Medicines & Healthcare products Regulatory Agency

MHRA

Guidance: frequently asked questions

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Latest published guidance can be found at:
www.gov.uk/government/collections/new-guidance-and-information-for-industry-from-the-mhra

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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 Northern Ireland can be included in MRP/DCP so it will not be possible to include the UK in those procedures. However, where the UK and Republic of Ireland 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 – is the licence number in NI to remain as PL xxxxx/xxxx and for GB as PLGB xxxxx/xxxx? Will joint packs or GB / NI packs not be 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 where 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. **Can purely national licences remain as they are?**

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

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

8. **Section 15 of the CAP conversion guidance clarifies some of the requirements for the UK MAH following the UK's exit from the EU. 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 states that 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 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 already been automatically allocated PLGB numbers for converted EU MAs, do they need to submit a COA application when they submit the baseline? 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 provide 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 standstill period? What are the timescales for assessment?**

    The reliance route will also apply for variations. Further procedural guidance has been published. https://www.gov.uk/guidance/variations-to-marketing-authorisations-mas

12. **For in-flight procedures, where should we put the assessment reports in the eCTD?**

    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 as soon as possible 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 needed.

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. 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.

16. Please can we have more guidance on the timings and details for pre-vetting of materials for products which are 'In flight' at the start of 2021 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.

17. At what point will we need to add NI details to the pack?

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.

18. 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.

19. 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.

20. What information do I need to submit to the MHRA for marketing authorisations, variations and renewals to be approved by EMA for products in the community marketing authorisation procedure that have effect in Northern Ireland?

Marketing authorisations approved in the community marketing authorisation procedure (via the EMA) take effect in Northern Ireland. The MHRA no longer has access to EMA common repository and rapporteur assessment reports. Applicants for marketing authorisations, variations and renewals should submit the same information (eCTD) to the MHRA at the time of submission to the EMA. Submissions should be sent via the MHRA portal.

21. Some companies typically file centralised applications and wish to follow the Reliance model. However, is there a need for MHRA approval of the tradename for GB after the end of transition period, or are the EU proposed tradenames still applicable for both GB and NI?

Pre-submission naming advice is available through inventednames@mhra.gov.uk. The name will be assessed as part of the MA application, as it is now, and wherever possible will accept the product name agreed for the centralised application in Great Britain.

22. In the case of UK wide national MAs, if the batch release site is currently in the UK (e.g. for a product which is manufactured in the UK) will this be acceptable after 31 December 2021 for a product being supplied to NI?

Yes, this will be acceptable.

23. Will a UK-based MAH be acceptable where a product is being supplied to NI under a UK-wide national licence?

Yes this will be acceptable.

24. Does the MAH for the UK(NI) element need to sit in NI/EU/EEA for nationally authorised products outside of MR/DCP?

For products authorised nationally outside of the MRDC procedure, the MAH may be located anywhere in the UK or in the EEA.

25. To comply with EU guidance, companies are in the process of removing UK sites of release from EU licences under MR procedures. If NI remains part of the MR/DCP procedure and they retain a UK wide national licence, how can UK site of release be maintained especially for UK manufactured product? Also noting that EU testing will not be recognised after 2023 and a UK site will need to be on the licence.

Commission Technical Notice (2021/C 27/08) permits the use of batch testing and batch release done in GB until 1/1/22. These facilities should be named on the Marketing Authorisation to permit their use.

It will be possible to remove the GB batch test laboratory and batch release site (thereby staying in MRDC) and maintain supply to GB under the standstill provisions until 1 January 2023, when GB recognition of EU/EEA batch testing ends.

In the case of UK(GB) manufactured product, this does not impact the approved site of batch release. The QP of the GB manufacturer will be required to confirm compliance of the manufacturing process, whereas the batch release site for QP certification may be in EU/EEA. This is described in EU GMP Annex 16.

26. If a company chooses to retain NI in MR/DCP with a NI specific licence and request that separate MAs are issued for UK(NI) as a CMS, and Great Britain – how would this be managed? Is there a time limit on when this decision, or a decision to remove UK(NI) from the MR/DCP and maintain a national MA in GB only, needs to be taken?

It can be taken at any time before the procedure closes. Requests should be sent to MR-DCprocedures@mhra.gov.uk

27. For MRP/DCP, if following the new default position linking the GB approval to the NI approval as CMS, with one overall UK licence, what happens with regard to products supplied with devices? At some point a UKCA mark for the devices will be needed but companies won't be able to make this update via the MRP/DCP as it is UK specific. Will this necessitate companies either removing GB/NI from the procedure completely or having separate GB and NI licences?

The impact on co-packaged devices will be considered and advice issued. The UKCA mark is not required until June 2023.

28. If a UK-wide licence is being managed through UK(NI) MR/DCP Procedure, will submissions need to be processed through CESP or the MHRA Portal?

These applications will need to be submitted through CESP.

29. Are duplicate CP products (clones – i.e. identical dossier, different tradenames) included in the scope of non-GB converted CP dossiers?

Yes, they are included.

30. Does the MHRA envisage that joint packs could be possible for CPs between NI and GB? An EMA meeting at the end of November said *"for CAPS we can have joint GB/NI pack so long as the leaflet is in line with the EU aquis. Package leaflet must be in line with EU licence. UK administration information will go in the bluebox and other countries in the multi pack proposal will have to agree to this".* This would be helpful to understand which packs companies can supply to NI and which other markets they can be shared with.

Yes, we envisage that this is possible. Joint packs with EU MS are also possible in line with EU guidance. For example, the HPRA has published advice on this.

31. What is the update on MAH location for MR/DCP products, given the EU position?

The UK position is that the MAs granted by MHRA at the end of a- MR or DC procedure may continue to have the MAH located anywhere in the UK. A GB based MAH will not be accepted for the MAs granted in the Member States at the end of the procedure.

32. With regard to being out of compliance to the EU position – there are issues starting with the submission of the new version of the eAF which now no longer includes UK as an option.

New applications made through MRDC procedure will have to choose NI as the target market.

33. For licences which are being Grandfathered to GB licences, will the MHRA be using these dossiers for the purposes of Northern Ireland as well as GB?

A separate application form will be needed for GB but duplicate submission of the supporting technical dossier is not required.

34. How will differences between the CAP and GB licences be managed e.g. Batch release site as EU have requested removal of UK Batch Release from CAP licences, MAH details?

If the MAH intends to use UK batch release sites for GB these can be named on the application form.

35. If a licence is not being Grandfathered because it is not and will not be marketed in the UK, including NI, will a baseline dossier still be required?

Yes, it is still required as the product may still be marketed in Northern Ireland in the future.

36. If the National Assessment Route is to be used for a new MAA or a Variation, will the EMA submission package provided to the MHRA for NI be used to support the PL (GB) application or will a separate submission be required?

If the EU reliance route is used there is no need to resubmit the supporting data package.

37. Can MAHs submit PIP amendment applications/PIP Annual Reports before submitting the baseline application (for converted CAPs)?

Yes, if an EU-PIP has been agreed prior to 1 January 2021, MAHs are able to submit PIP modifications, annual reports and compliance check requests via the PIP portal of MHRA Submissions irrespective of whether the baseline application has been submitted. The PIP portal should accept EU-PIP numbers for those agreed prior to 1 January 2021. Relevant paediatric supporting information can be uploaded into the submission, including anything amended or new since the currently agreed PIP. Paediatric User Guides for each submission type are available from the guidance tile of MHRA Submission PIP portal.

38. The table in the grandfathering guidance just says " - If the identical changes have already been approved for the corresponding centralised product and provided evidence of this is included as part of the submission to the MHRA, the variations will be processed under the recognition route." Will a 'letter of intent' be needed for this process?**

No letter of intent is required for variations.

39. It is understood that CESP can still be used for NI as a CMS in MRPs/DCPs. Can it also be used for UK wide Marketing Authorisations (including NI)?

CESP can only be used if NI is a CMS in a DC or MR procedure.

40. The guidance 'Procedural advice for Northern Ireland on applications for EC Centralised MAs' states CP MAs not grandfathered into GB MAs require a baseline submission and all subsequent lifecycle maintenance submissions to EMA are also to be submitted to the MHRA. Does this also apply to grandfathered CP MAs for which a variation is only submitted to EMA, and not for the GB MA?

Yes, it applies to all submissions made to EMA because MHRA does not have access to the common Repository, but the EU MA is valid in NI.

41. Is it possible for Northern Ireland to be RMS in MR/DCP procedures?

No, the Northern Ireland Protocol is clear that UK(NI) cannot lead assessments on behalf of the EU.

42. Can the MHRA comment during the procedure on variations submitted with UK(NI) as a CMS in an EU procedure?

Yes, MHRA can submit comments as CMS.

43. Is the MHRA going to issue its own set of application forms as the eAF form only gives the option of United Kingdom (Northern Ireland)?

The UK may issue its own application form in due course but until then companies can continue to use the EU eAF. We will shortly be publishing an interactive tool to assist companies to complete the form and advise what information should be included in the cover letter.

44. For NI as CMS in MRP-DCP, can the MAH be based in mainland GB, and will MHRA (acting as NI regulator) confirm to RMS during validation?

The MAH can be located in GB for UK wide MAs including those applied for through the DCP procedure. MHRA will confirm this if asked.

45. Is it possible for a product to have two MAs with a single MA number; one for NI which will still be in the DCP/MRP and one for GB which will be national?

No, it is not possible to have two MAs with a single number.

46. Can the MHRA confirm that the MAH can be located anywhere in the UK or EU/EEA both now and after the end of the two-year standstill period? If the guidance changes once again and a MAH is required to be located in the UK after the end of the standstill period, will MHRA give industry at least 12 months' notice to make the Change of Ownership applications in the future?

The MHRA will give sufficient notice to companies if changes are proposed to the current arrangements.

47. Where can MAH be located for UK wide MAs where NI is a CMS in a MR/DCP?

The MAH can be located anywhere in UK.

48. The MHRA states that the MAH can be in the EU. Is this an interim measure or likely to be in place permanently?

The MHRA will give sufficient notice to companies if changes are proposed to the current arrangements.

49. Can the MHRA grant UK wide Marketing Authorisations?

Yes, unless a product fall within the mandatory scope of the EU centralised procedure.

50. Can a company submit nationally to MHRA to get a UK wide MA or does NI have to form part of the MR/DCP?

A national application for a UK wide MA can be made.

51. Provided MAHs have not opted out, can MHRA confirm that the CAP MA will be valid in NI and GB until the baseline submissions have been submitted (deadline 1 January 2022)?

The EU centralised authorisation remains valid in NI regardless of whether or not the MAH has opted out from GB. The CAP is deemed to have been converted into a GBMA unless the company has opted out on or before 21 January 2021.

52. Is the reliance/recognition of CPs only in place for 2 years (standstill guidance) or will this continue longer term?

This route of application will be reviewed in due course.

53. Will the DCP/MRP reliance procedure continue after standstill (2021, 2022)?

This route of application will be reviewed in due course.

54. If UK(NI) remains in a DCP and GB is aligned to it, it is clear that variations will be processed via the DCP/MRP (CESP). Will any additional submission be required for the purpose of the GB MA?

No additional submission will be needed if there is a UK wide MA.

55. Can the MHRA comment during the procedure on variations submitted with UK(NI) as a CMS?

Yes, UK(NI) as CMS can submit comments.

56. For UK wide licenses (PL xxx/xxx) which are already granted as part of MR-DC variations, companies will continue to select UK(NI) in the MR-DC eAF and submit via CESP. Do companies also have to submit to the MHRA for the identical variation via the Portal?

No a separate submission is not necessary.

57. For variations submitted for DCP/MRP with UK(NI) as CMS – will the MHRA be expecting a parallel submission for GB?

A separate submission will not be necessary if the MA is a UK wide MA.

58. Regarding Type IA variations for products authorised under EU DCP or MRP, please confirm that where a UK wide MA is involved, since the MR/DC variation decision applies UK wide, it can be implemented unless the MHRA notifies the MAH within 30 days of the RMS decision that it cannot be accepted in Great Britain.

Type IA variations are ‘do and tell’ and are therefore regarded as already implemented unless the MHRA advises the MAH within 30 days that they have not been accepted.

59. What is the fee for the Accelerated Assessment 150-day licensing procedure?

The UK national fees apply. Please visit https://www.gov.uk/government/publications/mhra-fees

60. Where NI remains within a MRP/DCP, and GB is separate and MHRA recognises MRP/DCP variation decisions, will there be two fees payable to MHRA (CMS fee plus a national follow on)?

If there are two separate MAs the variation to NI will attract the relevant CMS fee and the GB MA variation will attract the relevant reliance fee.

61. Does a GB wholesale dealer who will be importing Qualified Person (QP) certified medicines from the EEA, and ensuring certain checks are made by the Responsible Person (import) (RPi) need to get title in order to import such products?

The guidance on sourcing medicines from an approved country says (penultimate paragraph of section 1.1; emphasis added):

"An EEA manufacturer or wholesaler may only supply a licensed medicine to a wholesaler in Great Britain. The sale and supply to an authorised person (hospital, doctor or retailer) must be from a UK licensed wholesaler."

Authorised medicines may only be sold or supplied on the UK market if they are in accordance with their marketing authorisation (i.e. QP certified). The first step of placing the product on the GB market is for the product to be imported into GB by a wholesaler (who performs the necessary checks). The wholesaler can then sell or supply that medicine to another wholesaler, or to an authorised person.

The UK wholesaler who places medicines on the GB market must therefore take title to each batch to sell or supply.

62. It is noted that the reliance route has been included for Type IB and II CP variations. Will consideration be given to introducing the reliance route also for CP renewal applications?

We will take the EU decision on the renewal into account, but we will also consider introducing the reliance route.

63. Please confirm that the MHRA will continue to accept a shortened renewal for products authorised under Article 10(1) and for generic products previously authorised via the Centralised Procedure.

We will continue to accept a shortened renewal procedure for products authorized on a national basis. For converted CAPS we expect the same renewal dossier as that submitted to the EMA.

64. For CP renewals that were submitted before 01 January 2021 to EMA for products authorised under Article 10(1), can a company resubmit these renewals to MHRA as shortened renewals? Please can you confirm that this will be acceptable?

We expect the same dossier to be submitted to us as for the centralised product.

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).

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 January 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 January 2021, should the results be posted onto the publicly accessible database that the study was registered on (for e.g. clinicaltrials.gov)?**

   This is correct. Please see guidance here: 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. 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

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 January 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.

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, needs 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 January 2021? Do these need to have the UK Responsible person identified on the packaging from January 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 need to have either a UKCA marking 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 marking on your device, you will not be required to re-label the device with a UKCA marking until 1 July 2023 for placement on the Great Britain market. Devices can have both markings 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, needs to be included on product labelling where the UKCA marking 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.

6. **Does the deal deliver anything bespoke for medical devices?**

   The deal contains several important provisions which will benefit medical devices. The agreement ensures that EU member states continue to cooperate with the UK on market surveillance and includes provisions on marking and labelling. It also includes a commitment that allows conformity assessment bodies to use subcontractors in the other territory to perform testing or inspections in relation to required procedures. These provisions will ensure that both parties are able to work together to remove unsafe devices from their markets, that medical devices are effectively labelled and there is ongoing opportunity for further collaboration.

7. **Will the UK seek to agree recognition of conformity assessment for medical devices outside of the FTA?**

   The UK will continue to cooperate closely with the EU on the regulation of medical devices and seek out opportunities, where appropriate, to agree new ways of working.

8. **Will the EU recognise the UKCA marking? And if they do will the UK continue recognising the CE marking after the 30 June 2023?**

   The UKCA marking will not be recognised in the EU after the end of the transition period. The UK has been clear that CE marked devices will only be accepted for a period of 2.5 years.

9. **How do I register with the MHRA? What does the registration process involve?**

   Detailed information on how to register with MHRA can be found in the MHRA's registrations guidance. (https://www.gov.uk/guidance/register-medical-devices-to-place-on-the-market)

10. **Is the UK Responsible Person required to have any specific qualifications or experience?**

    There aren't any specific requirements for qualifications or experience, so long as the UK Responsible Person is competent to carry out the responsibilities of a UK Responsible Person as set out in our guidance. (https://www.gov.uk/guidance/regulating-medical-devices-in-the-uk#responsible)

11. **Do manufacturers need to report incidents to the MHRA?**

    Where there is a medical device incident, the report should be made to the National Competent Authority in the country where the incident occurred. In cases where Great Britain or Northern Ireland are affected, we would expect the manufacturer to notify the MHRA as the UK's standalone medical devices regulator.

    Where the manufacturer initiates a Field Safety Corrective Action, they should issue a notification to the Competent Authorities of all countries affected at the same time and also to the National Competent Authority responsible for the manufacturer.

If the incident did not occur in the UK, the manufacturer would not be required to report this to the MHRA.

Further information about reporting adverse incidents and corrective actions to the MHRA is available for manufacturers of medical devices.

https://www.gov.uk/government/collections/medical-devices-guidance-for-manufacturers-on-vigilance

12. What are the responsibilities of importers/distributors?

In cases where the Great Britain or Northern Ireland importer is not the UK Responsible Person or NI Authorised Representative, the importer will be required to inform the relevant UK Responsible Person or NI Authorised Representative of their intention to import a device. In such cases, the UK Responsible Person or NI Authorised Representative will be required to provide the MHRA with a list of device importers. We will provide further guidance in due course.

Other than the above requirement, there will be no additional obligations on distributors or suppliers of medical devices. Existing obligations around storage, transportation and checking device labels for the CE marking or UKCA marking will continue to apply. The importer's name and address will not need to be present on the label unless the importer or distributor is acting as the UK Responsible Person for the purposes of the UKCA marking.

13. Will the MDR and IVDR apply in NI?

The Medical Device Regulations (2017/745) and the in vitro Diagnostic Medical Device Regulations (2017/746) will apply in Northern Ireland from 26 May 2021, and 26 May 2022 respectively, in line with the EU's implementation timeline.

14. When can I start to use the UKCA marking?

Manufacturers will be able to use the UKCA marking from 1 January 2021 on a voluntary basis. The legal obligation to use it will not apply until 1 July 2023.

15. Will devices requiring the UKCA marking need to undergo a completely new conformity assessment route?

Yes, this will require a new conformity assessment for the purposes of the UKCA marking. The conformity assessment process for the UKCA marking mirrors the processes set out under the MDD, IVDD and AIMDD which have been transposed into UK law through the UK Medical Devices Regulations 2002. The assessment time will vary depending on the devices under assessment and the resources of the Approved Body performing the assessment.

16. For class I devices when the manufacturer is not based in the UK then the devices must be registered from 1 January 2022 for the GB market. For the NI market the requirement to register with the MHRA in Jan 2021 is for class I devices when the manufacturer or Authorised Representative is based in NI. Class I devices where the manufacturer is not based in NI are not included on the list, therefore what is the requirement for registration class I devices?

For the purposes of the NI market, where the Class I manufacturer or its Authorised Representative are not based in NI, they must register in the EU country where the manufacturer or the Authorised Representative is based. There is no requirement to register this Class I device for the purposes of NI.

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.

3. **Is the MHRA negotiating with EMA for access to the common data repository to avoid duplicate submissions?**

   The MHRA is in correspondence with the EMA regarding access to the Common Repository

F. Supply (including OCABR)

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, on which the MHRA can provide details. However, it will not necessarily be as simple as moving stock, as a GB licence will be needed for the product, but this can be gained via a UA.

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

   RoI does permit wholesalers to supply products licensed for another market. This is 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. **Will the UK's National Institute for Biological Standards and Control (NIBSC) continue to be a member of the EU OCABR network, and will the UK and EU still mutually accept each other's OCABR certificates?**

   No, NIBSC is now a standalone National Control Laboratory. Manufacturers are asked to follow this guidance https://www.nibsc.org/about_us/latest_news/guidance_for_mfrs.aspx for independent control testing of batches of biological medicines for use in the United Kingdom.

4. **Is there any possibility post 1 January 2023, that the UK would continue to accept EU testing and release sites?**

   As with all our trading partners, we remain open to agreeing further arrangements with the EU to address regulatory barriers to trade. The TBT chapter in the UK-EU FTA is intended to be a framework for bilateral cooperation that can be built on in future. Continuity of supply, patient access and safety will always be the priority for government and we will continue to work with the sector to understand the impact of the UK's standstill measures on the supply of medicines to the UK.

5. **If UK QC testing is required from 1 January 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 January 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 January 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 January 2023.

6. **A company has multiple contract batch releasing sites in EU which are currently certifying the finished product packs imported into UK for marketing in UK. Will the MHRA continue to recognise and 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 of 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 that batches 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 considering the EEA QP batch certification (with both the UK and EEA sites named on the marketing authorisation as site of batch release).

7. **In accordance with the MHRA guidance, products 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 products 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: https://www.gov.uk/guidance/importing-medicines-on-an-approved-country-for-import-list-from-1-january-2021.

8. Will we need to add export to our Wholesale Distribution Authorisation (WDA) licence when products are recalled to the EU?

No, as a 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 continues to be the case from 1 January 2021. The scope of the UK PSMF is 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 like EVWEB?

The MHRA will send XMLs directly to MAHs via Gateway. When using ICSR Submissions, the MHRA will automatically send to this system and the 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. 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.

16. Is it acceptable to include the most recent copy of the PSMF summary in baselines in accordance with the update that was made to the Article 57 database in 2020?

According to guidance published on our website, *"Historical EU information about the PV Master File, etc. in module 1.8. is not required. New information must be submitted as a later type IA variation."*
Detailed guidance on the submission of type IA variations for converted EU marketing authorisations (following submission of the baseline initiating electronic Common Technical Document (eCTD) sequence) is already published on our website here:

Guidance on qualified person responsible for pharmacovigilance (QPPV) including pharmacovigilance system master files (PSMF) - GOV.UK (www.gov.uk)

17. How will PRAC recommendations be managed by the MHRA? Will they be considered for UK products?

MAHs should continue to implement PRAC decisions and should continue to monitor the EMA website. MHRA will contact MAHs regarding UK specific requirements.

18. Once a company has a UK specific PSMF number, what is the time frame for submission of the respective variations?

This is covered in detail on our website at the following link:

Guidance on qualified person responsible for pharmacovigilance (QPPV) including pharmacovigilance system master files (PSMF) - GOV.UK (www.gov.uk)

19. For ongoing PASS for Centrally authorised products, are there any specific separate submissions (interim/final reports) to MHRA as well as PRAC?

For PASS studies, where progress or interim reports are required you will be notified by MHRA Where such requests are made the progress/interim reports must be submitted to the competent authorities of the Member States in which the study is conducted for products authorised in respect of Northern Ireland. We request that you inform us where you have a progress/interim report via Pharmacovigilanceservice@mhra.gov.uk and we will advise you on the appropriate means of submission.

For non-interventional PASS, MAHs must submit a final study report to the MHRA and to the PRAC (unless the study is to be conducted in the UK only) for products authorised in respect of Northern Ireland, and to the MHRA for products authorised in respect of Great Britain only.

20. Will MHRA be producing versions of the GVP documents which include the exceptions and modifications alongside the existing text? To aid review of the 100-odd page document. Any plans for a new MHRA GVP "Purple Guide"?

We have no plans to produce a consolidated document that merges EU GVP with the exceptions document. The MHRA will consider in the future producing standalone guidance for the UK but there is no timescale for this. There are no plans to update the Purple guide.

21. The MHRA has requested that If the PSUR includes signal correspondence to an important medical risk or if the MAH has been requested to assess a signal by another regulatory authority the MAH must notify the MHRA. Can you clarify why this has been requested as it's a duplication of work since this info is provided in the PSUR?

The MHRA has requested this to ensure the effective tracking and management of signals. MAHs should notify us via e-mail: SignalManagement@mhra.gov.uk

22. Does the MAH need to notify the MHRA of all requests they get from HAs to perform signal assessments, irrespective of the which HA the request is from? There are other HAs with a similar requirement but MAHs only need to notify them if gets requests from certain HAs (e.g. FDA, EMA, TGA), but not all?

We are reviewing our requirements in this area and will update the guidance in due course. In the meantime, please notify us of all requests.

23. Has the MHRA provided their expectation with regards to the timelines for sending validated signals that are published on the EMA site for PRAC discussion and are not emerging safety issues?

This guidance was developed prior to clarity on our regulatory position with NI. As we do now have a formal regulatory need for monitoring EMA materials in respect of NI we have reviewed this requirement and can confirm that MAHs will not need to send signals raised by EMA/PRAC to the MHRA. We will shortly be updating guidance to reflect this.

24. MHRA has published a list of cases received on 31 December 2020 from the European Medicines Agency. If there are more cases that were submitted to EMA between 28th and 31sT Dec which are not listed on the MHRA list then the expectation is to resubmit those cases to the MHRA via the new reporting process?

The MHRA published a reconciliation report of all reports received from the EMA between 28 and 31 December 2020. Any MAH reports that are not in list need to be resubmitted directly to the MHRA. If MAHs have any questions on this please contact E2B.Support@mhra.gov.uk.

25. Is there any available guidance on how ICSRs will be sent to MAHs (i.e. ASPRs)? and how to avoid duplication of NI ASPRs coming from MHRA and reports downloaded from EVWEB?

The MHRA is only sending ICSRs regarding Great Britain to MAHs. Any Northern Ireland ICSRs are being sent from the MHRA to the EMA only. MAHs are then expected to download these from the EMA. This was done to ensure the MHRA meets its reporting requirements as the regulator of Northern Ireland and to prevent the duplication of reports sent to MAHs.

26. Can MAHs submit a PSUR before submitting the baseline application (for converted CAPs)? If so, how should it be submitted to the MHRA?

Yes, the PSUR can submitted before the baseline. The submission should be made via the submissions portal for PSURs following the instructions.

27. Do PSURs for centralised products with respect to NI need to be submitted to the MHRA?

PSURs for centrally authorised products should be submitted to the EU PSUR Repository only.

28. For converted CAPs, what is the procedure number for PSUR to indicate on MHRA submissions. Is this the same as to EMA or specific UK number?

The procedure number included on the EURD list should be used.

29. Will the MHRA issue a UKRD list and if so, what will be the timelines and when will further information be available?

This will be in the future and we don't have any timescales for this. We will provide information on this well in advance of any change.

30. Please confirm whether PSUSAs ongoing at 31 December 2020 will be concluded by MHRA and not via the EMA procedure? If so, when should recommendation be expected?

PSUSAs ongoing on 31 December 2020 will be concluded by the EMA and MAHs should follow the PRAC outcome.

31. Will the MHRA still accept EU PSURs and EU RMPs after 1 January?

We will continue to accept the EU version of the PSUR and RMP. There are no anticipated changes to the format. UK-specific information should be included in an annex. We have not developed templates for these annexes but will keep the need for templates under review.