Combined Ways of Working Pilot: Post approval submissions

PLEASE NOTE: This guidance relates to post approval submissions for applications which have been submitted and approved via the Combined Ways of Working Pilot only.

Substantial Amendments

Step 1: Submission

Complete the Notification of a Substantial Amendment to a Clinical Trial form and the amendment tool (https://www.myresearchproject.org.uk/help/hlpamendments.aspx). The Notification of a Substantial Amendment form can either be completed as part of the amendment tool or found here.

A PDF version of the form and the amendment tool should be submitted along with any documents which are being amended via the new part of IRAS.

Where information in the EudraCT Annex I form is being amended, an updated version of the xml should also be provided. The changes may be highlighted but this is not mandatory.

Only substantial amendments should be submitted via this route. Amendments to studies taking place in the NHS (or HSC in Northern Ireland) which do not meet the criteria for a substantial amendment (substantial amendment details for the MHRA can be found here and details for the REC and HRA/HCRW Approval can be found here) should be submitted via e-mail to the REC. This is because the e-submission functionality for these types of amendments is still in development.

- A covering letter should be provided which contains the following table (in addition to what would standardly be included in the covering letter). Please indicate in the right hand column which documents are being submitted with the substantial amendment and, where relevant, the updated version number and/or document date.

Substantial amendment	**Yes/No**
Information	**Amendment**
1. SUBSTANTIAL AMENDMENT FORM:	
2. PROTOCOL	
3. INVESTIGATOR'S BROCHURE (IB)	
4. DOCUMENTATION RELATING TO COMPLIANCE WITH GOOD MANUFACTURING PRACTICE (GMP) FOR THE INVESTIGATIONAL MEDICINAL PRODUCT	

5. INVESTIGATIONAL MEDICINAL PRODUCT DOSSIER (IMPD)	
6. AUXILIARY (ie non-IMP) MEDICINAL PRODUCT DOSSIER	
7. CONTENT OF THE LABELLING OF THE INVESTIGATIONAL MEDICINAL PRODUCTS	
8. RECRUITMENT ARRANGEMENTS	
9. SUBJECT INFORMATION, INFORMED CONSENT FORM AND INFORMED CONSENT PROCEDURE	
10. NEW INVESTIGATOR	
11. NEW SITE	
12. PROOF THAT DATA WILL BE PROCESSED IN COMPLIANCE WITH UNION LAW ON DATA PROTECTION	
13. OTHER: PLEASE STATE BELOW	

Step 2: Validation

Validation checks will be completed on the substantial amendment by the MHRA within 3 days. This will involve checking that all of the relevant documents (as stated in the substantial amendment table copied to the covering letter) have been submitted and are readable, and that the correct organisation (REC / MHRA) and Part (Part 1 / Part 2) has been selected in the system. One validation check will be undertaken for the entire substantial amendment and only one validation letter will be issued by the MHRA. For substantial amendments to trials which involve sites in the NHS, the confirmation of categorisation will not be provided with the validation but will follow shortly afterwards.

Step 3: Co-ordinated assessment

The MHRA will determine whether the substantial amendment needs to be reviewed by the MHRA, the REC or both. This will be based on the information which is provided in the substantial amendment form (section A) and the information provided in the covering letter. Substantial amendments that need to be reviewed by the REC only will not incur a fee.

Where applicable, the relevant documents will be provided to the REC by the MHRA.

Step 4: Issuing an opinion

The final decision will be issued within 35 days. This will be a single e-mail with decision letter(s) attached.

Post approval reporting

Step 1: Submission

The following post approval reports should be submitted via the following routes:

Report	Submission route
Suspected Unexpected Serious Adverse Reaction (SUSAR)	Eudravigilance (EV Gateway or EVWEB) or eSUSAR website
Annual safety reports	CESP & E-mailed directly to the REC which approved the trial
Annual progress reports	E-mailed directly to the REC which approved the trial
End of trial notifications*	CESP & E-mailed directly to the REC which approved the trial

*If the trial has ended prematurely then a substantial amendment should also be submitted where it is necessary to seek ethical review of related actions such as informing participants and arranging continuing care and follow-up outside the trial. Please complete the end of trial notification form which can be found here.

Step 2: Acknowledgement

You will receive confirmation that the notification has been received.

Summary of changes

Summary of document changes			
Section	Change	Version	Date
Step 1 Submission	To confirm non-substantial amendments should be sent to the REC email.	2.8	4.6.2020
Step 1 Submission	Updated to refer to the amendment tool	2.7	1.6.2020
Throughout	Updated to reflect the roll out of the new part of IRAS	2.6	21.4.20
End of trial notification	To become post approval reporting	2.5	3.2.20
Document title	To reflect the broader scope of the document to include post approvals submissions other than amendments and end of trial notifications	2.3	7.10.19
Safety reports and progress reports	Section added to confirm that these reports should continue to be submitted as per normal process	2.3	7.10.19
Submission	Submission of substantial amendments should be via Eudralink and no longer via IRAS (until further notice)	2.1	3.5.19
Submission	All substantial amendments should be numbered sequentially, including the addition of a new site and PI	2.1	3.5.19
Submission	The submission of a new substantial amendment when an existing substantial amendment is under review should be avoided where possible.	2.1	3.5.19
Submission	Clarify that substantial amendments to add a new site and PI should be submitted via Eudralink	2.1	3.5.19

Submission	Clarification that substantial amendments which are an update to the IB should only be submitted when required	2.1	3.5.19