LIFE SCIENCES COLLEGE

What to Know: Key Takeaways From the 2021 Sidley Life Sciences College

Senior members of the European Commission, life sciences industry leaders, and Sidley lawyers gathered for the 2021 virtual Life Sciences College—Sidley's annual legal life sciences conference—to discuss the emergent regulations, trends, and tensions that are shaping the industry. Here, we recap the crucial takeaways from this year's summit.

EU Regulatory General Update

- **Pharmaceutical Strategy:** The Commission's Pharmaceutical Strategy is the most comprehensive legislative and policy exercise undertaken to date, covering the full life cycle of medicinal products, from R&D to health technology assessment and procurement.
- **Taking action:** In the context of that exercise, the Commission is working on 55 separate actions, including incentives to address unmet needs, accessibility, and affordability. Several of these would establish new powers at the EU level.
- **Pandemic response:** In response to the COVID-19 crisis, the Commission is working on setting up a Health Emergency Preparedness and Response Authority, expanding the mandate of the European Medicines Agency to include monitoring and mitigating shortages of medicines and medical devices, and coordinating studies and clinical trials, as well as granting new powers to the European Centre for Disease Prevention and Control.
- **Establishing a framework:** Since the Pharmaceutical Strategy relies to a large extent on the pharmaceutical industry to develop new and improved treatments, a predictable framework enabling companies to incur the risks and costs of product development will be of great importance.

Orphan and Paediatric Regulations

- **Inception Impact Assessment:** The European Commission published an Inception Impact Assessment that identifies the key problems that it needs to address during its review of the orphan and paediatric legislation. This includes targeting insufficient development in areas of greatest unmet medical needs for patients and the issue of availability and accessibility of orphan and paediatric medicines across different Member States. The Inception Impact Assessment puts forward a number of potential options to change the available incentives, obligations, and rewards in order to tackle these problems.
- **Industry concerns:** Disruption to the existing framework of incentives and rewards could undermine progress made so far in stimulating innovation for medicines development in Europe and may lead to greater industry uncertainty. The scope and definitions for important terms such as "unmet need" need to be carefully considered.
- **Regulatory review:** The interaction between the regulations and areas of national competence (such as pricing and reimbursement) will need to be carefully reviewed, as will the practicalities of any new obligations, including potential requirements to place medicines on the market in most or all Member States.
- **Future outlook:** Some further light was also thrown on the possible use of novel incentives, such as transferable vouchers, and how certainty for regulatory incentives may be achieved through reaching certain milestones. All options for amendments of the orphan and paediatric regulations remain on the table, and these will continue to be shaped by further consultation and more detailed analysis as part of the full impact assessment.

Fair Pricing

- **A "fair" price:** What is, or what should be, a fair price for medicinal products remains a hotly discussed topic. Stakeholders—at both the European and international level—are heavily involved in the discussion.

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- **World Health Organization (WHO):** While WHO guidelines and resolutions are not legally binding, they increasingly serve as a blueprint for national regulations on pricing. As the WHO continues to work on the fair pricing of medicines, vaccines, and health technologies, national regulations on pricing will likely also gain momentum.
- **Cost-plus pricing:** Stakeholders across Europe, including national pricing and reimbursement authorities, are calling for pharmaceutical pricing to use "cost-plus" pricing. Competition authorities use "cost-plus" as a benchmark to assess price increases for several older (off-patent) medicinal products.
- **Innovative products:** Now there is a broader call to assess prices of innovative products, including orphan medicinal products, based on "cost-plus." This shift raises a number of concerns (i) because a "cost-plus" analysis does not adequately factor in the probabilities of success or risks of failure that companies are facing when developing innovative products; and (ii) because it is accompanied by discussions in the context of the European Commission's Pharmaceutical Strategy about a possible reduction of existing product development incentives. These concerns are further exacerbated by the fact that prices of authorised medicinal products are increasingly compared to those of unauthorised products. It remains to be seen how those discussions will evolve over the months to come.

International Reference Pricing (IRP)

- **IRP status:** While the approach of IRP sounds simple, its practical application is not straightforward. Significant diversity exists regarding the timing of price evaluations, the choice of the "list" price to use, which countries to include, the comparison of different pack sizes, exchange rate issues, and the treatment of confidential discounts. The assumption underlying IRP—namely that some countries will determine the right "value for money"—and its impact on patient access is problematic.
- **Future of IRP:** There is increasing pressure for reference pricing to use net prices and be adopted globally. The rules will continue to evolve. The requirement to disclose net prices paid is increasingly discussed, as is a potential shift from "value-based" pricing to "cost-plus" pricing.
- **Competition law:** As IRP systems evolve, local price-setting decisions will have greater effect in other countries and potentially across the globe. This raises the question how agreements on price-setting and governance (in joint ventures, commercialisation licenses, and distribution agreements) will be assessed under competition rules predating these developments.
- **IRP impact on distribution agreements:** Significant regulatory price reductions in one market (e.g., based on the entry of an aggressively priced generic) may make it uneconomical to continue distributing a drug in that market and risk a significant impact on the prices in other markets. Without a specific contract provision that allows a drug to be taken out of reimbursement or the distribution contract to be terminated, a reliance on economic hardship or a floor price clause faces significant hurdles. A floor price clause may only offer some protection if it contains the option to terminate the contract and if the trigger price takes into account the effect on other markets. Even if a contractual termination right exists, ethical, regulatory, or antitrust duties may complicate withdrawals from a market or its reimbursement system.

Real World Evidence (RWE)

- **RWE framework:** RWE is intended to make payers confident in their decision-making and close data gaps. It does not replace randomised clinical trial data but rather complements it. Good quality data is key to enabling a health technology assessment (HTA) that incorporates RWE.
- **Industry alignment:** There is increasing regulatory and HTA alignment on RWE collection and utilisation. The National Institute for Health and Care Excellence, especially with its new Innovative Licensing and Access Pathway, is seeking to align with the Medicines and Healthcare products Regulatory Agency as much as possible.

- **Federated data sets:** A number of initiatives at the European and international level are aimed at creating federated data sets to achieve better coherence and international collaboration in the space of real-world data sharing.
- **Digital health:** Authorities are now embracing the promise of digital health tools—such as apps and wearables—in generating RWE. European-level incentives such as DARWIN and the European Health Data Space will facilitate the proper technical infrastructure and interoperability of data.

Artificial Intelligence (AI)

- **Commission proposal:** The European Commission is scheduled to publish a draft proposal on artificial intelligence in the coming months. It will cover various aspects of AI that are relevant to—and will supplement—sector-specific legislation.
- **Current medical devices framework adequate with supplements:** Medical Device Regulation (MDR) and In Vitro Diagnostic Regulation (IVDR) are adequate to cover AI and other new technologies. However, further guidance, such as the Medical Devices Coordination Group's guidelines on "Artificial Intelligence under MDR/IVDR framework," whose publication date is unknown, will be needed. The guidance may lend inspiration from the FDA's approach to AI in the healthcare sector.
- **Key hurdle:** With an adequate regulatory framework, the key hurdle is access to reimbursement for these new technologies. Data shows that healthcare systems can save significant sums by utilizing AI.

Schrems II

- **Schrems II:** While awaiting final guidance on Schrems II from the European Data Protection Board (EDPB), in parallel, companies are working through the EDPB's six-step roadmap with a primary focus on transfers previously addressed by Privacy Shield and steps three and four (i.e., assessing third-country laws and supplementary measures).
- **Supplementary measures:** When considering the supplementary measures in the EDPB's step four, it is important to consider the position both internally and externally—vendors are already starting to indicate some of the supplementary measures they are considering.
- **International data transfers:** When designing the Schrems II project, make sure to adopt a forward-facing approach to address the EDPB's requirement for reviews and have a compliant process in place to address new international data transfers.

Post-Brexit: The New Regulatory Legal Framework

- **Northern Ireland Protocol:** A big industry challenge is the Northern Ireland Protocol and adapting it to comply with two regulatory regimes in one country. To address these concerns, the UK government is engaging with the European Commission on the operation of the protocol. Additionally, British Cabinet Office minister Michael Gove wrote to the European Commission to request a 12-month extension for the phased implementation of medicines regulation in Northern Ireland, which will provide companies with additional time to prepare for the new arrangements, including complying with batch testing and Falsified Medicines Directive requirements.
- **Marketing authorisations:** Another challenge is understanding how marketing authorisations that have been approved under mutual recognition and decentralised procedures will be dealt with in the UK—since there seems to be a difference in opinion between the UK and the EU.
- **National licensing procedures:** The pharma industry is particularly excited about the new national licensing procedures in the UK (e.g., rolling review being available more widely, when it was previously restricted to public health emergencies, and the 150-day accelerated assessment procedure, which will speed up the access of a wider range of products to the market). The UK's participation in Project Orbis and the Access Consortium also helps to achieve more alignment and convergence in the requirements and thinking between the different jurisdictions.

- **IP regulatory rights:** The EU may reduce the IP regulatory rights protections afforded to pharmaceutical products as the UK continues to maintain a high level of IP protection for innovative products (including IP regulatory rights, such as regulatory data protection or orphan exclusivity).
- **Confidentiality:** The UK is not planning to change the confidentiality protecting the pricing negotiations between the authorities and the pharma companies.

Sanctions and Export Controls

- **Manufacturing and distribution:** The country of origin of certain products, raw materials, or APIs can trigger the application of limitations further down the supply chain and restrict the ability of companies to offer their products to certain parties or in certain countries. Companies need to closely monitor distribution channels in certain regions to ensure that onward sales of their products comply with sanctions and export control laws.
- **Nationality issues:** It can be challenging for companies to find financial institutions willing to process payments for transactions involving countries targeted by sanctions. In their own organizations, companies need to pay attention to the nationalities of their employees (especially, for dual nationals). Nationality might have broad jurisdictional implications for companies on the ability of some nationals (e.g., U.S., EU, or UK) to hold positions in regions close to or covering sanctioned markets.
- **Business activities:** Acquisitions of new companies should also be reviewed for sanctions and export control risks to mitigate risks of historical liability for the acquirer in case of previous violations. There might be other adverse effects, e.g., on the value of the new company due to loss of future revenue streams in case certain businesses need to be wound down post-closing.
- **Compliance program development:** To mitigate sanctions and export control risks, life sciences companies are developing compliance programs: stand-alone or integrated with broader compliance programs or codes of conduct. Those sanctions and export control compliance programs generally cover a number of issues, such as due diligence and screening of third parties, export classification of items, specific contractual clauses to address sanctions and export control risks with different third parties, identification of dual nationals in the company, anti-boycott provisions, training of employees and management, etc.

Compliance

- **Whistleblower directive:** The long-awaited EU Directive on the protection of whistleblowers (Directive) introduces minimum EU-wide standards for the protection of whistleblowers against retaliation, including the requirement that companies put in place safe reporting channels. A wide range of breaches or abuses of EU law are covered under the Directive, e.g., breaches in the area of public procurement, financial services, public health, consumer protection, privacy, data protection and IT security, and EU competition law. If whistleblowers acquire information of such breaches in their work-related context, they have the option to make a report internally (through the company's internal reporting channels), or externally (to the public authorities). Only in limited circumstances can the whistleblowers report to the wider public (e.g., the media) and still maintain legal protection.
- **Protection for whistleblowers:** The Directive seeks to provide protection to a wide range of reporters, going beyond the traditional employee-employer relationship and covering, amongst others, former employees, self-employed personnel, trainees, and management, among others. Under the Directive, whistleblowers are provided protection against punishments of retaliation, in all its possible forms, for making a report. For whistleblowers to qualify for such protection, they need to have reasonable grounds to believe that the information reported is true at the time of reporting and falls within the scope of the Directive.

- **Obligations for companies:** Companies with more than 50 workers have the obligation to set up confidential internal channels for reporting and provide clear and easily accessible information on procedures for reporting. When a report is received, they must follow up and give feedback to the whistleblower within a reasonable time frame. Companies with more than 250 employees will have to comply with these obligations by 17 December 2021—the deadline for EU Member States to implement the Directive into national law. This deadline may be extended by Member States until 17 December 2023 for companies with 50 to 249 employees.

Data Integrity

- **Enforcement trend:** The enforcement of data integrity at life sciences companies has spiked during the last several years. Governments worldwide demand accurate information to ensure product quality, safety, and efficacy. Unfortunately, both regulators and prosecutors continue to identify numerous instances of deliberate information fraud, missing data, or suspect paperwork.
- **Government action:** Invalid or non-credible data points are often interpreted as a signal that the entire operation could be vulnerable—and the government has responded accordingly. In the United States, for example, breaches in data integrity expose a company not just to FDA Warning Letters and import alerts but also to Department of Justice criminal investigations, congressional scrutiny, and whistleblower litigation.

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