ASPHALION

Els efectes del Brexit en el sector Farma y MedTech

Brexit situation

There's still a lot of uncertainty.

The possible Brexit date has been postponed again until 31st January 2020 by the EU.

Before Brexit

UK, an Additional Regulatory Area in the world

Brexit's impact

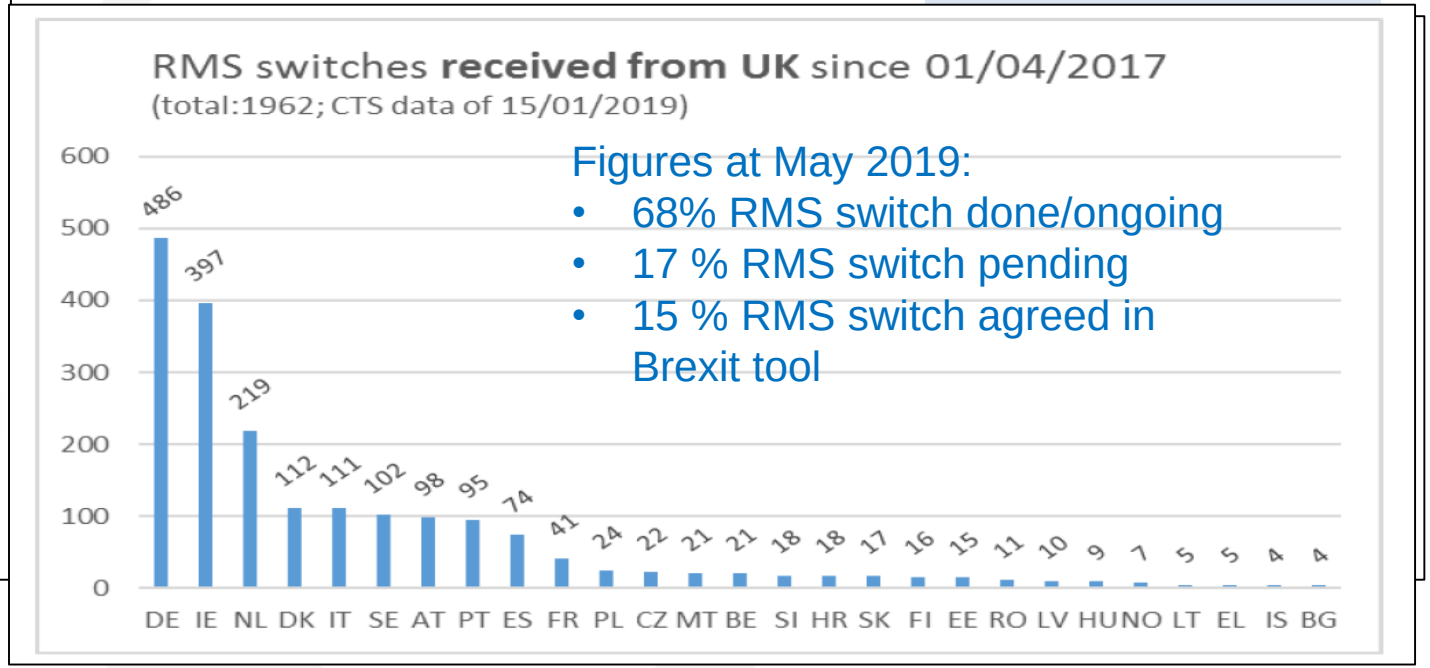
PHASE I; UK→ OUT
To keep current EU Marketing Authorisations

PHASE II; Stay in UK Market
How to keep UK Business

Brexit's impact

PHASE I; UK→ OUT

To keep current EU Marketing Authorisations



Brexit's impact - Summary

PHASE I; UK→ OUT

To keep current Regulatory, Pharmacovigilance & Manufacturing Activities

Local Representative located in the UK

- Nominated for MS other than UK: will have to be changed to a local representative located in the Union (EEA)
- Nominated for UK: After 31 October 2019 becomes obsolete

EU QPPV

The Qualified Person for Pharmacovigilance (QPPV) will need to change place of residence to carry out tasks in the Union (EEA) or a new QPPV will need to be appointed

Manufacturing site in the UK

Active substances and medicinal products manufactured in the UK will be considered as imported after 31 October 2019

UK sponsor for an orphan designation

Need to transfer the designation to a holder established in the Union (EEA) or change the place of establishment to the Union (EEA)

PMSF located in UK

Need to change the location of the Pharmacovigilance System Master File (PSMF) to a MS within the Union (EEA)

UK batch release site

Needs to be changed to a site in the Union (EAA)

UK batch control site

Upon importation batch control need to be conducted (repeated) in a site in the Union (EEA)

Brexit's impact

PHASE I; UK→ OUT
To keep current EU Marketing Authorisations

PHASE II; Stay in UK Market
How to keep UK Business

Phase II: Stay in UK market

How to keep UK Business

1. UK Legal presence requirements
2. Pharmacovigilance
3. Procedures for Medicinal Products
4. Medical Devices


NO DEAL
BREXIT
SCENARIO

Què és necessari per seguir amb les operacions a UK després de Brexit?

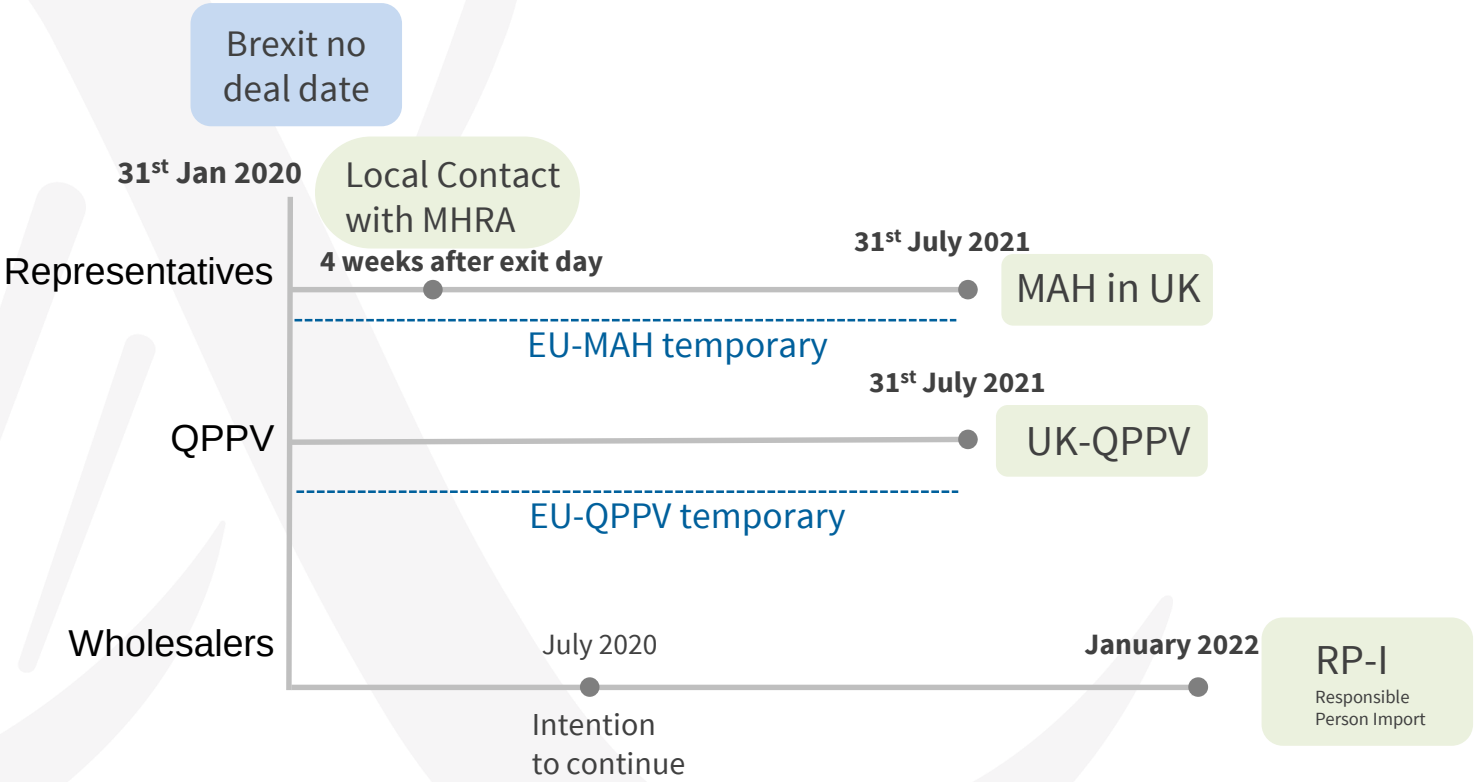
Brexit's impact, Legal Presence requeriments

- **Do I need a MAH based in the UK?**
  YES, by 31st July 2021
- **Do I need an UK-local representative?**
  YES, 4 weeks after Brexit day (until I have the MAH in UK)
- **Should the QPPV be based in the UK?**
  YES, by 31st July 2021
- **Do I need a QP in the UK?**
  YES, in certain cases (depending on the country of import)
- **What happens to the UK wholesalers importing QP certified medicines?**
  The UK will continue to recognize QP certification from EU / EEA countries after Brexit
  Importers should notify MHRA within 6 months of Brexit
  Responsible Person for Import (RP-I) will be appointed in 2 year period after Brexit

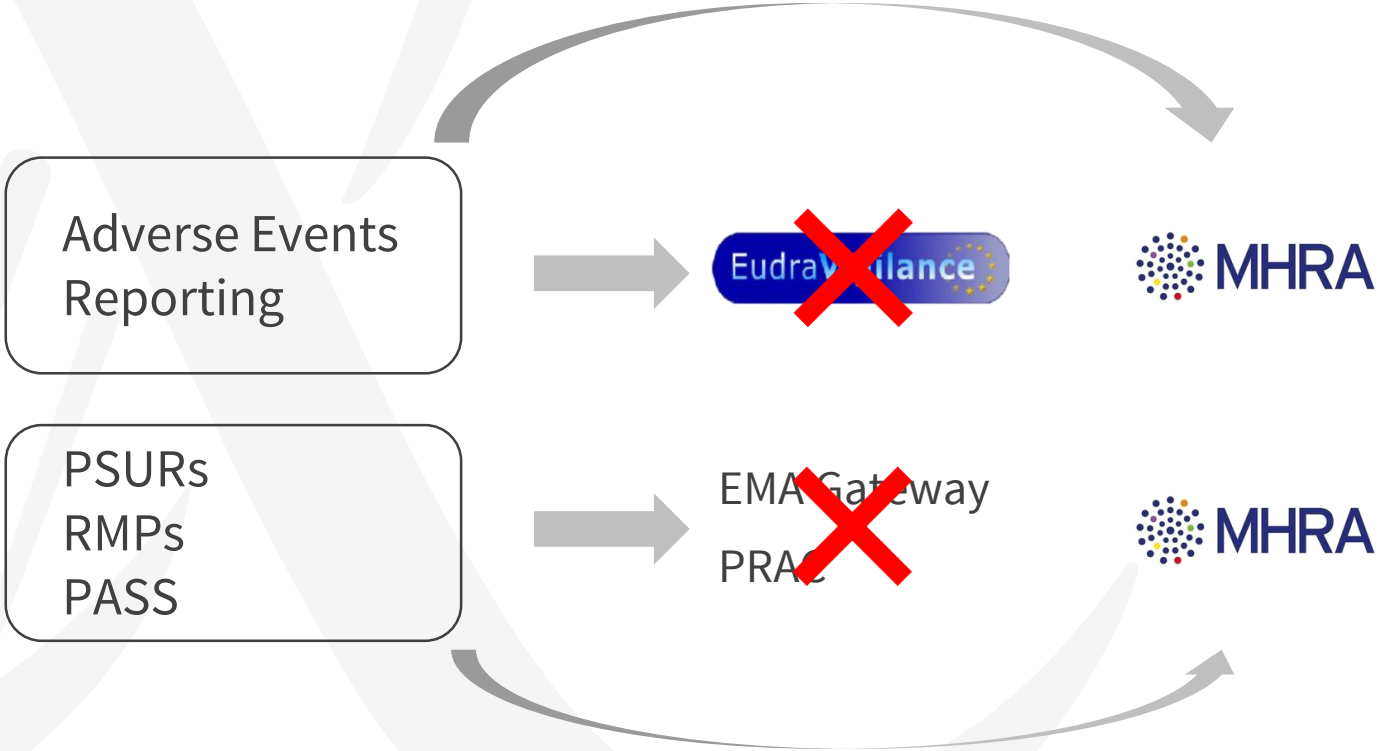
Brexit's impact Wholesalers

- Licensing regime for wholesalers importing QP certified medicines
  - The UK will continue to recognise **QP certification from EU / EEA** countries after Brexit.
  - all existing holders of UK Wholesale Authorisations will be permitted to purchase medicines that have been QP certified in the EU/EEA -> Notify MHRA within 6 months of Brexit of their intention to continue
  - **Responsible Person for Import (RP-I)** will be appointed **in 2-year period after Brexit**
  - Holders of this amended authorisation will be required to put in place an assurance system to ensure any medicines they import have been QP certified.
  - Wholesalers who wish to trade only with authorised manufacturers and wholesalers located in the UK may continue to do so under their existing wholesale authorisation and Responsible Person arrangements.
  - **A Manufacturer's Licence for Import (MIA) will continue to be required for all other forms of import** of human medicines being supplied onto the UK market

New Roles Required in No-deal Brexit



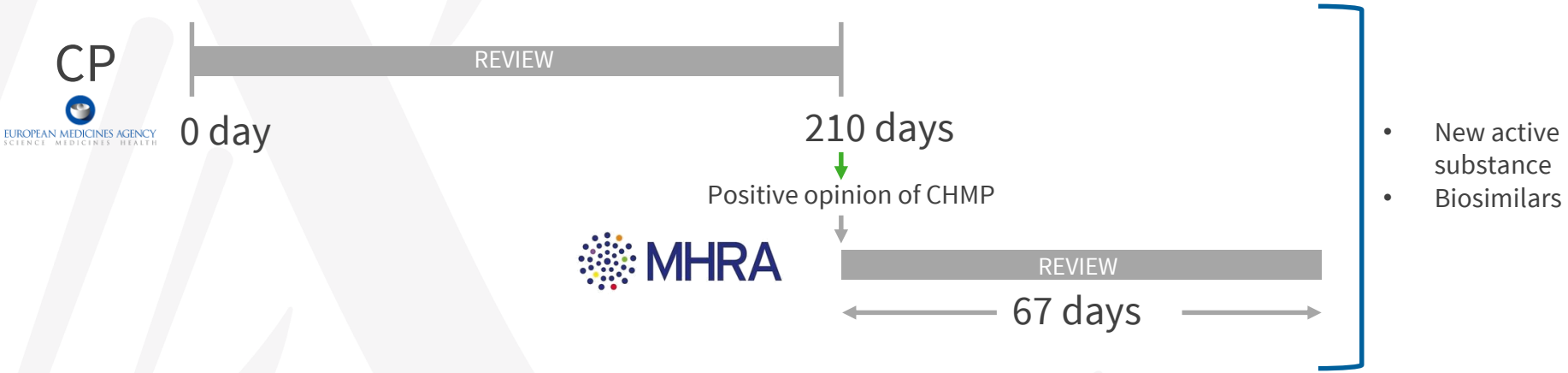
Pharmacovigilance new Flowcharts



A partir d’ara com registro un nou medicament a UK?

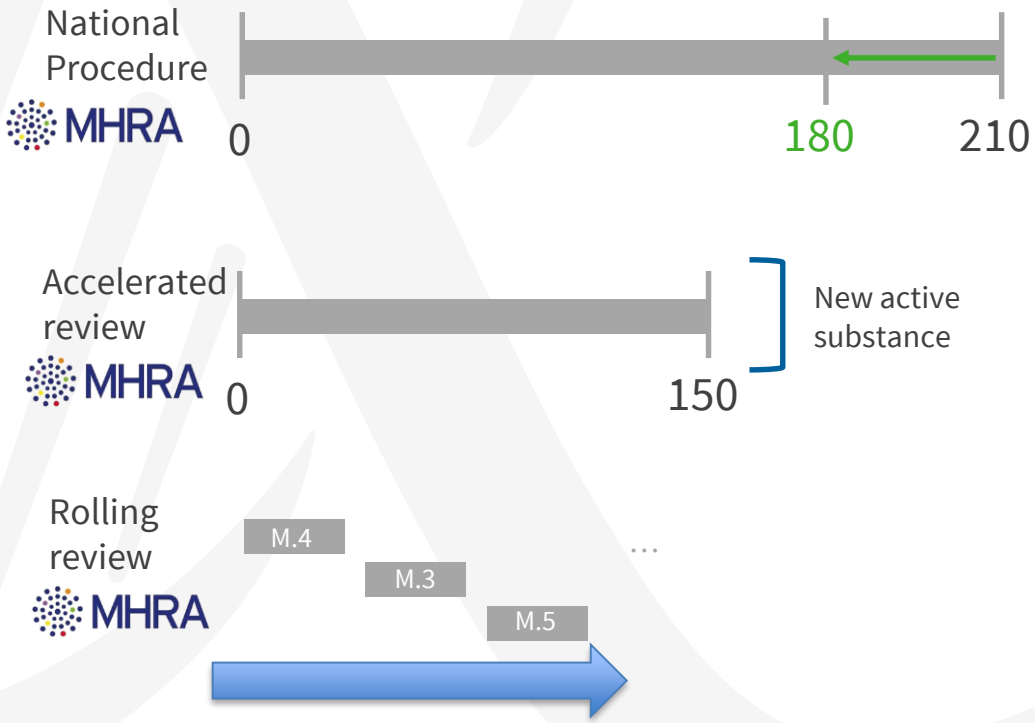
New Assessment Routes by MHRA

"Targeted assessment"



New Assessment Routes by MHRA

"Making from Brexit and advantage"



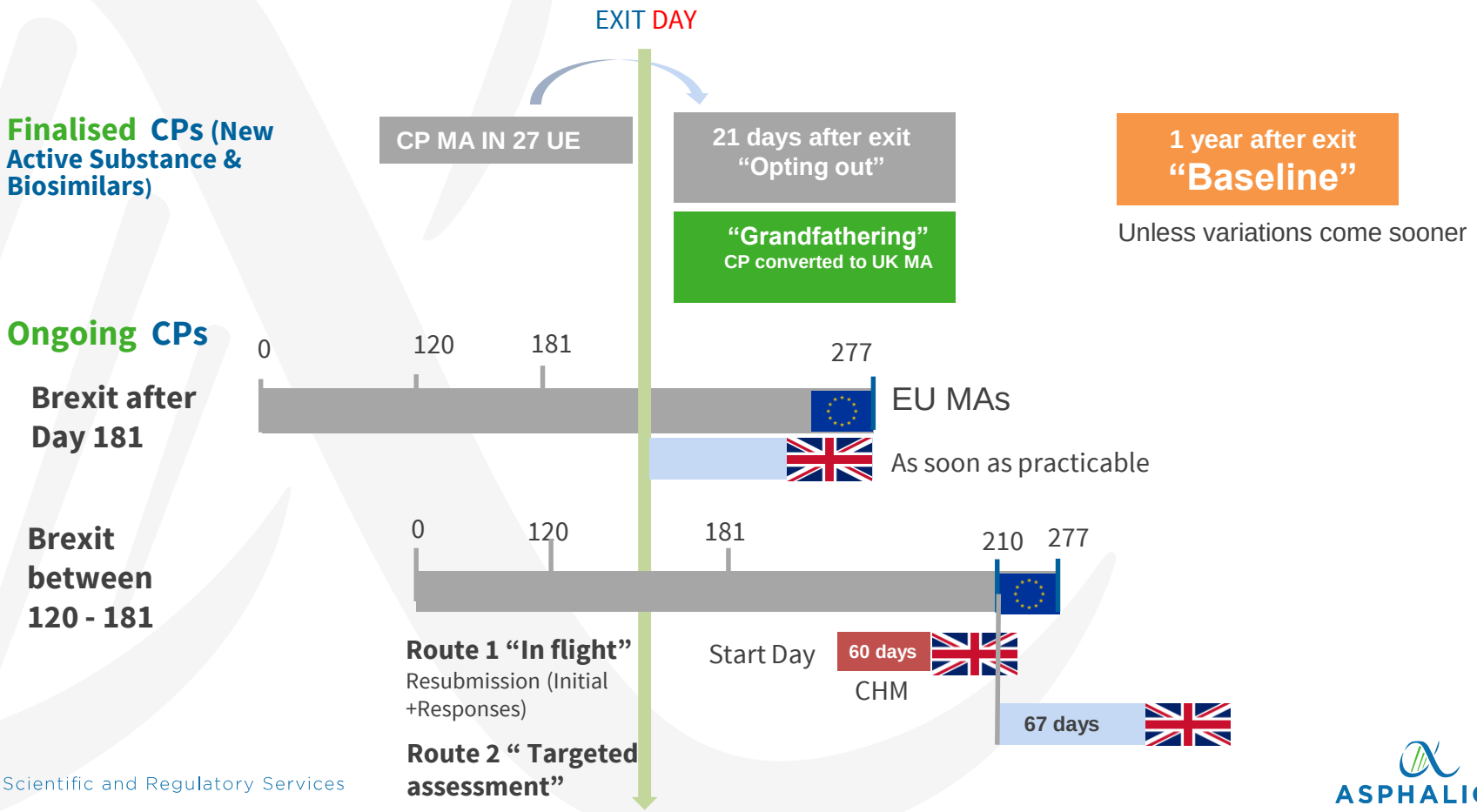
Brexit's impact, Conditional Marketing Authorisations and Exceptional Circumstances

- The MHRA will introduce a national **Conditional Marketing Authorisation (CMA) scheme for new medicinal products**
  - Same eligibility criteria as the EU
  - for medicinal products that fulfill an unmet medical need.
  - Where comprehensive clinical data is not yet complete, but that such data will become available soon.
  - CMAs will be valid for one year and will be renewable annually.

- The MHRA's existing scheme for **applications under exceptional circumstances** will continue.
  - Same eligibility criteria as the EU scheme
  - Comprehensive data package cannot be provided, because the condition is rare or because collection of full information is not possible or is unethical.

The designation by the EMA or another jurisdiction may be taken into account, but the final decision will rest with MHRA.

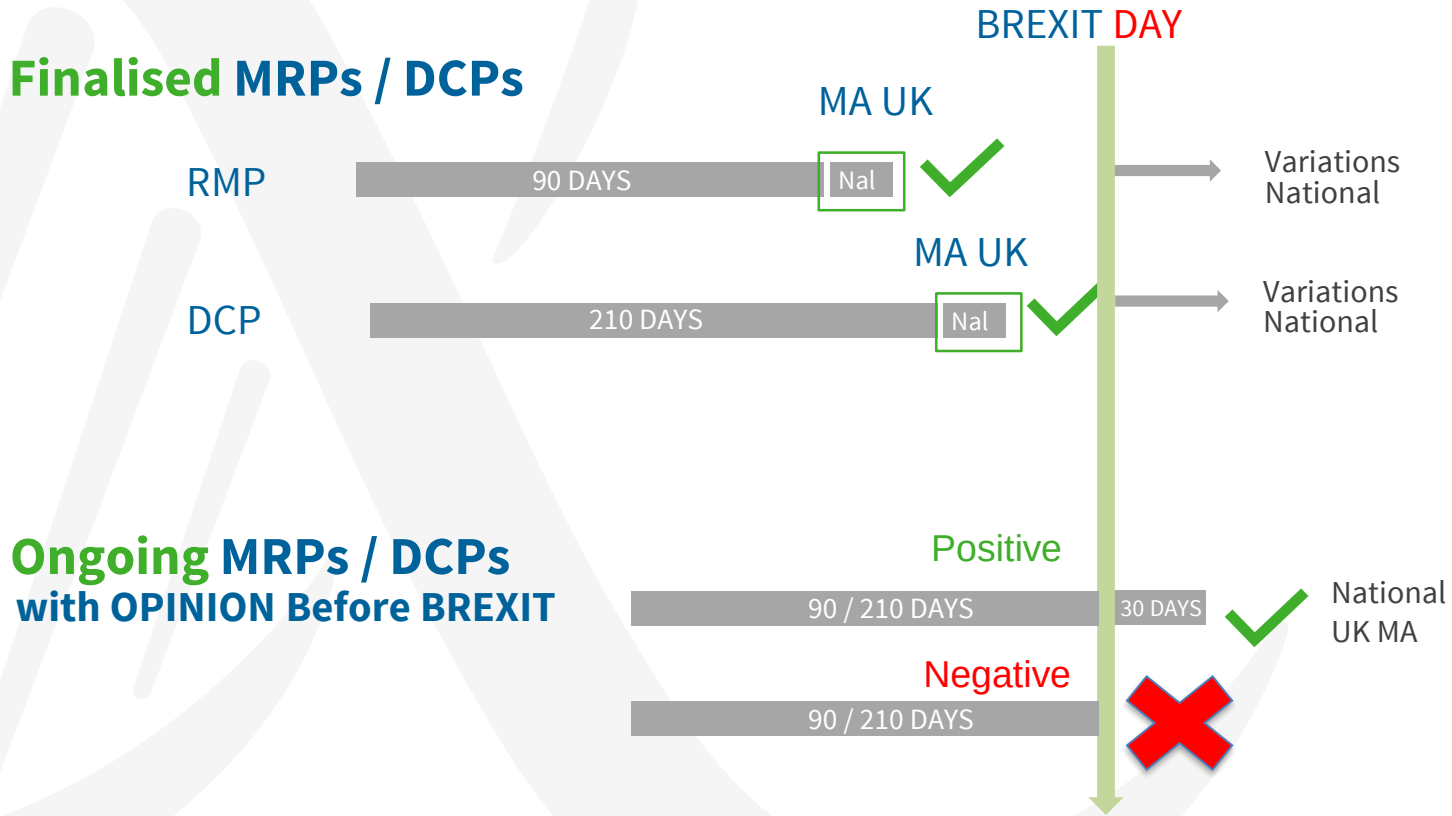
How BREXIT affects our current CP registration?



Variation	Positive CHMP Opinion Stage before exit day	MHRA Assessment	Fee Payable	Include in Initiating Sequence
Type IA (i) Submitted to EMA before exit day and not rejected or (ii) submitted to EMA after exit day and not rejected before data submission date	N/A	No	No	Yes (and list in summary of historical regulatory activity accompanying Initiating Sequence)
Type IB Submitted to EMA but not granted before exit day	Yes			
Type IB Submitted to EMA but not granted before exit day	No			
Type II Submitted to EMA but not granted before exit day	Yes			
Type II in clock stop Submitted to EMA but not granted before exit day And in clock stop	No	Yes Assessment of Replies	No	No Separate Submission needed along with or after Initiating Sequence (either minimal or complete)
Type II before clock stop Submitted to EMA but not granted before exit day. And before procedure first clock stop	No	Yes	Yes	
Type IB/II variations Submitted to EMA after exit day	N/A			

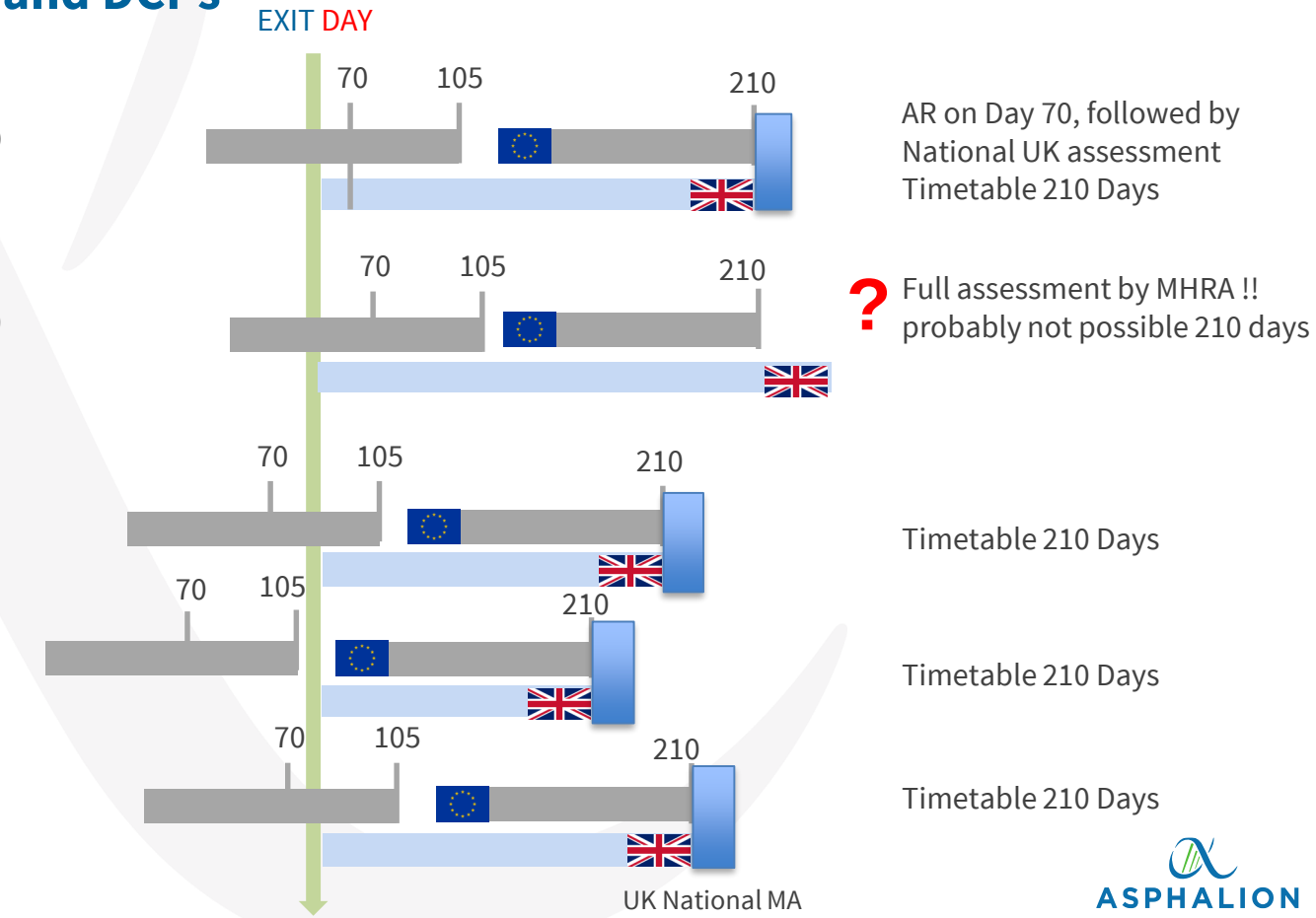
I si no son CPs els meus registres?

How BREXIT affects our current registration?



How BREXIT affects our current registration?

In progress RMPs and DCPs



How BREXIT affects our current registration?

- MHRA does not expect to be able to receive submissions through the Common European Submission Portal (CESP).
- A new national portal will be ready by exit day
  - https://www.gov.uk/guidance/converting-centrally-authorised-products-caps-to-uk-marketing-authorisations-mas-in-a-no-deal-scenario-grandfathering-and-managing-lifecycle-ch

Que hi ha d'especial pels genèrics (o hibrids)?

Brexit's impact, Abridged applications

- Abridged applications
  - Abridged procedures for obtaining an MA in the UK would remain in place.
  - However, **it would not be possible to rely on a European reference product for any new applications** submitted after the exit day.
  - **New abridged applications would need to be based on reference products that have been authorised in the UK**, including CAPs which have been converted to UK MAs or non-converted CAPs which were granted prior to exit day.
  - UK MAs based on EU reference products that have been granted (or are the subject of pending applications) prior to exit day will remain valid after exit day.

I per els productes comercialitzats, hi ha algun efecte al *packaging* ?

Brexit's impact Packaging and Leaflet

Some packaging and leaflets will have to be amended:

- **The MHRA will give until the end of 2021 to amend administrative details on the packaging and in the package leaflets for a product already on the market.**
  - UK administrative information: UK MAH's name and address (relocation),
  - UK product licence (PL) number,
  - information about the manufacturing site.

Falsified medicines:

- Legal obligations will be removed for all actors in the UK supply chain,
- Packaging containing Falsified Medicines Directive safety features will be acceptable.

I per productes en investigació?

Brexit's impact, National Scientific Advice

- The MHRA will continue to offer National Scientific Advice
- This service is available for developers of medicinal products and can be requested at any stage of the product's development
- Applications for scientific advice submitted by **UK-based SME** will be exempt from the fee. Applicants will be required to submit evidence of their SME status together with the scientific advice form.
- Requests for advice that is purely regulatory in nature will remain free of charge.

UK system for Rare Disease Medicinal Products

Marketing Authorisation Applicants should submit the
UK Orphan Drug Designation Application form with the MAA (module 1.2 eCTD)

- Orphan Criteria based on EU criteria, but **also** UK-specific aspects.
  - the prevalence of the rare disease in the UK,
  - the availability of satisfactory alternative treatment methods in the UK and the significant benefit.
- The evaluation of compliance with orphan criteria would be conducted in parallel with the review at the time of the MA application

- **Advantages:**
  - MA application fee refunded 100% for SMEs and fee waiver for variations 1st year
  - MA application fee refunded 10% for all other manufacturers.
  - **10 years** marketing exclusivity retained.

Brexit's impact, Paediatric Investigation Plans

UK-PIP in addition to EU-PIP and US-PSP

Compliance with a UK PIP or waiver should be demonstrated in applications for new medicinal products, as well as in new indications, new routes of administration, and new pharmaceutical forms for all products with supplementary patent protection

- EU-PIPs and modifications agreed by EMA prior to the exit day will be adopted as UK-PIPs.
- EU-PIPs with positive opinion by PDCO but not yet Decision by the Commission, will be adopted as UK-PIPs (if UK was still in at the time of opinion)
- EU-PIPs not yet given opinion by PDCO should be re-submitted to the MHRA.

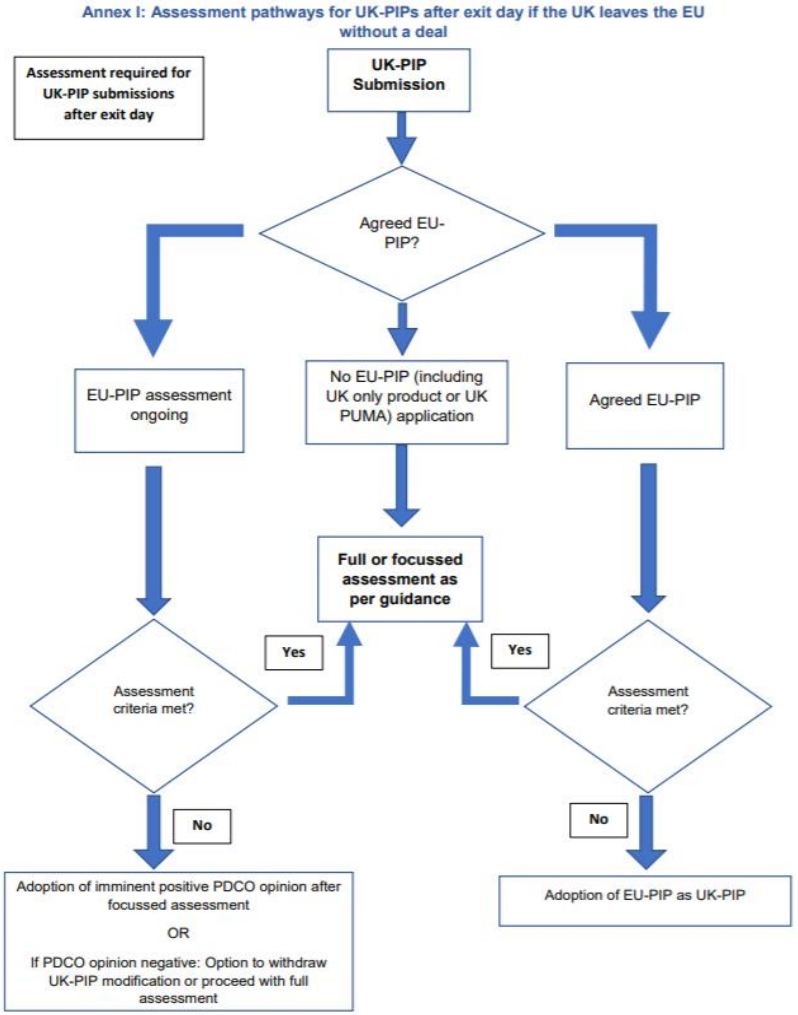
- **In principle, the MHRA will aim to accept a positive PDCO opinion**
- UK-PIP with no EU-PIP after the UK leaves the EU: Full assessment of the UK-PIP is required.

- The same rewards for PIP compliance would be available - a 6-month extension of a UK Supplementary Protection Certificate (SPC) (an SPC extends patent protection for medicinal products), as well as 2 years' additional market exclusivity for orphan products complying with a PIP.

https://www.gov.uk/guidance/procedures-for-uk-pips-in-the-event-the-uk-leaves-the-eu-without-a-deal
https://www.gov.uk/guidance/completed-paediatric-studies-submission-processing-and-assessment-in-the-event-of-a-no-deal-scenario

Brexit's impact,

Paediatric Investigation Plans



Brexit's impact investigational medicinal products

- Scientific Advice
  - Free for SMEs established in UK
- Orphan Drug Designation
  - At the time of submission
- Pediatric Investigation Plan (PIP)
  - the MHRA will take decisions on paediatric matters post Exit -> UK PIP
  - Same requirements and rewards

Hi ha altres consideracions legals pels medicaments?

Brexit's impact Legal Topics

- Data and market and exclusivity
  - Data and market exclusivity in the UK will start on the date of authorisation in the UK or EU, whichever comes first.
  - This will also apply in relation to marketing exclusivity for orphan products..
  - To be reviewed 2 years later.
- Parallel imports
  - Medicinal products that hold a marketing authorisation in another Member State, or are CAPs, and are essentially similar to a product that has been granted a UK marketing authorisation, will still be able to be imported under a parallel import licence
  - The parallel import regime will remain limited to EU and EEA countries.
  - Parallel import licence holders will in future need to be established in the United Kingdom.
  - Those currently holding licences will have until 31 July 2021 to effect this change if currently established elsewhere in the EU/EEA. Until they have done so, companies will be expected to put in place a UK-based contact person within 4 weeks of Brexit.

Com afecta el Brexit als medical devices?

Brexit's impact Medical Devices

- UK's current participation in the European regulatory network for medical devices would end.
- The MHRA would take on the responsibilities for the UK market that are currently undertaken through the EU system.

- UK-based NBs will no longer be recognised by the EU after Brexit, meaning the devices they have certified will no longer be in conformity with the applicable EU Directive. As such these products will not be able to be placed on the EU market.
- UK-based Authorised Representatives will no longer be recognised in the EU.

- UK-based NBs will be given by the MHRA an ongoing legal status and UK will continue to recognise the validity of certificates that they issued prior to exit day.

- A **UK Responsible Person**, will be created for manufacturers based outside of the UK.

Brexit's impact Medical Devices

- The EU MDR and EU IVDR will fully apply in EU Member States from 26 May 2020 and 2022 respectively, but devices can already be placed on the market under these new Regulations.
- Manufacturers wishing to place a device on the UK market must first register with the MHRA.
- Where a manufacturer is not established in the UK, it must designate a UK Responsible Person to register and act on its behalf: **A new role – the UK Responsible Person** – has been created under the UK MDR 2002 (as amended by the UK MDR 2019), applicable in a no-deal Brexit.
- The requirement for a manufacturer to have in place a UK Responsible Person is in line with **the grace period** for registering your devices

Brexit's impact Medical Devices
Timing for the registration at the MHRA

4 months	Class III medical devices Class IIb implantable medical devices Active implantable medical devices IVD List A
8 months	Class IIb non-implantable medical devices Class IIa medical devices IVD List B Self-test IVDs
12 months	Class I medical devices General IVDs Class A IVDs (if complying with the EU IVDR 2017/746).

Brexit's impact Medical Devices

The UK Responsible Person OBLIGATIONS:

- ensure that the declaration of conformity and technical documentation have been drawn up and, where applicable, that an appropriate conformity assessment procedure has been carried out by the manufacturer
- keep available a copy of the technical documentation, a copy of the declaration of conformity and, if applicable, a copy of the relevant certificate, including any amendments and supplements for inspection by the MHRA
- in response to a request from the MHRA, provide the MHRA with all the information and documentation necessary to demonstrate the conformity of a device
- forward to the manufacturer any request by the MHRA for samples, or access to a device, and ensure that the MHRA receives the samples or has been given access to the device
- cooperate with the MHRA on any preventive or corrective action taken to eliminate or, if that is not possible, mitigate the risks posed by devices
- immediately inform the manufacturer about complaints and reports from healthcare professionals, patients and users about suspected incidents related to a device for which they have been designated
- terminate the legal relationship with the manufacturer if the manufacturer acts contrary to its obligations under these Regulations and inform the MHRA and, if applicable, the relevant notified body of that termination

Brexit's impact Medical Devices

Notified Bodies that can be used from after the UK leaves the EU

- Certificates that have already been issued by UK-based Notified Bodies prior to the UK's departure from the EU will continue to be valid for the UK market.
- The MHRA will continue to oversee the activities of UK-based Notified Bodies.

- From Exit Day, if you wish to place a new device, which requires a Notified Body to carry out a conformity assessment, **on to the UK or EU market**, you will need to use a Notified Body based in an EU Member State.
- Once the conformity assessment has been successfully completed, you can place a CE mark on your device and place the product **on the UK or EU market**.

Questions?
Thank you!

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