Brexit Implications for UK Pharmaceutical Administration

By Pete Gough

With the historic vote by the UK to leave the European Union I have been asked by many of our clients and colleagues “What will the vote to leave the EU (Brexit) mean for pharmaceutical quality management and the role of the Qualified Person (QP)?” So this is my attempt to provide some answers.

The only thing that is certain is that we are facing at least two, and probably more, years of unprecedented uncertainty. So much of the following inevitably contains a high degree of educated guess work. This uncertainty is likely to impact investment decisions by companies, but I am not qualified to speculate on this area and will focus primarily on the possible legal and administrative impacts.

The European Medicines Agency (EMA) will move its headquarters from London to another EU Member State. Discussions are already underway regarding the relocation; the Member States most keen to host the Agency at the moment are Sweden, Denmark and Italy. Only around seven percent of the current EMA management and secretariat come from the UK at the moment, so the activities of the EMA should actually be largely unaffected.

One possibility is that the UK will seek to join Norway, Lichtenstein and Iceland in the European Economic Area (EEA). If this were to be the case, then in practical terms for medicinal products comparatively little would need to change.

If the UK does not elect to join the EEA and chooses to adopt what I will call the “Swiss model” for medicinal products, the UK will then be required to make much more profound changes. This would mean the UK would adopt EU pharmaceutical legislation into UK law so that UK medicines law shadows EU medicines legislation while it remains outside of both the EU and the EEA. This strategy would be less disruptive if a Mutual Recognition Agreement (MRA) or an Agreement on Conformity Assessment and Acceptance (ACAA) is agreed upon with the EU. Historically such agreements usually take much longer than two years to negotiate but given the unique circumstances of a Member State leaving the EU, this may be possible within the two-year exit timeframe.

Pharmaceutical Legislation

Until recently most EU pharmaceutical legislation has been issued as directives, which means that these directives have already been transposed into UK legislation; mostly in The Human Medicines Regulation 2012 (Statutory Instrument 2012-1916). However, this statutory instrument (SI) will almost certainly have to be revised as it has been issued under the authority of the European Communities Act 1972, which will have to be repealed, and contains numerous references to EU directives. The replacement legislation could revert to the Medicines Act 1968, which was the governing legislation in the UK prior to 2012, but hopefully will be substantively unchanged.

So what will UK pharmaceutical legislation look like moving forward outside of the EU? It all depends on the outcome of the negotiations between the UK and the EU. The most logical outcome for medicinal products would be for the UK to adopt the Swiss model. This would require the minimum re-writing of the existing UK legislation and could be applied to future EU changes whether they are issued as directives or regulations.

GMP and Other Regulatory Guidance

The UK Medicines and Healthcare products Regulatory Agency (MHRA) has always had significant input into the development of GMP and other medicinal product guidance. This will undoubtedly continue via organizations such as PIC/S, where the MHRA currently has chairmanship, and probably the International Council...
for Harmonisation (ICH). I would expect the MHRA will become members of the recently re-organized ICH so they can continue to participate in this highly influential forum and continue to provide their valuable contributions to the evolution of GMP and other guidance.

Qualified Persons (QPs)

The role of the QP is already enshrined in UK law by SI 2012-1916 so providing that the UK agrees to mirror EU legislation, as described above, there should be no change in terms of the requirements to become a QP or in the QP’s role in the certification of batches.

Obviously, if the UK is no longer in the EU, UK QPs will no longer be able to accept certification of products by EU QPs and vice versa. This is likely to increase the workload for QPs in the UK and in the EU for product coming from the UK.

If the UK can quickly agree to an MRA or an ACAA with the EU, there will be no need for re-testing when product moves between the UK and the EU. Without an MRA or ACAA, the required re-testing will create a significant barrier to trading medicinal products between the UK and the EU.

QPs who became eligible in another EU Member State and are named on UK Manufacturing Authorizations (MIAs) would be an issue. Hopefully, some sort of grandfather clause might be negotiable but it is possible that they may no longer be eligible. The reverse is also true with UK origin QPs no longer being able to be named on MIAs in the remaining 27 EU states.

Regulatory Inspections

If an MRA or an ACAA is agreed upon prior to the UK exiting the EU, not much will change between the UK and the EU. Without the MRA or ACAA, UK companies would be subject to inspections by EU authorities and the MHRA would be required to inspect in EU member states, which they do not have sufficient inspection resource to do at present.

The UK will need to agree on their own MRAs with the countries who currently have MRAs with the EU. This should be possible but will add to the MHRA’s work in the short term by conducting any assessments needed and additional inspections if there is a lag between the UK leaving the EU and the signing of UK MRAs.

The MHRA could lose its access to the EudraGMDP database and, in that case, their inspection outcomes would no longer be entered.

Another aspect of the split is the large quantity of inspection work subcontracted from the EMA to the MHRA. Presumably this will cease, which will result in a significant reduction in income for the MHRA. This is also likely to cause delays in EMA being able to perform “third-country” inspections.

Marketing Authorizations

(With thanks to Helen Erwood of ESPL Regulatory Consulting)

A lot is unknown but it is likely that the MHRA will have to mutually recognize centralized (EU) authorizations and introduce a process to issue a national MA (much like Norway and Iceland do at present).

If a centralized EU MA is held by a UK company the MA holder will need to have a legal entity within the EU/EEA.

For decentralized and mutual recognition procedures, companies will probably begin moving away from the UK quite quickly. For existing marketing authorizations linked to an EU procedure, where the UK is the Reference Member State (RMS), in the long term, the role of the RMS will need to migrate to another EU Member State. Transfer from one RMS to another currently requires the initial RMS to prepare an assessment report. The UK MHRA will be hard-pressed to do this for every mutual recognition procedure (MRP) and decentralized procedure (DCP) that it leads, so some form of interim process for this will be required.

Where the UK is a Concerned Member State (CMS) in an established EU MRP/DCP, pan-EU variations procedures will no longer apply in the UK, leading to a significantly bigger workload for the MHRA; the UK will have to assess changes for all previously EU-based MAs, with the consequential increase in approval times.

Degrees of regulatory disruption will be inevitable over the coming months, even if the MHRA introduces some pragmatic processes to migrate licenses linked to EU procedures into UK national procedures.

The EMA also subcontracts the large quantity of assessments to the MHRA, which again will presumably cease and this may in turn mean that the EMA response times increase for handling applications, etc.

Clinical Trials

This area is in the process of major change with the implementation of the Clinical Trials Regulation 536/2014. As this is a regulation, it has not until now required translation into UK law. This translation would now need to
occur when the UK leaves the EU, if we choose to follow the Swiss model. This regulation is due to be implemented before October 2018, which could well coincide with the UK formally leaving the EU.

Pharmacopoeia

The European Pharmacopoeia (PhEur) is prepared, published and distributed by the European Directorate for the Quality of Medicines and Healthcare (EDQM), which is part of the Council of Europe, not the EU. So, providing the UK remains a member of the Council of Europe, which has a total of 47 member countries including Switzerland, not too much should change.