EMA Brexit Interested Parties Meeting
Joint Industry Presentation – BREXIT

Industry Stakeholder meeting on Brexit and operation of the centralised procedure for human medicinal products

September 24, 2018

This is a joint industry presentation on behalf of the trade associations shown

March 23rd stakeholders meeting conclusion: Continue collaboration / dialogue to minimize resources impact

- Transition period: need for clear understanding of implications for EU regulatory system, role of UK, and MAHs

- Communication resources HMA/CMDh, EMA and MHRA: performance and delivery by the EU regulatory network

- Company-specific product portfolio dialogue on BREXIT preparedness with EMA and CMDh/HMA

- Post-Brexit future arrangements :
  - Exploration of all options for future regulatory and trade relationship between the UK and EU
  - Exploration of (extended) Mutual Recognition Agreement (MRA)

Industry Associations preparation for the ‘No Deal’ Scenario

- The political uncertainty presents a number of difficulties in making business continuity decisions

- Proceed with business continuity planning taking into account the EC/EMA Q&A and practical guidance documents:
  - Regulatory
  - Trade and supply
  - Clinical trials
  - Workforce

- Long term: in the interest of patients and public health, securing future cooperation on the regulation, trade and supply of medicines must be a priority

“No-deal”: facilitating continuity of supply

- Companies are taking into account EC/EMA guidance to prepare for “no deal” and be compliant with EU rules by time of Brexit

- Industry has highlighted challenges of completing all required activities in time for all products, and sought solutions to minimise adverse impact on continuity of supply of medicines to patients

- EMA’s Brexit preparedness survey results indicate EMA considers some products at risk of supply disruption or shortages in the EU, if changes not submitted and implemented in due time

- UK Government’s August 2018 guidance for “no deal” includes helpful solutions, including continued acceptance of EU testing & release of medicines for time-limited period

- **Are EMA, CMDh/HMA/ECHA and the European Commission considering the application of temporary arrangements to facilitate continuity of supply of medicines to EU patients?**
  - *E.g. acceptance of testing & release in the UK; confirmation of equivalence of UK GMP regulations to EU, so exemption from requiring MHRA written GMP confirmation for each batch of API imported post Brexit*

Life Science Industry Coalition:
Letter to Commissioner for Health and Food Safety

Mr. Vytenis ANDRIUKAITIS
Commissioner
Health and Food Safety
Rue de la Loi 200
BRUXELLES

Bruxelles, 03 August 2018

Dear Commissioner Andriukaitis,

This letter follows up on the Brexit discussion that you had with Medicines for Europe on 17 July 2018. We have agreed with our partner industry associations to send this response jointly as most of the issues are common to the pharmaceutical sector as a whole.

Our members have been preparing for the contingency of a 'no deal' scenario since the results of the referendum were known in 2016. Trade associations have called on its member companies stressing the need for readiness by March 2019. Despite these measures, we anticipate constraints in existing capacity of the system. Our immediate concern is the risk of disruptions to the supply of medicinal products in the advent of a disorderly withdrawal of the UK from the EU internal market. Maintaining uninterrupted supply of medicinal products is a shared public health responsibility of the EU27 and UK regulators, industry and supply chain stakeholders. We would like to underline that a disorderly withdrawal could occur at the same time as the implementation of the serialisation requirements of the Falsified Medicines Directive, which could also impact the supply of medicines and consume considerable resources of industry and regulators, resources that we would need to deal with a disorderly withdrawal. We therefore urge the EU and UK authorities to communicate what plans are being put in place to mitigate the risk of a disorderly withdrawal and to take appropriate steps to minimise the disruption in supply of medicines for patients.

<u>The main reasons for possible disruptions in supply include:</u>

The requirement to **re-test,** in either the EU-27 or the UK, batches of product that have already been tested by a manufacturer in the other jurisdiction.

<u>Industry's proposed solution to mitigate this risk is:</u>

The **application of the Article 51(2) arrangement under Directive 2001/83 as a pragmatic solution to maintain supply of medicinal products** until a **Mutual Recognition Agreement (MRA) on batch testing and inspections** can be agreed between the EU- UK (as exist already with several other 3rd country jurisdictions including Japan, Switzerland, Canada Australia and the USA).

Questions / Topics

Brexit related type IA (“do and tell”) variations

> Regarding the question on the Type IA variations, the proposed 2 months notification timeline for submissions after UK’s withdrawal from the Union (rather than total completion of these changes by the withdrawal date) has been agreed in order to allow MAHs sufficient time to notify Competent Authorities of changes that need to be implemented before 30 March 2019. We consider that the deadline of one year for submission of the notification(s) cannot be applied in this scenario, because it results in the previous situation becoming non-compliant with the Union Law, as a result of UK’s withdrawal from the EU.

EMA response letter (dd 28 August 2018)

- According to the current EU legal framework, any Type IA **notification** (submission to the Competent Authorities), however, has to be **submitted** within a period of **12 months** (“annual report”) **after implementation**;

- In addition, this administrative requirement will have an unnecessary impact on resources on both industry / regulators;

Please clarify the reasons for changing this general approach, as it is a fundamental part of the European regulatory framework, and for stipulating the 2 month period – taking into account the definitions and application of the implementation and notification date.

The possibility to market a multi-country pack which includes UK

For question 24, multi-country packs with a third country will normally not be possible. Marketing authorisation holders currently using multi-country packs that include the UK may therefore have to adapt their packaging. The use of the "blue box" and any other UK specific additional information on EU packaging materials may be acceptable only exceptionally, while complete alignment in product information is maintained once the UK has withdrawn from the Union, and if all other requirements of EU legislation are fulfilled (only non-promotional additional information that is useful for the patient is included, no negative impact on readability etc.). As it is deemed to be very challenging to fulfil such requirements, we expect that normally it will not be possible to maintain common EU-UK packs.

EMA response letter (dd 28 August 2018)

- Multi-country packs, shared with UK, are very important for several member state markets, including Cyprus, Malta and Republic of Ireland
- At the point of Brexit, UK product information will still be in complete alignment with EU
- UK packaging and labelling rules will also still be aligned

Therefore, industry understands EMA clarification to mean that **common packs can be maintained after Brexit, unless and until UK product information diverges from that of EU**

CPP Certificate of pharmaceutical product

- Please confirm that the European Medicines Agency will continue to issue CPPs within 10 working days (standard procedure) or within 2 working days (urgent procedure) following receipt of a valid application form.

Manufacturing and Supply

- Please advise what measures are being taken to plan for additional inspection resources to compensate for MHRA's departure from inspection collaboration programme?

21. How does UK's withdrawal from the Union affect the status of inspection outcomes by the UK competent authority? (NEW)

It is expected that findings of inspections, in particular to determine compliance with good manufacturing practice, good clinical practice and pharmacovigilance obligations, conducted by the UK competent authority before 30 March 2019 are implemented by the inspected entities in accordance with the applicable legislation, in particular Directive 2003/94/EC, Commission Delegated Regulation (EU) No 1252/2014 and Directive 91/412/EEC with regard to good manufacturing practice, Directive 2001/20/EC and Commission Directive 2005/28/EC with regard to good clinical practice and Regulation (EC) No 726/2004, Directive 2001/83/EC and Commission Implementing Regulation (EU) 520/2012 with regard to pharmacovigilance obligations.

- We understand that the inspected entities should implement the recommendations of MHRA inspection. Nothing is written regarding the validity of GMP certificates issued by MHRA. **Can EMA confirm that MHRA GMP certificates will remain valid in EU also after 29.3.2019?**

Bioequivalence Studies using UK comparator

CMDh updated guidance dated 19 June 18 included a revision regarding acceptance of Bioequivalence Studies using UK comparator: *"For Marketing Authorisation Applications submitted prior to 30 March 2019 for group procedures MRP/DCP that include a biostudy with the UK reference product as comparator, and where the study has been completed prior to 29 March 2019, will be accepted."*

There has been no corresponding change to the EMA Q&A guidance for the Centralised Procedure on acceptance of UK reference product for bioequivalence studies. The request is for the EMA to update their QAs to be in line with the CMDh interpretation.

Medical Devices (1/2)

Please advise whether the assembly and release (after Brexit) of a final medicinal product co-packaged with a third party medical device, having a certification from a UK Notified Body, could be considered acceptable, if the device component itself was released from the device manufacturer prior to Brexit. This would reduce the risk of supply issues.

- Several medicinal products are **co-packed** with third party device components that may be impacted by Brexit.
- As per European Commission communication, by 30-Mar-2019...
  - *...an EU distributor receiving product from the UK will become an importer for the purposes of Union product legislation and will have to comply with the specific obligations relevant to an importer,*
  - *...a device manufacturer or their designated authorized representative established in UK should be transferred in the EU, and*
  - *...a manufacturer must switch from UK Notified Body prior to the withdrawal date to EU Notified Body (either new certificate or transfer of the file).*
- All the above actions are under device manufacturer responsibility.
- Each of those aspects may impact device availability and may potentially lead to stock-out situations.
- If applicable, obligation to submit a variation to EMA is under MAH responsibility for co-packed products.

Medical Devices (2/2)

- Latest Brexit Q&A published in Jun-2018 indicates that a change of Notified Body (NB) would be regulatory relevant.
- Delays are anticipated to report such changes on time:
  - Due to the new Medical Device Regulation (EU) 2017/745 and 2017/746, many manufacturers of devices have not yet identified alternative NBs outside of the UK.
  - Long procedural timelines for manufacturers of devices to change NB.
- Planned mitigation for all affected devices:
  - Stockpile affected devices (prior to Brexit) for future use in co-packaged products to bridge until relevant changes are implemented after Brexit.
  - The assembly and release (after Brexit) of the final co-packaged medicinal products could be considered acceptable, if the device component itself was released from the device manufacturer prior to Brexit. Devices released prior to Brexit are not affected and remain in circulation.
  - This approach will be important to reduce the risk of supply issues and potentially stock-outs for co-packaged products.