Amendment Tool

v1.6 06 December 2021

For office use

QC: No

Section 1: Project information

Short project title*:	Toxicity from biologic therapy (BSRBR-RA)
IRAS project ID* (or REC reference if no IRAS project ID is available):	64202 (minimal dataset) / REC Ref: 00/8/053
Sponsor amendment reference number*:	Substantial Amendment 30 (SA 30)
Sponsor amendment date* (enter as DD/MM/YY):	13 February 2024
Briefly summarise in lay language the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study. If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained (note: this field will adapt to the amount of text entered)*:	1) Change to method of collection for patient follow up data: Previously in the BSRBR-RA, follow-up Patient Reported Outcome Measures data (PROMs, e.g. HAQ, EQ-5D) was captured via paper questionnaires posted directly to study participants. Mailing of paper questionnaires was halted due to the move to the BSRBR-RA web-based data collection system for collecting data from clinicians. We would like to reintroduce the follow-up PROMs data collection from study participants using this same existing BSRBR-RA web-based data collection system. Baseline ePROMs have always been collected via the rheumatology teams when the participant is first registered in the study and this aspect will remain unchanged. 2) Increase in the size of the existing BSRBR-RA biosimilar cohort due to new drug licensing

Project type (select):	**Specific study**			
	Research tissue bank			
	Research database			
Has the study been reviewed by a UKECA-recognised Research Ethics Committee (REC) prior to this amendment?:	**Yes**		No	
What type of UKECA-recognised Research Ethics Committee (REC) review is applicable? (select):	**NHS/HSC REC**			
	Ministry of Defence (MoDREC)			
Is all or part of this amendment being resubmitted to the Research Ethics Committee (REC) as a **modified amendment** (i.e. a substantial amendment previously given an unfavourable opinion)?	Yes		**No**	
Where is the NHS/HSC Research Ethics Committee (REC) that reviewed the study based?:	England	Wales	Scotland	Northern Ireland
	Yes	No	No	No
Was the study a clinical trial of an investigational medicinal product (CTIMP) OR does the amendment make it one?:	Yes		**No**	
Was the study a clinical investigation or other study of a medical device OR does the amendment make it one?:	Yes		**No**	
Did the study involve the administration of radioactive substances, therefore requiring ARSAC review, OR does the amendment introduce this?:	Yes		**No**	
Did the study involve the use of research exposures to ionising radiation (not involving the administration of radioactive substances) OR does the amendment introduce this?:	Yes		**No**	
Did the study involve adults lacking capacity OR does the amendment introduce this?:	Yes		**No**	
Did the study involve access to confidential patient information outside the direct care team without consent OR does the amendment introduce this?:	Yes		**No**	
Did the study involve prisoners or young offenders who are in custody or supervised by the probation service OR does the amendment introduce this?:	Yes		**No**	
Did the study involve children OR does the amendment introduce this?:	Yes		**No**	
Did the study involve NHS/HSC organisations prior to this amendment?:	**Yes**		No	
Did the study involve non-NHS/HSC organisations OR does the amendment introduce them?:	Yes		**No**	
	England	Wales	Scotland	Northern Ireland
Lead nation for the study:	**Yes**	No	No	No
Which nations had participating NHS/HSC organisations prior to this amendment?	**Yes**	**Yes**	**Yes**	**Yes**
Which nations will have participating NHS/HSC organisations after this amendment?	**Yes**	**Yes**	**Yes**	**Yes**

Section 2: Summary of change(s)

Please note: Each change being made as part of the amendment must be entered separately. For example, if an amendment to a clinical trial of an investigational medicinal product (CTIMP) involves an update to the Investigator's Brochure (IB), affecting the Reference Safety Information (RSI) and so the information documents to be given to participants, these should be entered into the Amendment Tool as three separate changes. A list of all possible changes is available on the "Glossary of Amendment Options" tab. To add another change, click the "Add another change" box.

Change 1				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Other significant change to study documents (e.g. information sheets, consent forms, questionnaires, letters) that can be implemented within existing resource in place at participating organisations - Please specify in the free text below			
Further information In particular, please describe why this change can be implemented within the existing resource in place at the participating organisations (free text - note that this field will adapt to the amount of text entered)*	The amendment includes updated participant information and consent materials (now version 11, 01/03/2023) to reflect changes in how we collect follow up information from patients directly. Hospital/clinical follow-up remains unaffected and will continue to be provided by participating organisations via the same BSRBR-RA web based data collection system.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Remove all changes below	

Change 2				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Protocol - Non-substantial changes (e.g. not affecting safety or the scientific value of the trial)			
Further information (free text - note that this field will adapt to the amount of text entered):	The amendment includes an updated study protocol (now version 2.1, 13/02/2024) to reflect changes in how we collect follow up information from patients directly. Hospital/clinical follow-up remains unaffected and will continue to be provided by participating organisations via the same BSRBR-RA web based data collection system.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Remove all changes below	

Change 3				
Area of change (select)*:	Study Design			
Specific change (select - only available when area of change is selected first)*:	Data collection, transfer or processing of identifiable participant information - Changes in arrangements or organisations involved (other than the addition of new participating organisations)			
Further information (free text - note that this field will adapt to the amount of text entered):	Previously in the BSRBR-RA, follow-up Patient Reported Outcome Measures data (PROMs, e.g. HAQ, EQ-5D) was captured via paper questionnaires posted directly to study participants. Mailing of paper questionnaires was halted due to the move to the BSRBR-RA web-based data collection system for collecting data from clinicians. We would like to reintroduce the follow-up PROMs data collection from study participants using this same existing BSRBR-RA web-based data collection system. Baseline ePROMs have always been collected via the rheumatology teams when the participant is first registered in the study and this aspect will remain unchanged. It is worth reiterating that this data has always been collected and that there is no change apart from the vessel used to collect this data.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Remove all changes below	

Change 4	
Area of change (select)*:	Participant Procedures
Specific change (select - only available when area of change is selected first)*:	Participant procedures - minor change that can be implemented within existing resource at participating organisations - Please specify in the free text below
Further information In particular, please describe why this change can be implemented within the existing resource in place at the participating organisations (free text - note that this field will adapt to the amount of text entered)*	Previously in the BSRBR-RA, follow-up Patient Reported Outcome Measures data (PROMs, e.g. HAQ, EQ-5D) was captured via paper questionnaires posted directly to study participants. Mailing of paper questionnaires was halted due to the move to the BSRBR-RA web-based data collection system for collecting data from clinicians. We would like to reintroduce the follow-up PROMs data collection from study participants using this same existing BSRBR-RA web-based data collection system. Baseline ePROMs have always been collected via the rheumatology teams when the participant is first registered in the study and this aspect will remain unchanged. It is worth reiterating that this data has always been collected and that there is no change apart from the vessel used to collect this data.

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	

Remove all changes below

Change 5	
Area of change (select)*:	Study Design
Specific change (select - only available when area of change is selected first)*:	Participant numbers - Significant change to sample size
Further information (free text - note that this field will adapt to the amount of text entered):	The BSRBR-RA has been collecting observational cohort data on patients receiving biologic therapy for rheumatoidarthritis in the UK for over 20 years. Biologic DMARDS (bDMARDS), including the TNF inhibitors (TNFi including Enbrel, Remicade, Humira), first became available to treat RA in the late 1990's, having a profound effect on the outcome of many patients with RA. In 2001, the BSRBR-RA was set up to monitor the long-term effects of these drugs. Since then, newer advanced therapies have been developed based on this knowledge. These later drugs included the IL-6 inhibitors (RoActemra) and biosimilars (Inflectra, Remsima, Benepali, Flixabi) which were also added as new cohorts to the BSRBR-RA study. As part of substantial amendment SA20 (approved 16/03/2015), we received approval to recruit a cohort of 2000 biosimilar patients. At the time, only two biosimilar drugs were available for use in the UK. Substantial amendment SA25 (approved 24/08/2017) increased the target sample size of this cohort to 6000 in order to accomodate the increasing number of biosimilar drugs available at that time (which had expanded to 7). Currently there are approximately 14 biosimilar drugs being prescribed to treat rheumatoid arthritis in the UK, with a new Tocilizumab biosimilar (Tyenne) having recently been approved also. In order to accommodate these new drugs, we propose to increase the sample size for this cohort to 10,000 patients.

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	

Add another change

Section 3: Declaration(s) and lock for submission

Declaration by the Sponsor or authorised delegate

- I confirm that the Sponsor takes responsibility for the completed amendment tool
- I confirm that I have been formally authorised by the Sponsor to complete the amendment tool on their behalf

Name [first name and surname]:*	Lynne MacRae
Email address:*	FBMHethics@manchester.ac.uk

Lock for submission

Please note: This button will only become available when all mandatory (*) fields have been completed. When the button is available, clicking it will generate a locked PDF copy of the completed amendment tool which must be included in the amendment submission. Please ensure that the amendment tool is completed correctly before locking it for submission.

Lock for submission

After locking the tool, proceed to submit the amendment online. The "Submission Guidance" tab provides further information about the next steps for the amendment.

Section 4: Review bodies for the amendment

Please note: This section is for **information only**. Details in this section will complete automatically based on the options selected in Sections 1 and 2.

	Review bodies																	
	UK wide:						England and Wales:				Scotland:				Northern Ireland:			
	REC	Competent Authority MHRA - Medicines	Competent Authority MHRA - Devices	ARSAC	Radiation Assurance	UKSW Governance	REC (MCA)	CAG	HMPPS	HRA and HCRW Approval	REC (AWIA)	PBPP	SPS (RAEC)	National coordinating function	HSC REC	HSC Data Guardians	Prisons	National coordinating function	Category:
Change 1:	Y					Y				Y				Y				Y	C
Change 2:	N					(Y)				(Y)				(Y)				(Y)	A
Change 3:	N					Y				Y				Y				Y	A
Change 4:	N					(Y)				(Y)				(Y)				(Y)	C
Change 5:	Y					(Y)				(Y)				(Y)				(Y)	A
Overall reviews for the amendment:																			
Full review:	Y					Y				Y				Y				Y	
Notification only:	N					N				N				N				N	
Overall amendment type:	Substantial																		
Overall Category:	A																		