The Windsor Framework

The impact to pharmacovigilance activities - for PV and Regulatory

A joint webinar, presented by

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26th February 2025

We will cover...

- A recap on the background of the Windsor Framework
- Windsor Framework measures and impact to Regulatory
- Overview of impact to artwork and supply
- Impact to Marketing Authorisations
- MHRA categorisation of products for PV purposes

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- Individual Case Safety Reports (ICSR)
- Periodic Safety Update Reports (PSURs)
- Post authorisation safety studies (PASS)
- UK-specific actions
- Implementation of EU Outcomes / Safety Referrals
- UK Qualified Person for Pharmacovigilance (QPPV)
- UK Pharmacovigilance Master File (PSMF)
- Notification of QPPV and PSMF to XEVMPD

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Leah Heathman BSc MTOPRA Dip CNM

- Managing Director and Senior Regulatory Consultant at Fusion Pharma
- 23 years in Pharma Industry
- Set up Fusion Pharma in 2013
- Supporting Industry through Brexit with webinars, articles and free consultations
- Our 7th webinar on the Windsor Framework

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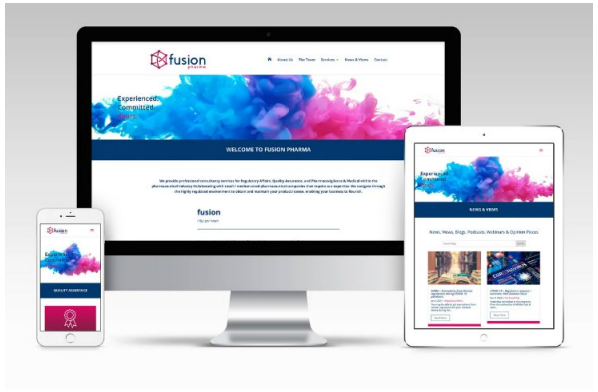

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The Windsor Framework: Recap on the background

2020

UK formally left EU

(voted to leave in 2016)

Transition period started

2021

Transition Period Ended

EU law no longer applied to GB

EU law continued to apply to NI via the 'Northern Ireland Protocol'

2023

The Windsor Framework announced

Amends and replaces the Northern Ireland Protocol and brings NI back into the UK trade laws

2025

Windsor Framework Applies

All measures implemented

1st Jan 2025

Regional explanation

United Kingdom (UK)
England
Northern Ireland (NI)
Scotland
Wales

Great Britain (GB)
England
Scotland
Wales

Ireland (IE)
A separate country and remains part of the EU

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The Windsor Framework: Measures commenced 1st Jan 2025

- **All new medicines for the UK market will be authorised by the MHRA**
- **All outer packaging* must state 'UK Only' and can only be distributed/sold within UK**
- **The Falsified Medicines Directive (FMD) will not apply to NI (anti-tamper devices should remain on packaging)**

* Outer packaging could be carton or label (depending on whether the medicine has secondary packaging)

Work carried out in Regulatory 2023 - 2025

- All GB and UK packaging has been updated to state 'UK Only' (sticker possible for 6 months)
- Art 61(3) / variations submitted to register updated artwork for all marketed products
- Project planning with Supply Chain to ensure:
  - implementation of new artwork from 1st Jan
  - continued supply to GB, NI and EU (complexity with shared packs and FMD)
  - early implementation where possible
- NI packs shared with EU markets are being updated to remove NI – work still in progress

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The Windsor Framework: Overview of impact to artwork and supply

GB / UK packs

- These have been updated to state ‘UK Only’ on the outer packaging
- Complete packs can no longer be shared since they state ‘UK Only’
- Since Brexit, the Falsified Medicines Directive (FMD) no longer applied in GB, since 1st Jan 2025 this also includes NI

EU packs

- Many EU packs were shared with NI, this is no longer permitted
- The EMA has given up to 36 months from 1st Jan 2025 to update artwork to remove NI, although it is expected to be removed at the next opportunity
- Individual member states have shown flexibility however check with them directly
- QPs can still release EU packs with NI details to EU markets (*these cannot be distributed to NI, GB, UK*)

All packs QP released prior to 1st Jan 2025, may continue to be sold

PILs and inner packaging can continue to be shared, as long as the content is authorised in all relevant markets

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The Windsor Framework: Impact to Marketing Authorisations

There has been a lot of changes to licencing in the UK:

Licence Type	Before 1st Jan 2025 (pre-WF)*	Since 1st Jan 2025 (post-WF)	Comments
EU	EMA continued to include NI in Centralised Procedure	N/A – no longer possible	NI has been removed from the CP.
PL	UK-wide licence, achieved through: • Existing PL licences (i.e. pre 2021), or • MRP / DCP (post 2021)	All new products will be UK-wide and authorised by MHRA.	Existing UK-wide MRDC licences can remain in the procedure unless the MHRA requires specific changes, at which point UK(NI) will need to withdraw from the procedure.
PLGB	GB-only licence, achieved through: • Grandfathering a Centrally Authorised Product (CAP), or • New licence granted by MHRA (through ECDRP or IRP)	N/A – no longer issued	**Note!** PLGBs previously granted will maintain their PLGB prefix, but will now be considered UK-wide and the same as PLs.
PLNI	NI-only licence, achieved through MRDC Procedures where NI is a non-voting Concerned Member State (CMS).	NI-only licence. Can be applied for or retained through MRP / DCP.	**Note!** It is not possible to have a PLNI and a PLGB for the same product.

* Since 2021

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The Windsor Framework: Category 1 and Category 2 Products

- The Windsor Framework changes only covers those products which fall under the **mandatory scope** of the Centralised Procedure.
- The MHRA have split products into two categories, **Category 1** and **Category 2**.
- The MHRA have released a **list of all Category 1 Products**: Link
- All new products submitted from 1st Jan 2025 will be requested to select the appropriate category within the MHRA submissions portal, this will be confirmed by the MHRA within the grant letter.
- There is detailed guidance on MHRA website to help you determine which category your products are, we have summarised in the next page.
- There are differences in PV responsibilities depending on your product's category so work with Regulatory to determine this.

Mandatory scope of CP includes:

- HIV or AIDS
- cancer
- diabetes
- neurodegenerative diseases
- auto-immune and other immune dysfunctions
- viral diseases
- biotech medicines
- advanced-therapy medicines e.g. gene-therapy etc.
- orphan medicines (rare diseases)
- veterinary medicines for use as growth or yield enhancers

Optional scope of CP includes products that:

- contain new active substances for indications other than those listed
- are a significant therapeutic, scientific or technical innovation
- would be in the interest of public or animal health

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The Windsor Framework: Category 1 and Category 2 Products

	Category 1 (C1)	Category 2 (C2)
Scope	Products that fall within mandatory scope of CP	All other products
Product/ licence description	• Products within mandatory CP scope that were grandfathered CAPs (i.e. PLGBs) or authorised by MHRA since 1st Jan 2021. • Products within optional CP scope authorised by MHRA since 1st Jan 2021 (unless authorised in EU through NP or MRDCP). • New applications for products within mandatory or optional scope of CP. • Generic, hybrid or biosimilar products of C1 reference products for future applications. • Generic, hybrid or biosimilar products of all already authorised products (regardless of reference category). • All conditional marketing authorisations.	• Products that do not fall within the mandatory scope of CP. • New applications for products not within the mandatory or optional scope of CP. • Products that fall under the optional scope that were authorised through NP. • Products authorised prior to introduction of CP (introduced in 1995). • Generic, hybrid or biosimilar products of C2 reference products for future applications. • PLNIs (under MRDCP).
Applicable legislation from 1st Jan 2025	These products will be authorised in accordance with UK law .	These products will be authorised in accordance with UK law and applicable EU law.
	• Human Medicines Regulations 2012, Part 11 • Human Medicines Regulations 2012, Schedule 12A	• Human Medicines Regulations 2012, Part 11 • Commission Implementing Regulation (EU) No 520/2012 • EU Regulation 2023/1182 and Directive (EU) 2022/642

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Key Guidance and Resources

While the information in this article is considered to be true and correct at the date of publication, changes in guidance and/or experience may impact on the accuracy of the information. Please refer to the relevant guidance for the latest information:

The Windsor Framework (UK Government announcement)

MHRA Windsor Framework Hub

MHRA guidance on UK-wide licensing

MHRA guidance on labelling and packaging

MHRA Pharmacovigilance guidance and Q+A

MHRA list of Category 1 products

HPRA Brexit updates

HPRA Q&A

EMA Brexit Q&A

Windsor Framework: Pharmacovigilance Update

26-Feb-2025, version 2.0
Presenter: Sarina Norris

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- 16 years in Pharmaceutical, CRO and Medical Devices Industry, including 9 years at ADAMAS
- Conducted GVP audits, Gap Analysis and Consultancy activities
- Supported MHRA GVP, GMP and GCP Inspections
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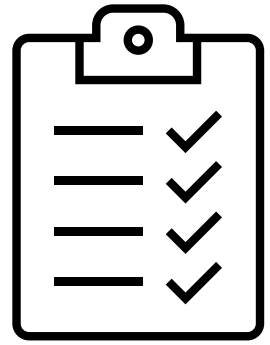
PV Process Updates:

Depending upon whether your product is a Category 1 or 2, this will determine the PV activities required from 01-Jan-2025.

Potential areas impacted by the changes could be:



- Individual Case Safety Reports (ICSR)
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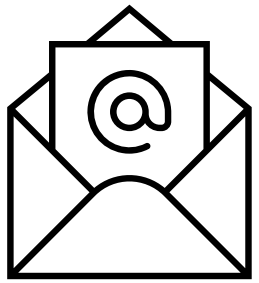
- Notification of QPPV and PSMF to the Extended EudraVigilance Medicinal Product Dictionary (XEVMPD)

ICSR Reporting

- MHRA Reporting:
  - All MAHs, irrespective of licence category (i.e., Category 1 or 2) must send all UK ICSRs and serious non-UK ICSRs which meet the MHRA reporting requirements to MHRA within 15 calendar days for serious ICSRs, and 90 calendar days for non-serious ICSRs

- EMA Reporting:
  - For Category 1 products where the MAH has an EU or EEA license for the same product, the MAH must continue to submit all serious UK and other country ICSRs to EMA within 15 calendar days and submit all non-serious ICSRs originating from NI in line with the EMA requirements.
  - For Category 2 products (and NI MAs) the MAH should submit all Serious UK and other country reports to EMA within 15 calendar days. Additionally, MAHs should submit all non-serious ICSRs originating from NI to EMA within 90 days.



PSURs

- MHRA can define UK-specific submission requirements for Category 1 product PSURs in the same way as for products historically authorised.
  - MHRA will define this at the time of authorisation or post-authorisation.

- Usually, PSUR submissions timelines will be in line with the EU and will follow the EU Reference Date (EURD) list. MHRA may define a UK-specific requirement, however this will be communicated to you. In the absence of this continue to submit in line with the EU.

- Submissions:
  - Category 1 – submit through the MHRA PSUR portal to MHRA. If the product is also licensed in the EU then also submit to the EU PSUR repository
  - Category 2 - submit via the EU PSUR Repository for EU single assessment. MAHs do not need to separately submit their PSUR to MHRA.

Note: Where the PSUR cannot be accessed from the EU PSUR Repository, the MAH may be requested to submit it directly to the MHRA via the MHRA PSUR Portal.

PSURs

Product Category	Territory	MHRA Portal Submission	EU PSUR Repository	Comment
Category 1	UK Only	Yes	N/A	
Category 1	UK and EU License	Yes	Yes	
Category 2 and NI MAs	UK Only	Not required*	Yes	*(providing MHRA can access PSUR in the EU PSUR Repository)
Category 2 and NA MAs	UK and EU License	Not required*	Yes	*(providing MHRA can access PSUR in the EU PSUR Repository)

Taken from:
[Pharmacovigilance following agreement of the Windsor Framework - GOV.UK]

Post Authorisation Safety Studies (PASS)

Category 1 Products

- Draft Protocols, significant amendments, and final study reports for all studies should be submitted to MHRA

Category 2 Products (and NI MAs)

- The draft study protocol should be submitted to both the EMA's PRAC and MHRA
- Significant amendments to the draft protocol should be submitted to both PRAC and MHRA

Note: if the study was requested by MHRA and conducted in the UK only, then only submission to MHRA will be required.

Major Safety Reviews and UK-specific actions

- MHRA may conduct a major safety review of medicines authorised in the UK, where concerns are identified related to product safety. MHRA will review the available data and consider what regulatory action may be needed, which will be communicated with you.

- Other safety reviews for UK products are conducted by the MHRA, which may be triggered by identification of a new safety signal or another piece of new information related to the product. MHRA will review the information and provide actions to you for implementation.

Note: If a UK-specific action impact on products authorised via the MRP/DCP procedure, and the action does not align with the Mutual Recognition position, then the MAH will need to withdraw from the MRP/DCP, which will result in a purely national, UK-wide MA i.e. a standalone UK authorisation.

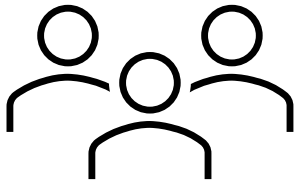
Implementation of EU Outcomes / Safety Referrals

Category 1

- There is no legal requirement for an outcome of an EU procedure to be implemented for a Category 1 product marketed in the UK only

- However, MAHs have an obligation to keep the marketing authorisation up to date with current scientific knowledge

- MAHs should continue to monitor the EMA and the MHRA websites for new information and update the authorisation as necessary within the context of the UK License, for example, where the terms of the MA differs between the UK and EU product.



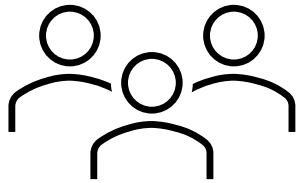
Implementation of EU Outcomes / Safety Referrals

Category 2 (and NI MAs)

- MAHs should continue to implement the outcome of relevant EU procedures, e.g. PSUR single assessments, EU pharmacovigilance referrals (Article 31 referrals) in line with EU timelines.

- MAHs should submit the relevant documentation to the MHRA and may be requested to submit additional information regarding the procedure to the MHRA.

Note: In exceptional circumstances where the outcome of an EU Safety Referral does not align with the interests of patient safety in the UK the outcome should not be implemented. MHRA will inform MAHs of the action to take as soon as possible, usually within 14 days of the publication of the EU decision, which will result in a standalone UK License.



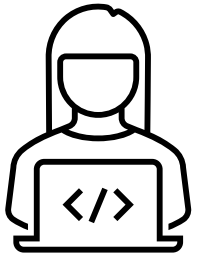
UK QPPV

- No changes to the UK requirements of the UK QPPV.

- The legislative reference for a product may change if a product is subject to HMR schedule 12A, rather than the EU Commission Implementing Regulation (CIR) 520/2012 due to product category.

- Legal requirements concerning the qualification and responsibilities of the QPPV:
  - Category 1 - now outlined within HMR Schedule 12A paragraph 10
  - Category 2 - requirements stated in the CIR Article 10

Note: The requirement in HMR schedule 12A mirrors the CIR requirements, therefore no differences exist in practical terms.



UK QPPV

Product Category	Territory	UK QPPV	EU-QPPV	EU-QPPV
		Can reside in EU/EEA or UK	Must reside in EU/EEA	Can reside in UK or EU/EEA
Category 1	UK only	Yes	No	No
Category 1	UK & EU license	Yes	Yes	No
Category 2	UK only	Yes	Subject to EU Directive 2022/642(13)*	Subject to EU Directive 2022/642*
Category 2	UK & EU license	Yes	Yes	No

Taken from:
[Pharmacovigilance following agreement of the Windsor Framework - GOV.UK]

UK National Contact Person for PV (NCP)

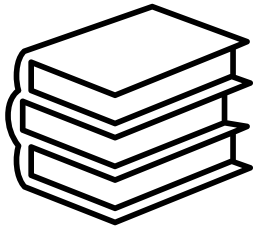
- There are no changes to the requirements to operate an NCP within the UK following the implementation of the arrangements for human medicines under the Windsor Framework on 01-Jan-2025.

UK PSMF

- A UK PSMF will be required for all UK marketing authorisations regardless of the route of authorisation.

- No changes to the operational implementation of the UK PSMF, but the current legislative reference for a product may change if a product is now subject to HMR schedule 12A rather than the CIR due to the product category concerning the format and content of the PSMF.
  - Category 1 - the legal requirements are outlined in HMR Schedule 12A Part I.
  - Category 2 - the legal requirements are outlined in Chapter I of the CIR will continue to apply.

Note: The HMR requirement mirrors that of the CIR and therefore no differences exist in practical terms.



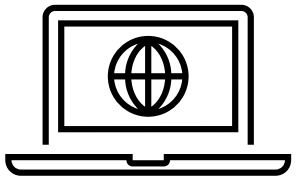
Notification of QPPV and PSMF to Extended EudraVigilance Medicinal Product Dictionary (XEVMPD)

Category 1 products

- Continue to follow the existing notification requirements.

Category 2 products

- MAH must notify the UK QPPV and UK PSMF details to the MHRA.
- Additionally, MAHs must also submit information on the UK QPPV and the location of the UK PSMF to the Article 57 database (XEVMPD) in accordance with Regulation (EC) No 726/2004 Article 57(2).

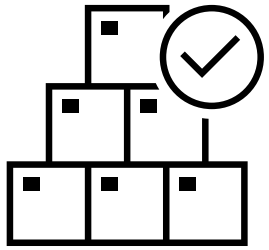


Summary

- Implementation due date was 01-Jan-2025 so please take any pending actions as soon as possible to maintain compliance

- The categorisation of your products determine which processes are impacted
  - Check product categorisation on the Category 1 list published by MHRA and any products not listed there are by default Category 2
  - Determine the impact to each of your PV systems and processes accordingly

- The legal basis has been updated. Category 2 products now fall under the EU legislation and as such there have been several changes to reporting and updates to EMA and the Article 57 database



References:

Guidance on pharmacovigilance procedures, updated 08-Jan-2025 - Guidance on pharmacovigilance procedures - GOV.UK

Guidance: Pharmacovigilance following agreement of the Windsor Framework, published 30-Aug-2024 - Pharmacovigilance following agreement of the Windsor Framework - GOV.UK

Exceptions & modifications to the EU guidance on good pharmacovigilance practices that apply to UK marketing authorisation holders and licensing authority Guidance note, Published 07-Feb-2025 - https://assets.publishing.service.gov.uk/media/67ab3564d41dfb0b59cec46d/Exceptions_and_modifications_to_the_EU_guidance_on_good_pharmacovigilance_practices_that_apply_to_UK_MAHs.pdf

Category 1 lists of products - Category lists of products - GOV.UK

List of authorised products - Marketing authorisations: lists of granted licences - GOV.UK