Morgan Lewis

LIFE SCIENCES
INTERNATIONAL REVIEW

Welcome to the Q3 2018 issue of our *Life Sciences International Review*.

This issue covers life sciences developments within Europe, Asia, and the United States in the areas of intellectual property, regulatory, pricing and reimbursement, international trade, litigation, and competition, and provides the latest on the ongoing Brexit saga.

Major news this quarter includes a recent Court of Justice ruling that gives guidance on the Specific Mechanism for the parallel import of medicinal products, EU guidance on adapting existing good clinical practice to advanced therapy medicinal products, MedTech Europe's concerns about the implementation of the new Medical Devices Regulation and In Vitro Diagnostic Medical Devices Regulation, the US Food and Drug Administration's recently unveiled Biosimilars Action Plan, and much more.

Many of the topics covered in this issue are ongoing. The *Life Sciences International Review* team continues to monitor developments and will include updates in future issues to keep our readers up to date with the latest events and trends in the life sciences industry.

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INTELLECTUAL PROPERTY

Parallel Trade, Specific Mechanism, and SPCs

A number of the late EU accession member states did not then permit patenting of pharmaceutical products. Under normal EU rules, manufacturers could not prevent parallel import from a new accession state to other member states. The 'Specific Mechanism' addresses this; pharmaceutical product patents and supplementary protection certificates (SPCs) (see further below) can be used to prevent parallel imports from a new accession state if (1) they were filed when the accession state did not permit that sort of protection, and (2) the person intending to import or market the product has given one month's prior notice to the holder or beneficiary of the patent or SPC.

The Court of Justice has recently given some guidance on the interpretation of the Specific Mechanism ruling, namely, that where patents were not available for the medicine in the 'new' accession countries at the time of filing the patent in 'old' EU countries, but SPC regulations had been introduced in such new accession countries at the time SPCs were sought in the old countries, then an innovator possessing a patent and SPC in the old countries can rely on the Specific Mechanism to object to the parallel importation of a drug from those new countries. The guidance also confirms that paediatric extensions are covered under the Specific Mechanism, as they are extensions to the duration of protection offered by SPCs. See the decision **here**.

SPCs and Combination Products

The Court of Justice of the European Union (CJEU) recently decided the question on the position of combination products under Regulation (EC) No 469/2009 (SPC Regulation). The SPC Regulation provides medicines an additional term of patent protection (on top of the standard 20 years) to compensate in part for the development time between patent application and marketing. The case in question concerned invalidity proceedings against the SPC for Truvada, a treatment for HIV which contains two active ingredients. The CJEU concluded that a combination product is eligible for an SPC if the claims in the underlying patent relate necessarily and specifically to that combination of active ingredients (even if the combination of active ingredients is not expressly mentioned in the claims of the basic patent). See the decision **here**.

Manufacturing Waiver for SPCs

The European Commission has announced outline proposals to introduce a manufacturing waiver for SPCs. Under the proposal, generic drug companies would be able to manufacture new products for non-EU markets whilst SPCs are in force. The Commission's intention is to help Europe's pharmaceutical companies tap into fast-growing global markets and foster jobs, growth, and investments in the EU. However, companies would have to disclose to competent authorities the intended manufacturing operations, notify the supply chain that the drugs are only for export outside of the EU, and label the products as intended only for export to third countries. There also would be a restriction on stockpiling medicines pre-SPC expiry, with a view to supplying markets once the SPC has expired. See the proposal **here**.

Blockbuster Biologics Review

Blockbuster Biologics Review, produced by our intellectual property lawyers, covers developments in inter partes review (IPR) and patent litigation challenges implicating blockbuster biologic drugs. These quarterly reports provide updates on the following topics:

- Current status of IPR challenges
- Institution and invalidation rates for IPRs challenging blockbuster biologics
- Current status of blockbuster biologic-related patent litigations

Read the current issue **here**.

Patent Ruling by US Court of Appeals

The US Court of Appeals for the Federal Circuit upheld a district court ruling that four patents owned by Acorda Therapeutics are invalid for being obvious in view of certain prior art publications. The four patents are Orange Book listed patents for Ampyra, a drug commercialized by Acorda and approved by the US Food and Drug Administration (FDA) for the treatment of multiple sclerosis. In a 2-1 split decision, the Federal Circuit judges affirmed a ruling from the US District Court for the District of Delaware that the patented methods directed to improving the walking ability of multiple sclerosis patients were obvious to the skilled person in view of multiple prior art publications on this subject matter.

Acorda accused Roxane Laboratories and a generic drug company of infringement of five Orange Book listed patents associated with the filing of an abbreviated new drug application (ANDA) seeking FDA approval of a generic version of Ampyra. The district court found that four of the five patents were invalid. A fifth patent, licensed to Acorda from Elan Corp., was found valid and infringed by the district court, and an injunction was issued barring commercialization of a generic version of Ampyra until expiration of the licensed patent on 30 July 2018. The four patents found invalid did not expire until 2027. This ruling will now make it possible for commercialization of a generic version of Ampyra.

The claims at issue in these patents were directed to a method of increasing walking speed in a human multiple sclerosis patient through the twice-daily oral administration

of a sustained release composition of 10 milligrams of 4-aminopyridine (the active ingredient in Ampyra). The cited prior art publications used as the basis of the obviousness analysis a statistically significant improvement in timed gait for multiple sclerosis patients given 17.5 mg 4-aminopyridine twice daily versus a placebo, and also a statistically significant improvement in walking speed for multiple sclerosis patients given 10–40 mg of 4-aminopyridine twice daily versus a placebo. The Federal Circuit found that the district court did not clearly err in finding that a person of skill would have looked to the cited prior art publications, considered their limits, and had a reasonable expectation of success as to the efficacy of 10–20 mg 4-aminopyridine twice daily to improve walking.

The patents-at-issue are US Patent Nos. 8007826, 8354437, 8440703, and 8663685. The case is Acorda Therapeutics Inc. et al. v. Roxane Laboratories Inc. et al., case numbers 17-2078 and 17-2134, in the US Court of Appeals for the Federal Circuit.

See the ruling **here**.

BREXIT

UK Government White Paper

The UK government has published its white paper, 'The future relationship between the United Kingdom and the European Union', which sets out the proposed post-Brexit relationship with the EU and is part of the UK's effort to reach a deal with the EU. The paper marks a shift in the government's public position towards a 'softer Brexit', including seeking an 'association agreement' with the EU (a model most closely associated with countries seeking to join the EU, e.g., Ukraine), a 'common rulebook' for goods but provision for services, and the possibility of a preferential immigration deal for EU citizens.

With specific reference to healthcare and life sciences, the UK would participate in the European Medicines Agency (EMA)—including acting as a 'lead authority' on the assessment of medicines—but accepts that it would not have voting powers. In addition, the white paper states that good practices and batch release procedures would effectively continue as they do at present. Further, there would be mutual recognition of professional qualifications.

It is fair to say that the white paper has few friends in the 'leave' or 'remain' camps, and the EU has already expressed concern that the white paper amounts to 'cherry picking' even before any announcement as to the progress of negotiations. A recent summit has officially rejected the paper in its present form, but the Commission has suggested that it may still be the basis for future discussion. The October deadline for the conclusion of negotiations is almost certain to slip. The white paper is available **here**.

'No Deal' UK Unilateral Acceptance of EU Pharma Testing

The UK government confirmed in one of a series of technical notices on the ramifications of a 'no deal' Brexit that European pharmaceutical companies will be able to supply their medicines, including investigational medicines, in the UK on the basis of approved batch testing carried out in the EU for at least two years from 29 March 2019 (the scheduled date of Brexit). See the technical notices **here**.

This contrasts with the EU's continuing insistence that UK companies, in the event of a no-deal Brexit, would not be able to sell medicines to the EU based on UK testing. In an updated June 2018 Q&A document, the European Commission and EMA have indicated that, in a no-deal scenario, UK-based pharmaceutical companies will not be able to rely on marketing authorisations issued by the Medicines and Healthcare Products Regulatory Agency to sell products across the EU after Brexit. This would mean that the UK would become a third country as of 30 March 2019, and companies whose batch release activities are in the UK would need to move those activities to another EU member state after this date in order to supply to the EU.

The EMA/Commission paper indicates a list of issues the EMA considers that those working in relation to human medicinal products should take into account. These include establishment of marketing authorisation holders, choice of reference products for abridged applications, and pharmacovigilance. See the EMA/Commission Q&A paper **here**.

The UK secretary of state for Brexit said he hoped that the EU might change its mind and reciprocate, stating, "Given that we start from a position of common rules, we would also hope and I think expect, in good faith between close partners, that the EU would recognise medicines from this country with our regulatory approval. But in a no deal scenario, we can't guarantee it".

A recent vote in the House of Commons on the Trade Bill makes it the UK government's negotiating objective to secure an agreement with the EU that allows the UK to continue to participate in the EMA.

UK and the Unified Patent Court

The Unified Patent Court (UPC) will have exclusive competence over European patents and European patents which have not been opted out of the new system. The UPC project currently only allows participation by EU member states. The UK government, having ratified the UPC agreement in April, has confirmed that it will seek to ensure the country's continued participation in the UPC after its EU membership ends, with options being explored by the UK government as part of the broader Brexit negotiations. The fate of London's pharmaceuticals and life sciences section of the Unified Patent Court will also form part of the Brexit negotiation. Read the government's white paper (especially page 47) **here**.

EMA Move and Data Transparency

As a consequence of Brexit, the EMA is moving from London to Amsterdam. The EMA hosting agreement between the Netherlands and the EMA was finalised in June, and the EMA has implemented a business continuity plan (BCP).

Despite earlier optimism as to the number of resignations and Amsterdam's readiness, the EMA warns that 'some areas have been temporarily reprioritised, suspended or postponed to resource Brexit preparedness activities and safeguard core activities'. A notable consequence is a reduction in the operation of EMA's proactive publication of clinical data. The EMA announced in August 2018 that, as part of its Brexit BCP, it is temporarily suspending the publication of clinical data submitted to it as part of marketing authorisation applications. Data packages submitted before the end of July 2018 will be processed and formalised, but no new procedures will be initiated. The EMA also has advised that it is no longer in a position to process 'access to documents' requests issued outside the EU. See the update **here**.

PRICING AND REIMBURSEMENT

Strengthened EU Cooperation on HTA Is Agreed by Stakeholders

Support for EU cooperation on Health Technology Assessment (HTA) was shown in discussions between more than 300 policymakers, healthcare providers, patient representatives, and other experts. The stakeholders agreed in their discussions that HTA should have the chance to become more structured, sustainable, and efficient, and emphasised three key topics. See the Commission press release **here**.

EU Member State Pharmaceutical Policy Cooperation

In June, Ireland became the latest country to join the BeNeLuxA initiative on pharmaceutical policy for sustainable access to and appropriate use of medicines. BeNeLuxA, as the name suggests, was originally formed by the Netherlands and Belgium in 2015, and joined subsequently by Luxembourg and Austria.

The focus of the cooperation is threefold:

1. Sharing information on medicine policies
2. Performing joint HTA procedures
3. Sharing information and experiences on the reimbursement of specific medicines

Membership in the initiative is open to EU member states and other interested countries. See further information **here**.

REGULATORY

ATMPs

The EU has recently developed the draft guidelines intended to adapt existing good clinical practice (GCP) specifically to advanced therapy medicinal products (ATMPs) envisaged in Regulation 1394/2007 on ATMP.

The document considers how standard GCP rules would apply to clinical trials conducted in relation to an investigational ATMP. It complements the existing ICH GCP Guidelines and guidelines on good manufacturing practice specific to ATMPs.

Stakeholders may comment on the consultation by 31 October 2018. See the consultation **here**.

In addition, as part of the ongoing cooperation between the European Commission/EMA and FDA, the agencies agreed to work together to develop common scientific approaches on the regulation of ATMP medicines, particularly in relation to their preclinical and clinical development and optimising the collection and use of data. See further information **here**.

Orphans

In June, the EMA launched 'IRIS', an online portal for orphan designation applications to the Committee for Orphan Medicinal Products. The portal allows applicants to submit and manage information and documents related to applications and post-designation activities, and to check application status.

Use of IRIS is now obligatory for applicants. EMA has developed guidance documents on the use of the new system. See further information **here**.

MedTech Regulation

In a July 2018 position paper by MedTech Europe, the medical technology industry European trade association expressed 'significant concerns' about the state of implementation of the new Medical Devices Regulation (MDR) and In Vitro Diagnostic Medical Devices Regulation (IVDR), and the risk of products not being re-certified before the date of application of the regulations. The MDR and IVDR are due to take effect on 26 May 2020 and 26 May 2022, respectively.

MedTech Europe called for an extension of the transition period under the MDR and the IVDR, citing specific concerns, including the slow progress in designating Notified Bodies, which needs to occur before they can assess and certify or re-certify compliance with the new regulations; the Notified Bodies' capacity to perform these obligations; publication of only a few of the obligatory implementing acts; delays around several aspects of the review process; the need to have the Eudamed database in place; and the possible impact of Brexit given that up to 40% of CE markings are granted by UK Notified Bodies. See the press release **here**.

Clinical Trial Data Transparency

In July 2018, the EMA published a report on the first year of Policy 0070, its clinical data publication policy affording open access to clinical data submitted by pharmaceutical companies in support of marketing authorisation applications through the Clinical Data Publication (CDP) website.

The EMA reports that 54 procedures were published in the first year—representing a 100% compliance rate. Of these, 19 involved commercially confidential information (CCI) redactions by the EMA; 1.46% of the published documents contained CCI and only 0.01% of the total pages published included redactions. The EMA further reports that CCI redactions largely related to details on product composition, detailed information on analytics assays or methods, and future development plans. See further information **here**.

Cannabis Approval

The UK has approved the legalization of medical cannabis, which will allow medical cannabis to be made available to children and adults with a prescription. Over 30 countries have legalized medical cannabis, including a number of European countries. See the UK government press release **here**.

Anti-gift Laws in France

In addition to the better-known 2011 French Sunshine Act laws, there are 'anti-gift' provisions dating from 1993 which impose strict conditions under which companies active in the health sector are allowed to grant advantages, in cash or in kind, to healthcare professionals (HCPs), with such advantages being prohibited in most cases.

These 'anti-gift' provisions were amended last year and entered into force on 1 July, although certain implementing texts are yet to be published. The new provisions extend the prohibition to include unreimbursed medicines for prohibition to receive advantages to all HCPs. The new provisions also refine exemptions and the HCP submission and approval processes, and increase criminal sanctions for infringement. See further information **here**.

Orphan Diseases in China

In May, five key Chinese governmental authorities, including the State Drug Administration (SDA) and the National Health Commission, issued an initial list of 121 rare indications—the first time China has recognized rare diseases on a national level. The proposals include allowing foreign clinical data in new drug applications (if the sponsor can show that no racial differences exist) in order to shorten the timeline and streamline the process for the approval of new orphan drugs, including imported drugs to encourage more Western orphan drug developers to bring new drugs into the country.

Under the Technical Guidance, with respect to NDAs for rare diseases, even though the clinical trial data obtained overseas is considered partially acceptable due to concerns of potential racial differences, SDA may still accept such clinical trial data with conditions, and require the registration applicant to collect supplementary data regarding safety and efficacy of such drugs after market authorization.

Read the full LawFlash **here**.

China National Drug Administration Sets Guidelines for Overseas Drug Trial Data

In an effort to increase the availability of pharmaceutical treatments in China, the China National Drug Administration (CNDA) recently released guidelines to allow pharmaceutical drugs that have already undergone clinical trials in other countries to enter the Chinese market without undergoing domestic clinical trials, subject to certain requirements regarding trial data.

On 10 July, the CNDA published its Technical Guidelines for the Acceptance of Overseas Clinical Trial Data for Drugs. This followed the 10 January release of the CNDA's similar guidelines regarding the acceptance of such data for the registration of medical devices.

Together, these guidelines open the door for the registration in China of pharmaceutical drugs and medical devices that have already undergone clinical trials in other countries but previously could not be sold on the Chinese market without undergoing domestic clinical trials, allowing faster access to the Chinese market with much lower costs for pharmaceutical companies and medical device manufacturers.

Read the full LawFlash **here**.

US Biosimilars

On 11 May 2018, US President Donald Trump issued his blueprint to lower drug prices, which describes the administration's plan to reduce the price of prescription drugs by, among other actions, 'advancing biosimilars and generics to boost price competition.' To help achieve the administration's goals, the FDA recently unveiled its Biosimilars Action Plan (BAP).

Noting the 'anemic' competition for biosimilars, with only three biosimilars currently marketed in the United States being FDA approved at the time of the BAP release, FDA Commissioner Scott Gottlieb stated that the BAP would help the FDA achieve the goals of making the process for developing biosimilars more efficient and promoting competition and affordability across the market for biologics and biosimilar products.

Read the full article Morgan Lewis article **here**.

FDA: Probiotic Products Can Use CFUs on Supplement Facts Panel

In a draft guidance document, the FDA stated that in certain cases, it will allow probiotic products to use colony-forming units (CFUs) to quantify live microbial ingredients on the Supplement Facts panel, noting that this measurement tool is useful to consumers.

The FDA's draft guidance document states its intention to exercise enforcement discretion for certain probiotic products that declare the quantitative amount of live microbial ingredients on the Supplement Facts panel in terms of CFUs. The agency states that CFUs provide a useful description of the quantity of live microbial dietary ingredients, and use of that measurement on the Supplement Facts panel will help consumers identify the amount of living microorganisms in each product and make comparisons across dietary supplement products. Accordingly, while FDA considers whether to conduct rulemaking to formally change the unit of measure, it will allow the use of CFUs in certain cases.

Read the full LawFlash **here**.

INTERNATIONAL TRADE

Medical Device Exports to Iran After Resumption of Sanctions

After the decision to terminate US participation in the Joint Comprehensive Plan of Action (JCPOA), most EAR99 medical devices remain covered by general licenses for export or re-export to Iran, but medical device companies will need to identify financial institutions able to handle export-related transactions.

US sanctions against Iran prior to implementation of the JCPOA in January 2016 included secondary sanctions that subjected foreign parties to potential liability for transactions involving Iran, but, thanks to fairly broad general licenses and related exclusions, the sanctions exempted a large number of medical devices from the sanctions' purview. For humanitarian reasons, US and non-US companies were able to export a number of medical devices to Iran and engage in the associated dealings necessary to conduct that business. The general licenses and accompanying detailed guidance prior to the JCPOA identified many of the medical devices that could be exported to Iran, and the conditions for those exports.

The sanctions relief in the JCPOA did not initially address medical devices, but in a significant move in late 2016 and early 2017, the US Treasury Department's Office of Foreign Assets Control (OFAC) effectively relaxed the restrictions on exporting medical devices to Iran. OFAC's action allowed US and non-US companies to export to Iran all medical devices properly classified as EAR99 products under the US Commerce Department's Commerce Control List, except those identified on the List of Medical Devices Requiring Specific Authorization. This action opened the door to exports to Iran of many more medical devices than previously had been authorized, without the need for a specific license from OFAC.

Read the full LawFlash **here**.

Impending US Tariffs on China to Impact Manufacturers

Newly approved tariffs would impose 10% to eventual 25% tariffs on hundreds of chemical ingredients imported from China used for many US Food and Drug Administration–regulated products, including dietary supplements, over-the-counter drugs, and cosmetics.

US President Donald Trump announced on September 17 that additional tariffs on a total of approximately $200 billion of Chinese products will be imposed beginning as soon as September 24. These additional tariffs could go into effect either as a whole or in tranches over time, as with the initial $50 billion of tariffs imposed earlier this year. The tariffs initially will be imposed at the 10% level, but will later be increased to 25% by the end of 2018. The additional tariffs include hundreds of chemical ingredients that are used in dietary supplements, cosmetics, and OTC drug products. President Trump has also indicated that tariffs on as much as another $267 billion of Chinese products could be imposed in the future.

Read the full LawFlash **here**.

LITIGATION

Shanghai Regulator: Speaking Fees to Physicians Constitute Bribery

A local regulator in Shanghai has recently fined a domestic medical device company for commercial bribery after determining that the company had unduly influenced a group of seven physicians when it paid them speaking fees to give presentations at an industry conference featuring materials prepared by the company, including specific endorsements of the company's products.

Read the full LawFlash **here**.

COMPETITION

China Announces Crackdown Campaign Against Unfair Competition Activities

China's State Administration for Market Regulation recently announced an enforcement sweep to promote the

implementation of its amended Anti-Unfair Competition Law. The crackdown campaign, which began in May and will continue through October 2018, focuses on market confusion acts, trade secret infringement, commercial bribery, and internet-related misconduct. Key areas in the spotlight include online transactions and the pharmaceutical and education industries.

Read the full LawFlash **here**.

MORGAN LEWIS NEWS

Morgan Lewis Boosts US Disputes Capabilities with 7-Partner Life Sciences, Tech IP Team

Morgan Lewis has welcomed a seven-partner intellectual property litigation team that enhances the firm's trial and appellate capabilities, particularly in the life sciences and technology industries.

See the announcement **here**.

FDA Focus: What Morgan Lewis's Practice Chair Is Watching, *Law360*

Morgan Lewis partner Kathleen Sanzo is featured in a special *Law360* series interviewing FDA legal leaders on their practices and what they are watching for their clients. Kathleen tells the publication she is closely following food safety challenges in the global supply chain, changes in the manufacturing of drugs, and the FDA's approach to the regulation of in vitro diagnostics.

Read the *Law360* article **here**.

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