already being produced by 3D printers, Medical Device Regulation, which has not yet even come into force, is outdated in this area.

Until now, 3D printing has largely been unregulated, despite multiple legal issues. For example, if an implant is 3D printed by a hospital, who is responsible? The supplier of the printer, the supplier of the CAD files providing the blueprint for the implant, or the hospital itself? Is the implant a customized device? Which manufacturing standards and regulatory requirements apply? Do exemptions apply for devices made in health care institutions or are they manufactured on an industry scale?

The answers to all these questions have to be found by interpreting laws which do not explicitly regulate this new area of technical developments. Additional questions also arise from the direction of the machinery directive, the REACH Regulation, data privacy, intellectual property, and product liability.

These issues also impact the pharmaceutical industry, as 3D printers may soon be used to manufacture drugs. For traditional manufacturers, utilizing 3D printer compliance with GCP is in focus. However, 3D printers may soon be used by hospitals to print their own medicinal products or to do patient-individual compounding. Questions arise as to whether a hospital/pharmacy is allowed to manufacture outside the scope of pharma laws, and what traditional manufacturers can do about it.

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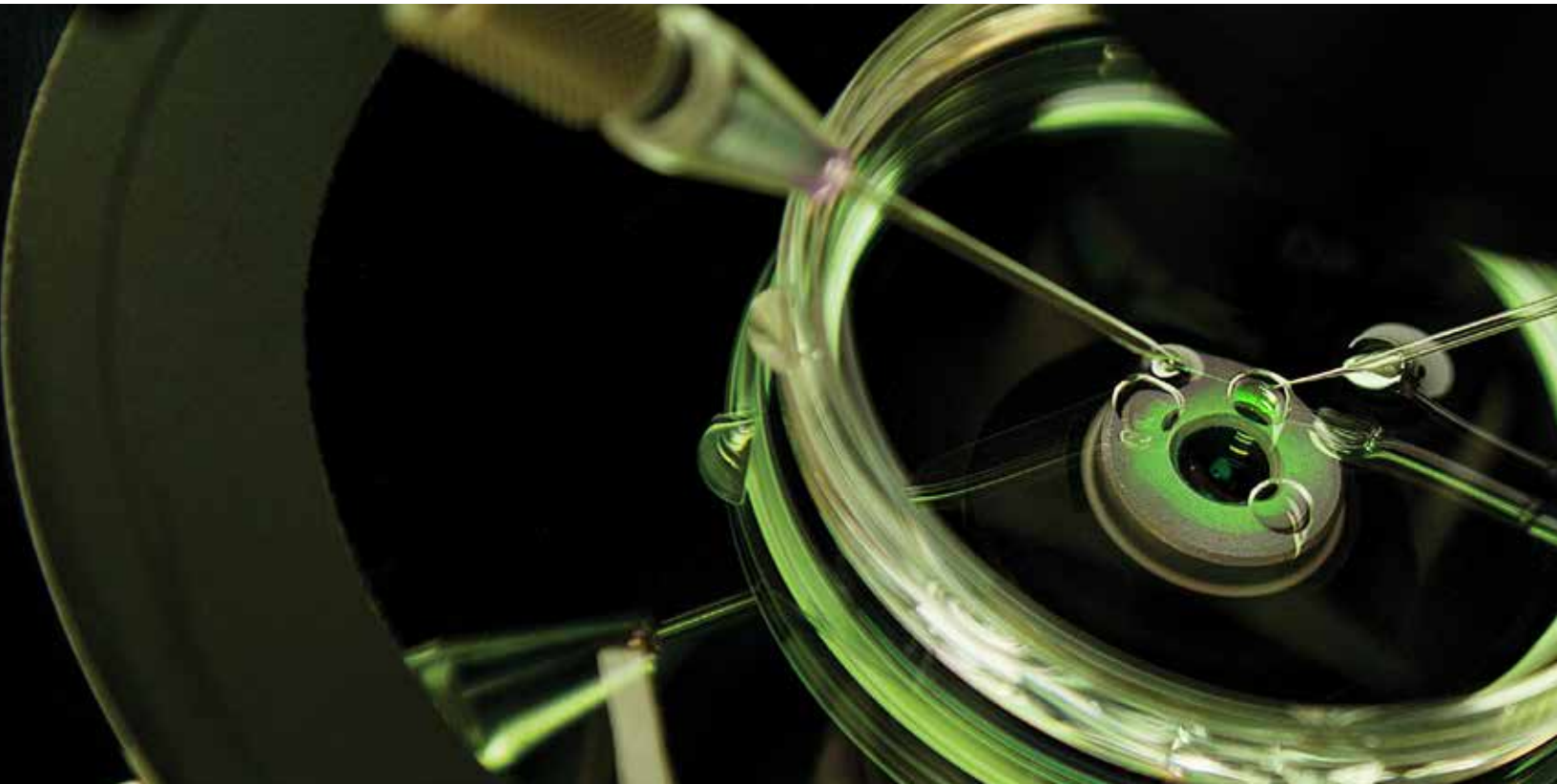

The application of blockchain to life sciences

The life sciences and health care sectors have issues with data storage due to the huge volume and need for interoperability across different organisations. When patients move between different health care providers, their medical data has to be transferred to different organisations making medical records difficult to track and trace. The data must be accessible by each organisation, which requires consistent methods of storage and access.

The use of blockchain technology would allow patients to have a unified medical record that can be accessed from a decentralized store. Systems such as the MedRec prototype, which uses blockchain smart contracts to create a decentralised data-management system, are set to improve the way that patients' medical records are stored and accessed.

One of the biggest challenges that will be faced by blockchain technology will be compliance with GDPR. A patient's medical records constitute sensitive personal data, which by the very purpose of a blockchain system, would be transferred to other users of the system. This conflicts with the objective of GDPR, which requires the party controlling personal data to safeguard the security and privacy on behalf of individuals. Systems will have to implement safeguards to ensure that data security and privacy is maintained. This could take the form of restrictions on jurisdictions that can participate in the system. Systems could also ensure that medical records are not stored on the blockchain themselves, but instead the blockchain holds a reference to where each medical record can be accessed.

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"They have great legal and regulatory knowledge, as well as litigation capabilities both at a national and international level. They are incredible and their technical understanding is fantastic."

Client, Life Sciences, Chambers Global-wide, 2019

CRISPR'ed and out

2020 is not going to be a very Happy New Year for He Jiankui. In a new twist to the CRISPR babies saga, on 30 December 2019, he was sentenced to three years in prison and fined ¥3 million (approximately US$430,000). This came a few weeks after his unpublished manuscript was leaked and was quickly pored over by experts. The verdict was damning; one expert commented that it was technically impossible to determine whether an edited embryo "did not show any off-target mutations" as claimed in the paper, without destroying that embryo by analyzing every single cell. Another noted that none of the embryos got the 32-base pair deletion to CCR5 that is known in humans. Instead, they gained novel variations whose effects are not known. The saga has illustrated that whilst it is relatively easy to carry out editing of human embryos, it is somewhat harder to carry it out successfully.

Preliminary results from the first two clinical trials to use CRISPR have been mixed. In November, CRISPR Therapeutics/Vertex announced that the first two patients to receive CTX001, a treatment for the inherited blood disorders beta thalassemia and sickle cell disease, have normal levels of haemoglobin several months later. If these results are replicated in larger trials, it shows the potential for CRISPR to cure two debilitating and relatively common diseases. However, another trial to treat HIV infection was less successful – only 5% of the transplanted cells were edited, not enough to cure the disease.

To great excitement, a new form of CRISPR – prime editing – has recently emerged. Unlike previous versions of CRISPR, this technique enables precise changes to be made to DNA without making cuts in the double helix. This is significant because DNA attempts to repair itself when cut but the repair process can introduce imperfections in the DNA sequence, reducing the efficiency of the editing and leading to off-target effects. Prime editing uses a modified version of the Cas9 enzyme which cuts only one of the two DNA strands and prime editing guide RNA (pegRNA) that both specifies the target site and encodes the desired edit. It has been used to make single base changes and insert and delete DNA sequences in a variety of cell types with much higher efficiency. According to the scientists involved, it has the potential to correct 89% of known disease-causing genetic variants in DNA.

Whilst CRISPR continues to dominate the headlines (and the hype), it is not the only gene therapy on the block. So far, fewer than 100 patients in the world have been commercially treated with a gene therapy, although more have received gene therapy as part of a clinical trial. However, despite the relatively small number of therapies approved to date, and the issues still to be overcome, the FDA is gearing up for an explosion in this field and predicts that by 2025 they will be approving 10-20 cell and gene therapies every year. The challenge for the industry will be how to price these novel therapies so that they are available to those that need them.

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For more information

Life Sciences and Health Care Horizons provides only a snapshot of some issues the industry will face in 2020. Our team is focused on tackling these issues to provide our clients around the globe with valuable and innovative solutions to their most complex challenges — present and future.

To learn more about our team or any of the issues covered, please contact Asher Rubin, any of the authors in this publication, or one of the partners you regularly work with at Hogan Lovells.

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Life Sciences and Health Care Horizons – Global Event Series

From spotting trends in digital health innovation to breakthrough cures and navigating fluid regulatory landscapes, the Hogan Lovells' Life Sciences and Health Care Horizons event series will span three continents and feature cutting-edge analysis, engaging panel discussions, and featured keynote speakers.

Stay tuned for more details.

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Our global life sciences and health care capabilities

Navigating complexities in the life sciences and health care industries is no easy task. Successfully competing in the space requires increasingly creative strategies and integrated solutions that protect and support your business day in and day out.

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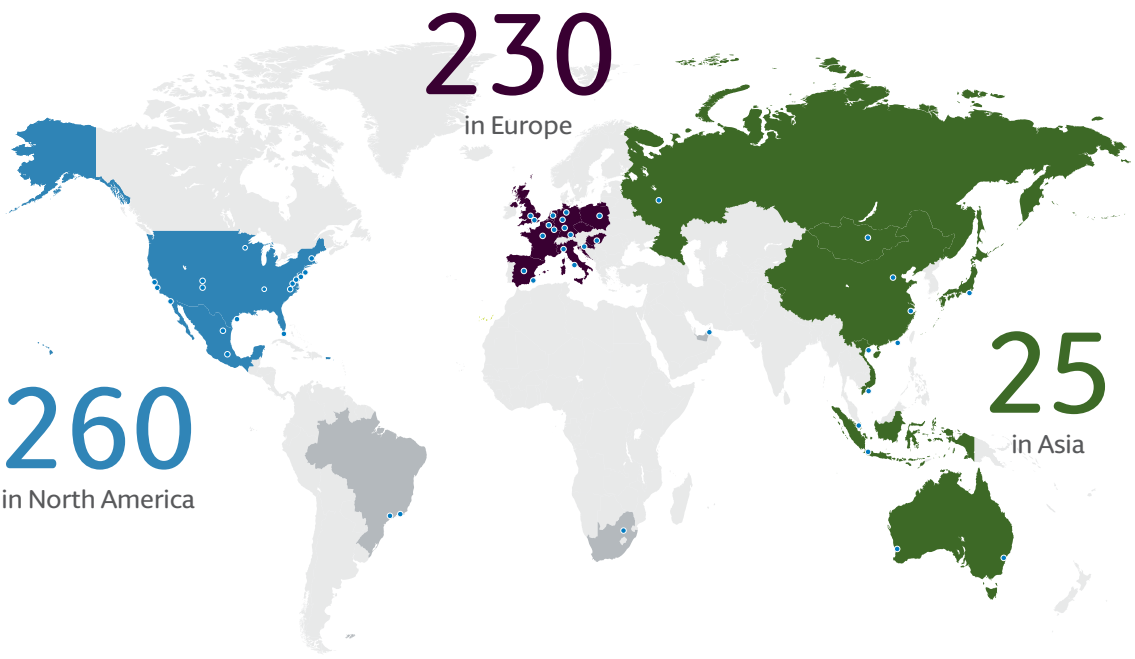

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