Morgan Lewis

EUROPEAN LIFE SCIENCES REVIEW

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Welcome to the sixth issue of our EU Life Sciences Review, which covers some of the most critical developments in the pharmaceutical and medical technology sectors in the last quarter and is produced by our life sciences lawyers in London, Frankfurt, Paris and Moscow. If you have any questions on any of these issues, please contact Paul Ranson.

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MORGAN LEWIS – UPDATE

Brexit

On 23 June 2016, the United Kingdom voted in favour of leaving the European Union (EU) 52%-48%.

On 24 January 2017, the UK Supreme Court ruled that the UK government cannot trigger Article 50 of the Treaty on European Union to begin the UK's withdrawal from the EU without the agreement of both Houses of Parliament, although it does not need to consult the devolved administrations of Scotland, Northern Ireland, and Wales. Once Article 50 is triggered, a member state has two years in which to conclude negotiations and exit the EU. See the judgment here.

There was, however, little appetite within the House of Commons to go against the 'will of the people' and the third reading was passed by a large majority on 8 February. The Bill then went to the House of Lords which passed two amendments including one which demanded that Parliament be given a 'meaningful vote' on the final Brexit deal before Britain's withdrawal from the EU. These amendments were rejected by the House of Commons meaning that Prime Minister Theresa May will now be able to trigger Article 50 before her end-of-March target.

In its 2 February 'White Paper', the Government sets out 12 'negotiating objectives' for the Brexit process and its future partnership with the EU. The paper seeks 'the most free and frictionless trade in goods and services that is possible' without membership of the EU's single market. See the White Paper here.

As far as the life sciences sector is concerned, concerted lobbying as to its special features including the EU regulatory regime seems to have paid off to a degree. A 'Green Paper' seeking views on the development of the UK's industrial strategy as the UK prepares to leave the EU (closing 17 April 2017) was published on 23 January and whilst not actually citing 'winners' and 'losers' which the Government would either prioritise or not during the negotiation phase, life sciences, along with the aeronautic, automotive and financial services sectors, was trumpeted as a clear success story. See the Green Paper here. Some commentators noted the absence of major takeover reform. Presumably attracting inward means that 'UK First' has been trumped by the need to show post-Brexit that the UK is open for business and internationally competitive. A policy proposal on takeovers is still expected but is likely to focus more on infrastructure issues.

Pricing and Reimbursement

Off-label Use of Medicines

On 24 January, the European Commission dismissed two complaints brought in 2015 by EFPIA, EUCOPE and EUROPABIO before the European Commission regarding off-label legislation in Italy and in France. The complaint was to the effect that the legislation promoted off-label use on economic grounds notwithstanding the existence of an authorised alternative treatment. The European Commission ruled that:

- off-label use is not regulated by EU law
- the doctors retain freedom in prescribing
- national reimbursement rules fall outside the EU pharmaceutical regime.

The complaints concerned measures adopted in France and Italy on the use and reimbursement of medicines (notably Avastin) outside the terms of their marketing authorisations (off-label use) and claimed that these measures undermined the EU regulatory system for pharmaceuticals. There was also a concern that these measures were driven by budgetary pressures, an issue which has been considered previously by the European Court in the *Commission v Poland* case (Case C-185/10) found here.

The European Commission has also published a report addressing off-label prescribing in the EU generally, considering benefits and risks of off-label use and the EU and national regulatory frameworks for off-label use as well as the reasons behind off-label prescribing. The report may be found here.

Value Assessment and Funding Processes in Rare Diseases

The European Multi-Stakeholder Group for Value Assessment and Funding Processes in Rare Diseases has completed its Principles on how to improve the consistency of Orphan Medicinal Products and the Pricing and Reimbursement (OMP P&R) assessments in Europe.

The paper addresses the OMP P&R decision-making in respect of rare diseases and formulated 12 Principles in order to improve the consistency of OMP P&R assessment in Europe and ensure that it reflects the specificities of rare diseases and contributes to the sustainability of healthcare systems and further development of this field. The agreed-upon Principles may be found here.

Product Regulation

Orphan Medicines - Notice on Significant Benefit Published

The European Commission recently published its updated Notice on the application of Articles 3, 5, and 7 of Regulation (EC) No 141/2000 on orphan medicinal products which *inter alia* addresses the concept of 'significant benefit'.

Although the Notice is not legally binding, it is helpful for interpretation of the regulation and needs to be followed.

The text of the Notice may be found here.

EU/US GMP Mutual Recognition

Regulators in the European Union and the United States have agreed to recognise inspections of manufacturing sites for human medicines conducted by regulatory authorities from the EU and the FDA in their respective territories on both sides of the Atlantic. Such inspections are intended to ensure that these sites operate in compliance with Good Manufacturing Practice. Under the agreement the respective regulatory authorities can now recognise and reply on each other's inspections of manufacturing sites in their respective territories. The agreement is an annex to the EU-US Mutual Recognition Agreement which, although signed in 1998, has yet to be implemented. Certain provisions of the agreement have entered into force and it is expected that more will enter into force on 1 November 2017. See the agreement here.

Proposed Amendments to the Paediatric Regulation

The European Commission held a consultation process regarding the effectiveness of the Paediatric Regulation (Regulation). When the Regulation was adopted in 2007, two of its main aims were to reduce the level of off-label use and increase the number of medicines specifically developed and tested for children.

In particular, the consultation aims to evaluate the current state of affairs relating *inter alia* to the costs related to paediatric investigation plans (PIPs), the functioning of the reward system, the implementation of the Regulation, waiver/deferrals, the paediatric-use marketing authorisation (PUMA), and clinical trials for children.

See the consultation paper here.

Roadmap for evaluation - EU Blood, Tissues and Cells Legislation

The European Commission has published a roadmap for evaluating EU blood, tissues, and cells legislation, namely Directives 2002/98/EC and 2004/23/EC. The two-year evaluation will concentrate on 'the coherence of the blood and tissues and cells legislation with other relevant Union legislation' but will not cover advanced therapy medicinal products or medical devices. See the roadmap here.

Draft Guidance for the Pharmaceutical Sector in Relation to the Nagoya Protocol

The European Commission published a Guidance concerning the interpretation of Regulation No 511/2014, which relates to the implementation of the Nagoya Protocol on 'Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilisation to the Convention on Biological Diversity' (Nagoya Protocol), which aims to lead to a shared interpretation of the terms 'utilisation' and 'research and development' in relation to the development of pharmaceutical products (including biopharmaceutical and veterinary medicine products).

The Nagoya Protocol was adopted in 2010 and aims to provide a legally binding framework on how researchers and companies can obtain access to the genetic resources of a country and to the knowledge associated with these resources.

See the Guidance here.

EMA Report on Conditional Marketing Authorisations

Conditional marketing authorisations (CMAs) are intended to allow early access of important medicines and are valid for one year. However, only 12 approvals were granted between 2007 and 2013 (when the European Commission conducted a review of CMAs). Although some 30 medicines (including 14 orphans) have now received a CMA, there is continuing evidence that regulators are not applying Conditional Approval rules pragmatically, and potential applicants are not always considering taking such a route.

The report setting out the benefits of CMAs may be found here. A revised guideline on CMAs came into effect in June last year and can be found here.

Public Consultation on EMA's Policy on Access to Documents

One of the major developments in EMA policy has been an increasing willingness to disclose regulatory documents submitted to the EMA by applicants. Currently there is a Regulation (Regulation (EC) No 1049/2001) on disclosure generally by EU organisations and EMA policies on responses to requests and proactive publication. The EMA has recently embarked on a three-month public consultation on access to documents. The new document now covers how the Agency deals reactively with requests for access to EMA documents or data submitted by third parties in line with the Regulation but also refers to the rules concerning proactive disclosure of clinical data according to EMA Policy/0070. In particular, Policy/0043 would be extended to include corporate documents, and it contains an Annex on arrangements for the implementation of Regulation (EC) No 1049/2001, but the broad intent seems to be to consolidate rather than substantially change the current position. The consultation continues until 16 May 2017. See the draft document here.

Medical Devices Regulation (MDR) and In Vitro Diagnostics Regulation (IVDR)

In June 2016 an agreement was reached between the EU Parliament and the European Commission in respect of the texts of MDR and IVDR.

The MDR will impact all device manufacturers and will establish requirements to the parties involved in manufacturing, distributing, and assessing medical devices. It will also regulate the entry of the devices onto the market.

The IVDR will similiarly apply to all parties involved in in vitro diagnostics manufacture, import, and distribution.

The EU Council of Ministers voted to adopt the new EU regulations on 7 March with the regulations due to be finalised in April. Full adoption of these documents is expected by August 2017 with MDR expected to take effect 2020, and the IVDR in 2022.

See the full text of the MDR here and the IVDR here.

Intellectual Property

UPC Planned for December 2017

The Unified Patent Court (UPC) is expected to be operational in December. A provisional timetable has been released by the Preparatory Committee which is now working via a conditional timetable whereby the Provisional Application Phase (PAP) will start at the end of spring 2017, and the agreement on the UPC can enter into force and the UPC become operational in December 2017. The start of the three-month sunrise period during which patent holders can opt out of European patents is now planned for early September 2017. See the press release here.

Morgan Lewis – Update

We recently held a webinar on the comparative EU/US experience and laws on pay-for-delay clauses around patent expiry. Please click here to view the webinar link (click "Playback" to access the recording).

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