



Brexit transition: frequently asked questions

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Latest published guidance can be found at: www.gov.uk/government/collections/mhra-post-transition-period-information

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A. Licensing

1. If a medicine has a UK national licence and not a CAP, can we work with EU Member States (e.g. RoI) where a national licence also exists, to extend MRP/DCP?

Only NI can be included in MRP/DCP so it will not be possible to include the UK in those procedures. However, where the UK and RoI products are the same, and the product information is the same, it will be possible to use a common pack including both the UK and IE MA numbers.

2. For CAPs, if we are changing the MAH as part the CAP conversion process, and we choose to submit updated packaging mock ups with the baseline reflecting this, do we need to implement the updated SmPC (and, where relevant, prescribing information) at the same time? i.e. do all items need to be aligned as regards MAH/licence number?

Yes.

3. Will it remain acceptable to align the implementation of MAH details/PL numbers in prescribing information with the next safety approval?

Yes. Any change to the clinical information, the SmPC and patient information should also include updated administrative details at that time.

4. For MR/DC licences – the licence number in NI is to remain as PL xxxxx/xxxx and for GB as PLGB xxxxx/xxxx? Will joint packs or GB / NI packs are not accepted, where of course for NI, FMD is active and the product routed accordingly. Again, it would make sense to have Ireland/NI packs to avoid regulatory divergence over time. However, the product portfolios can be different between Ireland and NI.

Joint packs can only be agreed with the MAs in all jurisdictions are aligned and the information on the pack and in the PIL within the pack are identical (except for a small number of administrative details). Further guidance will be published in due course on the requirements with respect to the safety features aspects of the Falsified Medicines Directive.

5. We need to understand if our purely national licences can stay as is.

Yes, purely national MAs will remain as they are.

6. Will the MHRA issue different PL numbers for the CAP converted products that they issued previously in 2019 or will the PL numbers remain the same?

As the MAs for the converted community authorisations will be valid only in GB, the format of the MA number will start with PLGB* but the previously issued company number and sequential product numbers will not be changed. *Note that the exact format is to be finalised.

7. Does MHRA have data on the number of products including both the UK and RoI in the same licensing procedure?

For CAPs the MHRA do not have data on the number of joint UK-IE packs.

8. Section 15 of the CAP conversion guidance goes some way to clarifying the requirements for the UK MAH following Brexit. However, the requirements to submit texts or mock-ups is still open to interpretation. - Will the MHRA allow submission of texts only for all licences, including for actively marketed products? - If so, will the MHRA then allow the submitted texts to reflect the new MAH, but continued release of packs with PILs and labelling that reflects the existing MAH until updated mock-ups are submitted via variation within the two-year grace period?

Section 15 of the guidance is clear. Current requirements will apply. A text version will be acceptable provided the product is not marketed. Full colour mock-ups will need to be registered prior to marketing and if it the intention is to market within 30 days of the submission being accepted, full colour mock-ups must be submitted at that time.

- 9. If a company has been automatically already allocated PLGB numbers for converted EU MAs, do they need to submit a COA application when they submit the baseline (based on this: “For grandfathered CAP MAs with a non-UK MAH, there is a requirement to establish an MAH in the UK within 24 months of 1 January 2021”)? Or, because they already have the PLGB numbers allocated, is no COA required? In one example, the MAH is currently in France but the company already has a legal presence in the UK.**

The format of the PL number is company number/sequential product number. Therefore, the first part of the number relates to the specific MAH. If there is a COA then we will need to update the PL number. However, the company can submit the COA within the baseline supported by the CoA form and the Information Processing Unit will sort out the number.

- 10. For applications submitted under Article 10(1) and 10(3), if it can be justified that the EU reference product used in the bioequivalence study was registered via the same assessment route as the UK reference product, is there still a need to provide comparative data to demonstrate that the product used in the bioequivalence study is representative?**

Data may be required depending on whether there had been any significant variations to the EU registered product used as a comparator product in a bioequivalence study e.g. composition that had not been approved for the UK reference product (and vice versa). It would be for the generic applicant to justify the absence of any comparative data to bridge to the RMP.

- 11. Leaving aside in-flight variations - how will other variations be handled? Will the MHRA use the reliance approach during the 2 year stand still period? What are the timescales for assessment?**

The reliance route will also apply for variations. Further procedural guidance will be published.

- 12. For in flight procedures where should we put the Assessment Reports in the eCTD? Should we attach them to the cover letter or is another location preferable?**

They can be put in the working documents folder.

- 13. If a new product has received PO from CHMP in November and expects a CD in January 2021, we would target an initial sequences submission asap in January so that we could obtain the UK licence at the same time as the CD. We are also proposing to launch new products quickly after approval with the packaging details as approved by the EMA, i.e., with the EU licensing number on the carton. Is this acceptable to the MHRA?**

Yes, this is acceptable. You should have been contacted by the MHRA to arrange a call to discuss options as need.

- 14. If a reference medicinal product (RMP) has been registered for 8 years in the UK but not in the EU can it still be used as an RMP for the purposes of NI? We recognise this is an unlikely scenario.**

Only if the MA is limited to the UK.

15. We might need to know as soon as possible if the MHRA will accept that the UK branch of an overseas company can be a UK Marketing Authorisation Holder. For example, this could occur where a company does not have a plc registered in the UK but has set up the UK branch of an overseas company (based in an EU Member State)

In accordance with EU rules, the MAH of a Community Marketing Authorisation for sale and supply in Northern Ireland cannot be established in the UK. For currently granted UK/GB MAs and MAs pending on the 1 January 2021, the MAH established in the EEA and must establish in the UK before 1 January 2023. If the MAH is not established in the UK, contact details are required of a named individual who resides and operates in the UK that may be contacted by the Licensing Authority on any matter relating to the MA. Those details should be provided within 4 weeks of 1 January 2021.

16. How will separate electronic PILs/ SmPCs need to be managed for NI (e.g. via eMC for UK/GB)?

The MHRA will continue to host electronic versions of the approved product information. Questions regarding the eMC should be forwarded directly to the eMC.

17. Please can we have more guidance on the timings and details for pre-vetting of materials for products which are 'In flight' on 01 Jan 21 and for future applications.

The advertising standards unit will continue to invite MA holders to submit promotional materials for pre-vetting once the statutory product information has been agreed.

18. At what point will we need to add NI details to the pack? At the next update after January in line with removing the UK details?

Marketing authorisations issued in respect of NI only, will need to reflect the details in respect of NI at that time. No changes are required to any MA currently authorised in respect of UK-wide supply.

19. For clarification, is the third route for CAPs, the 'NI route', not possible for those applications currently in assessment? Will it be a route for future CAPs? My understanding is that our current CAP has available to it 'reliance or in-flight' assessment routes only at present?

Currently pending and future applications for Community Marketing Authorisations will continue to include Northern Ireland, and when granted the authorisation will cover marketing of the product in Northern Ireland. The in-flight and reliance route are for pending Community Marketing Authorisations to obtain a GB MA.

20. For products with ASMFs, do we need to include this as part of the baselines, including submission of the closed part by the manufacturer?

Yes, if the ASMF has not already been submitted to the MHRA they will need to be submitted along with the baseline.

B. Importing and exporting

- 1. Taking into consideration that we have a contract with a wholesaler in the UK that has its proper WDA to import and distribute medicines in the UK, do you think that we, as the MAH, will need our own UK WDA because we are buying and selling the products (financial transactions only)?**

A WDA is required to buy and sell medicines, even if the logistics part of this activity is sub-contracted to another party.

C. Clinical trials

- 1. Can you clarify if we will need to use the IRAS form for all CTAs from January, not just the ones submitted via the CWOW process?**

Yes, the IRAS form should be used for all applications from January with submission via the MHRA portal rather than CESP. (Note that CWoW uses a different part of IRAS for application and submission and this will continue for the current pilot applicants only for now).

- 2. UK CTA – will the application form be revised? If IMP is certified by EU QP, is it needed to mention UK QP in file, if so, where?**

The current form in IRAS will continue to be used for now. Section D9.2 of the form allows for multiple sites to be included; details of both the EU QP release site and UK site can be added. The full supply chain should be transparent in the IMPD. If necessary, UK-specific supply chain information can be confirmed in either the covering letter or in a separate document.

- 3. Any trials which received approval prior to 1 Jan 2021 will have been loaded onto EudraCT, and the sponsor will still have access to EudraCT. Is the posting of results still able to be completed on EudraCT? Will this still meet the MHRA's requirements even though the MHRA will no longer have access to EudraCT?**

It is our understanding from EudraCT administrators that results will be able to be posted for UK trials entered in the database prior to January 2021. This will meet the UK publication requirement.

- 4. For trials which are approved after 1 Jan 2021, the results should be posted onto the publicly accessible database that the study was registered on (for e.g. clinicaltrials.gov).**

This is correct. <https://www.gov.uk/guidance/registration-of-clinical-trials-for-investigational-medicinal-products-and-publication-of-summary-results-from-1-january-2021>

5. Does the MHRA still require an email confirmation once this activity is complete or will this no longer be required as the results will be publicly available?

As per current requirements we will require email confirmation that this has been done.
<https://www.gov.uk/guidance/registration-of-clinical-trials-for-investigational-medicinal-products-and-publication-of-summary-results-from-1-january-2021>

6. If a study in the UK has completed before 31 December 2020 (and the EOTD has been submitted to the UK), but x-UK sites are still open, will the MHRA still want to receive safety reports from the x-UK sites?

The current requirement will not change. The legislation only requires the global end of trial to be submitted; however, a facility to inform us of the local (UK) end of trial via the end of trial notification form also exists. If a UK end of a global trial is submitted, we would still expect to receive relevant safety updates and substantial amendments for the ongoing trial until the global end of trial notification is received. See <https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial>

7. Phase 1 trials in healthy volunteers can request a deferral for the registration activity, therefore the study will not have been posted on a publicly accessible database such as clinicaltrials.gov. In this case, should the summary of results be submitted directly to the MHRA?

Yes, if your clinical trial is not on a public register, summary results should be submitted to the MHRA. This is specified in the guidance.
<https://www.gov.uk/guidance/registration-of-clinical-trials-for-investigational-medicinal-products-and-publication-of-summary-results-from-1-january-2021>

8. Additionally, if the results are posted onto the publicly accessible database, the study was registered on, we assume this will also make the results of the study publicly available. Currently for phase 1 studies in healthy volunteers the results posted to EudraCT are not made public, so in future is the MHRA expecting sponsors to make phase 1 healthy volunteer study results public?

If a sponsor wishes to request a deferral of study registration within the required timeframe, in accordance with current transparency rules (e.g. due to commercial sensitivity), they should contact the Health Research Authority (HRA) at study.registration@hra.nhs.uk. If your clinical trial is not on a public register, summary results should be submitted to the MHRA.
<https://www.gov.uk/guidance/registration-of-clinical-trials-for-investigational-medicinal-products-and-publication-of-summary-results-from-1-january-2021>

9. If a Phase I healthy volunteer study is approved before 31 December 2020, and will be listed on the EU Clinical Trials Register (but not visible to the public), does the MHRA want a copy of the EU Clinical Trials Register upload or a copy of the CSR synopsis please?

We will accept either.

10. Import of IMPs from approved countries' – Does IMP include ATMP, and does the same list apply for importing ATMPs?

Yes, this includes advanced therapy IMPs and the same list applies.

11. For Annex 3 (EOT) forms, these are currently not available in IRAS to complete and so the EudraCT template is submitted. From 1 Jan 2021, will the MHRA still accept the completed EudraCT template form or will this form be added into IRAS to complete?

We will still accept the completed Annex 3 form to notify the EOT but plan to include a version of this on our website soon.

D. Devices

1. How do I register to become a UK Responsible Person?

UK Responsible Persons are designated by the manufacturer. A UK Responsible Person is required to register devices on behalf of the manufacturer with the MHRA from 1 January 2021. It is at this point that a UK Responsible Person will be expected to provide their details and to provide written evidence that they have the manufacturer's authority to place the relevant device on the market. We plan to provide further guidance on device registration and UK Responsible Persons on gov.uk in future.

2. When will I be able to register new devices with the MHRA?

You will be able to register new devices from 1 January 2021. Please note that it is not possible to register Class IIa, IIb or III devices before this date. Please also note that the UK Responsible Person functions will not be available on the system until 1 January 2021.

3. How do I need to label my device to place it on the UK market?

As of 1 January 2021, medical devices placed on the Great Britain market will need to have either a UKCA mark or a CE marking, depending on which legislation the device has been certified under. Where relevant, the number of the Notified Body or UK Approved Body will also need to appear on the label. If you already have a valid CE mark on your device, you will not be required to re-label the device with a UKCA mark until 1 July 2023 for placement on the Great Britain market. Devices can have both marks present on the labelling prior to 1 July 2023, and dual marking will continue to be accepted on the Great Britain market after 1 July 2023. However, from 1 January 2021 the name and address of the UK Responsible Person, where applicable, will need to be included on product labelling where the UKCA mark has been affixed (including when devices have been dual marked).

4. With respect to devices, what are the artwork expectations for products that are sold in the UK from Jan 2021? Do these need to have the UK Responsible person identified on the packaging from Jan 2021 or will there be a transition period that would apply (in line with the registration of product timelines)?

As of 1 January 2021, medical devices placed on the Great Britain market will need to have either a UKCA mark or a CE marking, depending on which legislation the device has been certified under. Where relevant, the number of the Notified Body or UK Approved Body will also need to appear on the label. If you already have a valid CE mark on your device, you will not be required to re-label the device with a UKCA mark until 1 July 2023 for placement on the Great Britain market. Devices can have both marks present on the labelling prior to 1 July 2023, and dual marking will continue to be accepted on the Great Britain market after 1 July 2023. However, from 1 January 2021 the name and address of the UK Responsible Person, where applicable, will need to be included on product labelling where the UKCA mark has been affixed (including when devices have been dual marked).

5. Should manufacturers continue to notify the MHRA of clinical investigations?

The MHRA will assess clinical investigations in accordance with EU Directive requirements. However, we will accept studies designed in line with the EU MDR/IVDR, including any documentation prepared according to the requirements of these regulations e.g. GSPR checklist. Existing guidance will continue to apply.

E. IT systems

1. Will the MHRA will have a type of XEVMPD product database equivalent?

There is currently no established timeframe to develop an equivalent to the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) in the UK. However, this is something under consideration by the Agency.

2. How can I reactivate my accounts?

For account reactivation queries please contact submissions@mhra.gov.uk.

F. Supply

1. What are the legal and regulatory arrangements for stock movement from NI to GB?

Unfettered access for medicines has a number of transparency requirements, which the MHRA can provide detail on, but it will not necessarily be as simple as just moving stock, as GB licence will be needed for the product, but this can be gained via a UA MA as such.

2. Is it possible to move a medicine via RoI if the medicine does not have an MA in RoI?

RoI do permit wholesalers to supply products licensed for another market. This is all covered by EC Directive 2001/83 Articles 76, 77 and 80. HPRa updated their guidance on this on 2 October 2020. This applies for CAPs or products with a national licence. Wholesalers would not be able to sell such medicines as authorised packs to an RoI pharmacist. The product could be moved through RoI by a wholesaler or by the manufacturer itself. The MIA would also include authorisation to distribute by wholesale the medicinal products covered by the MIA.

3. Is there any possibility post 1st Jan 2023, that the UK would continue to accept EU testing and release sites?

We are not in a position to speculate. A mutual recognition agreement, if negotiated as part of the future trade deal between EU and UK, would enable continued recognition of batch testing by both UK and EU.

4. If UK QC testing is required from 01/01/2023, would this be under the remit of the UK Responsible Person for Import, with an EU QP still being able to perform the batch release, or will this also lead to a need for UK QPs to release all products?

UK will accept batch testing done in the EEA for a period of 2 years until 1 Jan 2023. After that time, batch testing will need to be done under the terms of a Mutual Recognition Agreement, or in the UK. QP certification done in the EEA will continue to be accepted after 1 Jan 2023, provided that this certification is based on batch testing done under the terms of a Mutual Recognition Agreement, or in the UK. The UK RPI (in respect of supply of medicines to the GB market) will be required to continue verification that QP certification has been done in EEA after 1 Jan 2023.

5. A company has multiple contract batch releasing sites in EU who are currently certifying the finished product packs imported into UK for marketing in UK. Will MHRA continue to recognise & accept the batch release certification done by EU QPs for the batches physically imported into the UK warehouse directly from a third country e.g. India? If so, for how long?

Batches or medicine may be imported into the UK via a wholesaler with RPI checks to verify that QP certification has been done in the EEA. this requires the batches to be sourced from the EEA and may not be shipped under pre-certification quarantine. This is covered in the guidance: <https://www.gov.uk/guidance/importing-medicines-on-an-approved-country-for-import-list-from-1-january-2021>. Product shipped to the UK from a third country must be received by a site named on a manufacture / import authorisation (MIA). The batch will require QP certification in the UK. This may be done either:

- by the UK QP in full (with the UK site named on the marketing authorisation as site of batch release)
- by the UK QP taking into account the EEA QP batch certification (with both the UK and EEA sites named on the marketing authorisation as site of batch release).

6. In accordance with the MHRA guidance, product can be imported into the UK from the EEA under a WDL. However, the HMRC guidance states that pharmaceutical products coming from the EEA into the UK require an import license (which to date has always been a MIA) but does not give any further clarity on this point. Could the MHRA clarify this point? For product coming from the EEA into the UK can this be done under a WDL or is an import license (MIA) required?

Batches of UK authorised medicines that have been QP certified in the EEA may be imported into GB by the holder of a wholesale dealer authorisation. This is covered in the guidance:

7. Will we need to add export to our WDA licence to cover for recalls back to the EU?

No, as recalled product would not be eligible for further distribution.

G. Northern Ireland

1. Does the year's derogation apply fully for Controlled Drugs?

The 12-month period of regulatory flexibility in respect of regulatory importation requirements extends only to the batch testing, import authorisation and QP certification required in NI or the EU.

H. Pharmacovigilance

1. When is it necessary to have a UK PSMF (pharmacovigilance system master file)?

There is an existing legal requirement to have a PSMF that describes the pharmacovigilance (PV) system applied to UK authorised products and this will continue to be the case from 1 January 2021. From 1 January, the scope of the UK PSMF will be UK nationally authorised products, including those authorised by mutual recognition or decentralised procedures.

2. What are the expectations for the UK PSMF?

Regulation 182(2)(b) of The Human Medicines Regulations 2012 as amended (HMR) requires that UK marketing authorisation holders (MAH) maintain and make available upon request of the MHRA a pharmacovigilance system master file (PSMF) for their UK authorised products (hereafter termed "the UK PSMF"). This requirement applies to nationally authorised products, including those authorised by mutual recognition or decentralised procedures.

The content and format requirements of the UK PSMF are outlined in Chapter 1 of the Commission Implementing Regulation (EU) No 520/2012 and Part 1 of HMR Schedule 12A. In summary, the UK PSMF must consist of the following:

- A cover page that includes:
 - the unique UK PSMF number assigned by the MHRA (when the request to register the UK PSMF is processed) and, for PSMFs that cover authorisations covering the whole of the UK or Northern Ireland only, the unique number assigned by the EV System to the PSMF when the XEVPRM is processed in the XEVMPD.
 - The name of the MAH, the MAH of the QPPV responsible for the pharmacovigilance system described (if different), as well as the relevant QPPV third party company name (if applicable).
 - The name of other concerned MAH(s) (sharing the pharmacovigilance system).

- The list of PSMFs for the MAH (concerning UK nationally authorised products with a different pharmacovigilance system).
- The date of preparation/last update.
- A PSMF main body consisting of seven sections that describe the global pharmacovigilance system applied to UK authorised products. Where the pharmacovigilance system for UK authorised products is the same as that for EU authorised products, it is likely that many of the main body sections could be interchangeable between the UK and EU PSMFs.
- A set of PSMF annexes specific to UK nationally authorised products, including those authorised for sale or supply in Northern Ireland only, Great Britain only or across the whole of the UK.

Statutory guidance on the UK PSMF is detailed in EU GVP Module II, which will be modified in a guidance note entitled “Exceptions and modifications to the EU guidance on good pharmacovigilance practices that apply to UK MAHs and the licensing authority”. This guidance note will be published shortly after The Human Medicines (Amendment etc.) (EU Exit) Regulations 2020 receive Parliamentary approval.

3. Is a separate UK PSMF required if we only have EU centrally authorised products?

No, centrally authorised products should be included in the EU PSMF required under Article 104(3)(b) of Directive 2001/83/EC.

4. My company has UK national marketing authorisations that are applicable in Northern Ireland. Does this mean I need a QPPV in the EU?

No, the QPPV for UK authorised products (including those that cover Northern Ireland and Great Britain) can reside and operate in the UK or the EU. This is because the Northern Ireland Protocol includes a specific paragraph in Annex 2 which states that the reference to ‘Union’ in the second subparagraph of Article 104(3) of Directive 2001/83/EC can be read as including the United Kingdom for national marketing authorisations issued by the MHRA in respect of Northern Ireland.

5. For how long can the UK QPPV reside and operate in the EU?

The legal presence requirements for the UK QPPV have been put in place to implement the Northern Ireland Protocol and they will remain in place for at least as long as the Protocol is effective.

6. The guidance on the MHRA’s website states that the UK QPPV can reside and operate in the UK or the EU. Does this mean that the previous requirement to establish a UK QPPV in the UK within 21 months of exit day does not apply anymore?

Under the Northern Ireland Protocol, the previous requirement to establish a UK-resident QPPV within 21 months of exit day no longer applies.

7. If an MAH decides to have a UK QPPV located in the UK and already has a EU QPPV based in the EU, will the UK QPPV only be responsible for the marketing authorisations specific to Great Britain whilst the EU QPPV will retain responsibility for the MAs that cover the whole of the UK or are specific to Northern Ireland?

No, the UK QPPV will have responsibility for all UK nationally authorised products, whether they are in respect of Northern Ireland, Great Britain or both. The EU QPPV has responsibility over EU authorised products, including CAPs. The requirement in UK law to have a QPPV for UK MAs applies to all MAs issued by the MHRA; UK-wide, GB-only and NI-only.

8. If there is currently an EU QPPV in Northern Ireland will this be acceptable by MHRA, or would there still be a need for a UK national contact person for pharmacovigilance?

From 1 January 2021, UK MAHs must appoint a qualified person for pharmacovigilance for UK authorised products (“the UK QPPV”) and this individual must reside and operate in the UK (GB or NI) or the EU. If the UK QPPV resides and operates in the EU, the MAH must establish a national contact person for pharmacovigilance who resides and operates in the UK. If the UK QPPV resides and operates in Northern Ireland, there is no requirement to establish a national contact person for pharmacovigilance. It should be noted that an EU QPPV (i.e. the QPPV responsible for EU nationally and centrally authorised products) cannot be located in Northern Ireland from 1 January 2021.

9. What is the difference in the role of the UK QPPV versus the UK national contact person for pharmacovigilance?

The UK QPPV will be responsible for the establishment and maintenance of the PV system that is applied to UK nationally authorised products.

The legal requirements for a national contact person (NCP) will be that they reside and operate in the UK, they report to the UK QPPV (not necessarily line management reporting) and they have access to the PSMF. They should have access to the ADR reports for UK authorised products, have knowledge of pharmacovigilance requirements in the UK and ensure that pharmacovigilance queries raised by the MHRA, including via inspections, are answered fully and promptly. There will be no requirement for 24/7 availability but, for periods of extended absence (e.g. maternity leave, long-term sick leave, etc.), we expect another individual to be notified to the MHRA as the NCP.

10. Do I need to appoint a deputy for the UK national contact person for pharmacovigilance?

There will be no requirement to appoint a deputy for the UK national contact person for pharmacovigilance but, for periods of extended absence (e.g. maternity leave, long-term sick leave, etc.), it is expected that another individual is assigned as the national contact person for pharmacovigilance and their details should be notified to the MHRA within two weeks of the change.

11. Does the UK national contact person for pharmacovigilance need to be available 24/7?

There will be no requirement for 24/7 availability but, for periods of extended absence (e.g. maternity leave, long-term sick leave, etc.), it is expected that another individual is assigned as the national contact person for pharmacovigilance and their details should be notified to the MHRA within two weeks of the change.

12. For ICSRs if testing is done by a MAH in 2019 do they need to perform testing again?

No, if testing was completed then no further testing is required.

13. What format will XMLs need to be in to be sent and received?

XMLs can be sent to the MHRA as either R2 or R3 via Gateway. The ICSR Submissions portal will create files in R2 format only but R2 or R3 files can be posted using the ICSR Submissions portal. The MHRA will send all XMLs to MAH in R2 format.

14. Is transmission expected to be a direct gateway to gateway communication or will MAH be expected to manually download E2B files similar to EVWEB?

The MHRA will send XMLs directly to MAHs via Gateway. If using ICSR Submissions the MHRA will automatically send to there and MAH will be expected to view and download from there.

15. Is MLM still applicable?

We will not be implementing a UK version of MLM, and companies are required to send MLM cases received from the EMA to the MHRA. We have implemented a technical solution to ensure duplicated submissions between companies will only be processed once. Marketing authorisation holders are expected to maintain awareness of possible publications through a systematic literature review of widely used reference databases (e.g. Medline, Excerpta Medica or Embase) no less frequently than once a week. The marketing authorisation holder should ensure that the literature review includes the use of reference databases that contain the largest reference of articles in relation to the medicinal product properties. In addition, marketing authorisation holders should have procedures in place to monitor scientific and medical publications in local journals in countries where medicinal products have a marketing authorisation, and to bring them to the attention of the company safety department as appropriate.