Beth Israel Deaconess Medical Center

Committee on Clinical Investigations
Beth Israel Deaconess Medical Center
330 Brookline Ave.
Boston, MA 02215

Notification of Activation

IRB Protocol #:	2018P000410
Principal Investigator:	Ciaran Kelly
Protocol Title:	Burden of Illness in Celiac Disease: A Retrospective Chart Review
Funding:	External - Takeda
Review Type:	Expedited - Categories: 5
IRB Approval Date:	09/11/2018
Expiration Date:	09/10/2019
Notification Date:	09/11/2018

All committee requirements for the research application referenced have been met. This research application is approved for recruitment and enrollment of subjects. This certifies that the research application was reviewed by the Committee on Clinical Investigations (CCI), the appropriately authorized Institutional Review Board (IRB) and Privacy Board appointed to review research involving human subjects. In their review, the IRB specifically considered the rights and welfare of the individual(s) involved; the appropriateness of methods used to secure informed consent; and the risks and potential benefits of the investigation.

The following documents have been reviewed:

1. CCI Application:

- Part A - Basic Information 07/31/2018
- Part B - Study Description 07/31/2018
- Part M – Expedited Review, received 07/31/2018
- Part P – Data Safety Monitoring Plan, received 07/31/2018
- Research Staffing Form, received 07/12/2018
- HIPAA Waiver, received 07/12/2018

2. Informed Consent:
The study is approved with waiver of informed consent.

3. Authorization:
The study is approved with waiver of authorization.

4. Contract Execution Status:
Contract has been fully executed, 09/11/2018.

PLEASE NOTE:
As Principal Investigator, you are responsible for ensuring that this project is conducted in compliance with all applicable Federal, State and Local Laws and regulations, BIDMC institutional policies, and requirements of the CCI IRB, which include, but are not limited to, the following:

1. No changes will be made to the IRB-approved research protocol without first submitting a request to the CCI IRB and receiving the IRB's approval. The only exception to this requirement to obtain prior approval is when it is necessary to eliminate an apparent immediate hazard to subjects (45 CFR 46.103(b)(4)). Changes made to eliminate apparent hazards to subjects must be reported to the IRB as a deviation.

2. Using the IRB-approved consent process(es), PI and research staff will obtain and document informed consent (unless waived) and HIPAA research authorization (when applicable) from participants or their legally authorized representative (LAR) prior to the participant's involvement in the research. Refer to CCI Consent Guidance on the portal: (**https://portal.bidmc.org/Research/Human-**

Subjects/CCI/CCIIRBFrms/InfoCnstnAuth.aspx) For most recent IRB-approved consent form(s) download and/or print for each participant to be consented from the following link:
https://research.bidmc.harvard.edu/CTPro/ProtocolList.aspx

3. Submission of any and all reportable events including adverse events, protocol deviations and new information consistent with the CCI policy on unanticipated problems (Section XII, XIII of the CCI Policy and Procedure Manual). Refer to CCI Post Approval Reporting Guidance on the portal:
(**https://portal.bidmc.org/Research/Human-Subjects/CCI/CCIIRBFrms/ReportableEvent.aspx**)

4. Informing all investigators and research staff listed on the study of protocol modifications and unanticipated problems, including adverse event(s), involving risks to subjects or others.

5. Obtain Continuing Review and approval of ongoing research at the interval determined by the IRB (at least annually) to avoid expiration of IRB approval and cessation of all research activities. PI will submit a final CCI Progress Report to the IRB and other required reports to sponsors or funding/regulatory agencies, as applicable, when all research activities have ended. **https://portal.bidmc.org/Research/Human-Subjects/CCI/CCIIRBFrms/ContRvwnTermFrm.aspx**

6. Investigators and research staff are responsible for informing the IRB whenever there is a change to the information contained in the initial COI disclosure if a) he/she has acquired new financial interest(s) related to the study protocol and/or b) any of their previously reported financial interests related to the study protocol have changed. (Section VII, C.5 of the CCI Policy and Procedure Manual)

If there are any questions you may contact the Committee on Clinical Investigations (CCI) at 617-975-8511.

cc: Jillian Tessing, Caitlin Barrett

Professor David S Sanders
Consultant Gastroenterologist
Royal Hallamshire Hospital & University of Sheffield
P39, Gastroenterology Unit
Royal Hallamshire Hospital
Sheffield
S10 2JF

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

19 November 2018

Dear Professor Sanders

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Burden of Illness in Celiac Disease: A Retrospective Chart Review**
IRAS project ID:	**251220**
REC reference:	**19/HRA/0464**
Sponsor	**Takeda Pharmaceuticals**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

How should I continue to work with participating NHS organisations in England and Wales?
You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).

It is important that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details of the research management function for each organisation can be accessed here.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) has been sent to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?
The attached document *"After HRA Approval – guidance for sponsors and investigators"* gives detailed guidance on reporting expectations for studies with HRA and HCRW Approval, including:

- Registration of Research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics and is updated in the light of changes in reporting expectations or procedures.

I am a participating NHS organisation in England or Wales. What should I do once I receive this letter?
You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Name: Ms. Sheena Kayaniyil

Tel: 001 2156168627

Email: sheena.kayaniyil@iconplc.com

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **251220**. Please quote this on all correspondence.

Yours sincerely

Joanna Strickland

Assessor

Email: hra.approval@nhs.net

Copy to: *Sheena Kayaniyil, ICON plc.[delegated sponsor contact]* *sheena.kayaniyil@iconplc.com*

Luke Barron, Sheffield Teaching Hospital NHS Foundation Trust [Lead R&D contact] *luke.barron@sth.nsh.uk*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Contract/Study Agreement template [modified CRO mCTA 2018]	1	15 November 2018
Costing template (commercial projects) [Sanders_site budget_HRA]	1.0	11 October 2018
IRAS Application Form [IRAS_Form_24102018]		24 October 2018
IRAS Application Form XML file [IRAS_Form_24102018]		24 October 2018
IRAS Checklist XML [Checklist_05112018]		05 November 2018
Letter from sponsor [Delegation letter]	1.0	05 November 2018
Research protocol or project proposal [Takeda celiac disease chart review - Protocol Final V1.0]	2.0	17 April 2018
Summary CV for Chief Investigator (CI) [CV - Sanders]	1.0	12 October 2018

Summary of assessment

The following information provides assurance to you, the sponsor and the NHS in England and Wales that the study, as assessed for HRA and HCRW Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England and Wales to assist in assessing, arranging and confirming capacity and capability.

Assessment criteria

Section	Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	This study is linked to 14/YH/1216 which was a research database study which received REC approval.
2.1	Participant information/consent documents and consent process	Yes	Not applicable
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	The sponsor intends to use a modified CRO mCTA 2018 model agreement with participating NHS organisations. The agreement has been modified for a non-interventional study as follows: • Amendment and deletions to definitions • Deletion of appendix 2 • 3.2 deletion of some regulations • 3.3 deletion of ICH GCP & addition of GPP and GEP • 3.7 amendment to adverse event reporting requirements • 3.7.1 deletion of adverse event reporting in phase I trials • 5 amendments for non-interventional study & deletions to IMP references. • Payment terms in the financial appendix are to be finalised with the NHS site. These modifications are within the limits of acceptability and the HRA and HCRW waive the requirement to use an

Section	Assessment Criteria	Compliant with Standards	Comments
			unmodified model agreement. Participating NHS organisations should now determine the acceptability of the modifications and liaise with the sponsor to confirm the content of the agreement. **Please note**, this waiver does not constitute approval of the agreement, nor does it require NHS organisations to use this agreement.
4.2	Insurance/indemnity arrangements assessed	Yes	No comments
4.3	Financial arrangements assessed	Yes	Commercial funding is available to the NHS site which is a fixed fee for retrospective data collection, payable through the CRO. A validated Industry Costings Template is not applicable.
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Not Applicable	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	No Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England and Wales

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.
There is one NHS site type acting as a full research site performing research activities as stated in the study protocol. The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England and Wales in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. Where applicable, the local LCRN contact should also be copied into this correspondence. If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England and Wales which are not provided in IRAS, the HRA or HCRW websites, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net or HCRW at Research-permissions@wales.nhs.uk. We will work with these organisations to achieve a consistent approach to information provision.

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and Wales, and the minimum expectations for education, training and experience that PIs should meet (where applicable).
A local PI is required to oversee the local research activities. GCP training is expected of the local PI. GCP training is not a generic training expectation, in line with the HRA/HCRW/MHRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken
Where arrangements are not already in place, a letter of access is required. No pre-engagements checks or occupational health clearance is required.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales to aid study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Leena Heinonen	22845522	13.06.2018	2010/2720 REK sør-øst A
			Deres dato:	**Deres referanse:**
			05.06.2018	

Vår referanse må oppgis ved alle henvendelser

Knut E. A. Lundin
Oslo universitetssykehus HF

2010/2720 Immunologisk basis for cøliaki (gluten indusert enteropati)

Forskningsansvarlig: Oslo universitetssykehus HF, Oslo universitetssykehus HF
Prosjektleder: Knut E. A. Lundin

Vi viser til søknad om prosjektendring datert 05.06.2018 for ovennevnte forskningsprosjekt. Søknaden er behandlet av leder for REK sør-øst A på fullmakt, med hjemmel i helseforskningsloven § 11.

Det søkes følgende endring i prosjektet:
- Endringer i oppbevaring av data: legge data inn i en retrospektiv database med formål å registrere forløp av sykdommen cøliaki.

Vurdering
REK har vurdert den omsøkte endringen, og har ingen forskningsetiske innvendinger til endringen slik den er beskrevet i skjema for prosjektendring.

Vedtak

REK godkjenner prosjektet slik det nå foreligger, jfr. helseforskningsloven § 11, annet ledd.

Godkjenningen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad, endringssøknad, oppdatert protokoll og de bestemmelser som følger av helseforskningsloven med forskrifter.

Klageadgang

REKs vedtak kan påklages, jf. forvaltningslovens § 28 flg. Eventuell klage sendes til REK sør-øst A. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst A, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Vi ber om at alle henvendelser sendes inn på korrekt skjema via vår saksportal: http://helseforskning.etikkom.no. Dersom det ikke finnes passende skjema kan henvendelsen rettes på e-post til: post@helseforskning.etikkom.no.

Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen

Knut Engedal
Professor dr. med.
Leder

Leena Heinonen
rådgiver

Kopi til: *oushfdlgodkjenning@ous-hf.no; oushfdlgodkjenning@ous-hf.no*