HRCDC
Health Research Consent Declaration Committee

Date: 13th April 2021
Location: Videoconference

Minutes of the Meeting

HRCDC Attendance

Name
Brigid McManus
Alyson Bailey
Kevin Clarke
Aideen Hartney
Claire Colins
Kathy Brickell
Evelyn Mahon
John Ferguson
Zubair Kabir
Dan Rea
Barry O'Sullivan
Sheelah Connolly
Cornelius Cooney
Mary Tumelty
John Woods
Barry Lyons
Emily Vereker (Secretariat)
Jonny Barrett (Secretariat)
Caroline Byrne (Secretariat)

Quorum for Decisions ☒ YES

Returning Applications – For Consideration

Applicant	Ref No.	Title
Ignacio Martin-Loeches	20-035-AF1	Effectiveness of treatment for infusion in ICU patients with complicated influenza

New Applications - For Consideration

Applicant	Ref No.	Title
Alistair Nichol	21-002-AF1	Mega ROX
Alistair Nichol	21-004-AF1	AP-recAP-AKI-03-01 (REVIVAL)
Tom Rogers	21-003-AF1	Investigating the Epidemiology of *Mycobacterium bovis* Infection in Humans

Meeting Items

1. **Opening**
   The Chair opened the meeting and welcomed the members.

2. Apologies
Simon Furney

3. Disclosure of Interest
Kathy Brickell (KB) declared her interest in two applications: 21-002-AF1 'Mega ROX' and 21-004-AF1 'AP-recAP-AKI-03-01 (REVIVAL)'. KB was absent for this part of the meeting.

4. Minutes of the last meeting
Draft minutes of the 2nd March 2021 meeting were circulated in advance of the meeting and were agreed by the HRCDC.

5. Matters arising

i. 19-040-AF3: *The Interaction between Noradrenaline dosage, Troponin level and Mortality in Septic Shock.*
The HRCDC was informed that the Applicant has withdrawn their application seeking a consent declaration and therefore the responses to the HRCDC's request for further information are no longer required (Ref: HRCDC meeting minutes 13th October 2020).

ii. 19-086-AF1/AMD1: *Sepsis Immunosuppression in Critically Ill Patients.*
The HRCDC noted that this amendment request was approved by written procedure, following the provision of responses to the HRCDC's request for more information (Ref: HRCDC meeting minutes 2nd March 2021). The following conditions and recommendations were attached to the amendment:

Condition 1: It is a condition of this amendment that the appropriate contractual arrangement (material and data transfer agreements as necessary) is fully executed between St. James's Hospital and Dalhousie University prior to the transfer of any data and associated biological samples. The terms and conditions of use of the biological samples and associated data should align with the processing activities outlined to the HRCDC. Only the minimal amount of data should be transferred to the Dalhousie University in accordance with the principle of data minimisation. Where applicable, the data controller should ensure all requirements are in place for transferring personal data outside the European Economic Area, as outlined in Chapter V of the GDPR. Please consult with the data controller's DPO as necessary.

Condition 2: If applicable, the patient information leaflets and consent-to-continue and assent forms being used for the study, should be updated to ensure it is clear that biological samples and data are being transferred to Dalhousie University in Canada.

In addition to the decision made by the HRCDC, all specific and standard conditions attached to the live consent declaration still apply to and must be implemented for this Amendment, unless these have already been met.

6. Returning Applications

Reference ID:	20-035-AF1
Lead Applicant:	Ignacio Martin-Loeches
Lead Data Controller:	GlaxoSmithKline Research and Development Ltd.

Title:	Effectiveness of treatment for infusion in ICU patients with complicated influenza ("IV Zanamivir Effectiveness Study")
Research objective:	See HRCDC minutes of 28th January 2021
Reason for declaration:	The HRCDC considered the Applicant's response to the HRCDC's request for further information in the decision letter of 5th February 2021. See HRCDC minutes of 28th January 2021
HRCDC comments:	The Chair introduced the agenda item and reminded members that additional information was requested from the Applicant. The Chair referred to the detailed discussion on this application from the previous meeting and summarised the key outstanding matters and the responses provide by the Applicant. The consensus of the HRCDC was that a conditional declaration should be made. The decision was based on the following discussion points: **Public Interest and Study Scale** • To determine the significance of the public interest case for this study, the HRCDC discussed the Applicant's response outlining why the inclusion of a small number of St. James's Hospital participants was important for the overall study and whether other Irish sites may participate in the study. • It was noted from the Applicant's response that the study needs to involve patients from across Europe and that only a small number of patients will be recruited at each site. Other Irish sites were approached to participate but were unable to do so due to COVID-19, however they will be contacted again and invited to participate as the COVID-19 pressures ease. • The HRCDC acknowledged that the responses did provide further detail to help determine the significance of the public interest case regarding the inclusion of the personal data of the St. James's Hospital participants. **Consent and Transparency** • The HRCDC discussed the Applicant's responses that obtaining assent or consent would involve a disproportionate effort and be complicated to implement as the study extends back to the 2017/2018 flu season. In addition, the Applicant stated that assent or consent could create data bias that could undermine the study's findings and may not be acceptable to the European Medicines Agency who have mandated the study. It was also noted that a consent waiver had been obtained in other countries where the study is underway. • The HRCDC discussed the feasibility and appropriateness of seeking to obtain assent or consent, including from the most recent 2020/2021 participant cohort. It was noted that while the participant number will be small, the HRCDC also noted that the study is retrospective chart review. After a measured discussion, on balance the HRCDC accepted the Applicant's rationale as to why consent shouldn't be obtained, namely the risk of data bias and that consent is not obtained in other sites outside of Ireland.

	• However, the HRCDC was of the view that the Applicant's response on enhancing current transparency measures was not adequately addressed. Given the importance of transparency as a data protection principle and the small number of St. James's Hospital participants, the HRCDC was of the view that it would be appropriate and feasible to make robust attempts to directly contact participants and inform them about the study, their data protection rights and provide them with the opportunity to withdraw if they wished to do so. **Irish Data Protection Legislation** • Given the international and multi-site nature of this study, the HRCDC discussed that it was important for the data controller to ensure that data processing activities, and correspondingly terms and conditions within legal agreements, reflect the data protection legislation that is applicable in Ireland, which includes the General Data Protection Regulation (GDPR) as well as the Health Research Regulations. **Research Ethics Committee (REC) Approval** • It was noted that the study has provisional REC approval, with full approval subject to confirmation of the HRCDC declaration. Confirmation of full REC approval from the Applicant will therefore be required. **Public and Patient Involvement (PPI)** • The HRCDC commented that the Applicant did not address the topic of PPI in their responses to the HRCDC and may reflect a misunderstanding or unfamiliarity about PPI by the non-Irish Data Controller. • Given the nature and purpose of the study, the HRCDC acknowledged that PPI may be challenging to implement and would not be a requirement under this consent declaration. However, the HRCDC was of the view that the Applicant should be informed about the importance of PPI when undertaking future health research in Ireland.
HRCDC decision:	The consensus of the HRCDC was that a Conditional Consent Declaration should be made.
Duration of declaration:	The Declaration is made on 13th April 2021 and is valid until 30th April 2022 and for 30 years thereafter or upon confirmation that the personal data has been destroyed or rendered anonymised, whichever is sooner. The declaration shall not however be effective until full REC approval is granted.
Conditions attached:	**Condition 1.** The Applicant must directly contact each participant whose data will be included in this study to clearly inform them about (i) the study, (ii) their data protection rights and (iii) provide participants with the opportunity to opt-out of the study and withdraw their data. As part of this enhanced transparency and communication activity, the Applicant must provide participants with an easy-to-reach

	contact point should they wish to discuss the study, exercise their data protection rights or withdraw. For the avoidance of doubt, in order to meet this condition substantively, this enhanced transparency activity must include the option for participants to withdraw from the study. Where participants are 'lost to contact', the applicant needs to demonstrate the robust efforts that were made to contact them and report on these efforts in the Annual Review. **Condition 2.** Further to Condition 1, this condition sets out the scope of the consent declaration as follows: i) It shall apply to the personal data of participants who do not withdraw from the study and/or do not respond to the Applicant's direct communication, including where participants are lost to contact. NOTE: The declaration does not extend to participants who choose to withdraw from the study. ii) It does not extend beyond the 2020/21 participant cohort. Any future waves will require an amendment to the consent declaration. **Condition 3.** The Applicant must ensure that the appropriate legal agreements, including terms and conditions governing the transfer and use of data collected in Ireland, are in place with St. James's Hospital and the other study parties where relevant, prior to the transfer of personal data. In addition, the Applicant must ensure that the terms and conditions of the legal agreements accurately reflect data protection legislation as it pertains to Ireland, including the General Data Protection Regulation. **Condition 4.** Confirmation of full research ethics approval, when obtained, must be provided to the HRCDC as soon as possible. The conditional declaration shall not be in effect until this condition is met.
HRCDC Comment	The HRCDC recommends that careful consideration should be taken by the data controller and the Applicant as to how public and patient involvement (PPI) should be implemented for future studies that maybe undertaken in Ireland. The HRCDC strongly views PPI as an important activity and a key data protection safeguard in situations where consent is not or cannot be obtained from participants for research. PPI helps to create a more patient-centred approach by ensuring that the perspective of the public, patients, carers and their families are taken into account when designing and conducting a study. Furthermore, PPI also provides a valuable way of enhancing the level of transparency, which itself is an important data protection principle and a requirement under the Health Research Regulations. The data controller Applicant should inform the HRCDC of any progressive activity carried out in the area of PPI as part of the Annual Review.

7. New Applications

Reference ID:	21-002-AF1
Lead Applicant:	Alistair Nichol
Lead Data Controller:	Medical Research Institute of New Zealand (MRINZ)

Title:	The Mega Randomised Registry Trial Comparing Conservative vs. Liberal Oxygenation Targets (Mega-ROX)
Research objective:	The Mega-ROX study aims to determine the effect of two approaches to oxygen therapy on the risk of death in patients who need emergency life support (a breathing machine) in the ICU. Oxygen is essential for life and is given to all patients on life support. Often these patients receive more oxygen than they need to make their body oxygen levels normal. Some research suggests that giving more oxygen than is needed to achieve normal oxygen levels may be harmful while other research suggests that it is not, and it may even be beneficial. This study compares two ways of giving oxygen to patients on life support. The first is to give a little more oxygen and the second is to give a little less. Both approaches are safe, but it is not clear which approach is the most effective. All patients in this study can be allocated to either of the approaches to oxygen therapy being tested.
Reason for declaration:	For the purpose of processing personal data of individuals who lack decision-making capacity for this specific study, until such time deferred consent can be obtained from the individuals. Data processing activities includes data collection, pseudonymisation, analysis, sharing of pseudonymised data, storage, archiving, destroying.
HRCDC comments:	The HRCDC noted that provisional ethics approval had been granted by the Research Ethics Committee (REC) for the study where the design, methodology and ethical aspects of the study, including consent protocols are considered. Only studies that have ethical approval or provisional ethical approval, can be considered by the HRCDC to consider if the public interest outweighs the requirement for explicit consent. The Chair requested each HRCDC member to indicate whether a consent declaration should be made. After discussing the application, and based on the information provided by the Applicant, it was the consensus of the HRCDC that a conditional consent declaration should be made. **Public Interest** • The HRCDC was of the view that the study has a strong degree of public interest. **Assent/Consent Process** • The HRCDC queried the timeline for obtaining deferred proxy assent from the participant's proxy next-of-kin/relative. The HRCDC discussed that, where possible, attempts should be made to obtain prospective proxy assent prior to study enrolment. • The HRCDC also discussed that, as an additional safeguard, where participants lack decision-making capacity for a prolonged period, proxy assent should be reaffirmed from the individual who provided it on behalf of the participant, as appropriate and without causing any distress.

Transparency and Study Information Leaflets

- The HRCDC noted that effective transparency measures by way of information leaflets are to be implemented.
- From the information set out in the study information leaflets, the HRCDC discussed that the participant's data protection rights are not clearly outlined, including the right to withdraw from the study or what will happen to the data if proxy assent and/or deferred consent is not provided or withdrawn. It is noted that the Applicant is to engage with their data protection officer (DPO) to understand how to improve these forms.
- The HRCDC further noted that the information leaflets state that the bio-samples will be destroyed if the participant does not provide deferred consent, with no reference to personal data.
- It was discussed that the information leaflets should be reviewed carefully and amended for accuracy and clarity more generally when using terms such as 'assent' and 'consent' across documentation. Some phrases in the information leaflets could also be revised for enhanced readability.
- The HRCDC also discussed that the information leaflets could usefully reference the requirement for a consent declaration as a safeguard.
- In addition, the HRCDC noted that the proxy assent forms reference future use of data and bio-samples. The HRCDC discussed that it should be clear to the Applicant that the scope of the declaration does not extend to other unknown, research studies beyond the Mega-Rox study and therefore consideration should be given to amending this section of the proxy assent forms.

Research Ethics Committee (REC) Approval

- It was noted that provisional REC approval has been granted for this study. The HRCDC noted the responses to the REC's queries also provided by the Applicant.
- The HRCDC stated that confirmation of full REC approval, when available, is required.

Data Transfer Agreements

- The HRCDC noted the Applicant's response that a collaborative agreement is currently being developed between the data controller, MRINZ, and St. Vincent's University Hospital (SVUH). The HRCDC discussed that robust agreements governing the processing of personal data must be in place between the relevant parties.

Data Minimisation

- The HRCDC queried the 15-year archiving period and discussed whether this could be reduced in line with the principle of data minimisation. It was discussed that it is the responsibility of the data controller to determine how long personal data needs to be retained for.

Public and Patient Involvement (PPI)

	• The HRCDC discussed the Applicant's response with regards PPI activities. It was commented that the Applicant should be requested to report on PPI as part of the Annual Review. **Other** • The HRCDC noted that Applicant's response in the DPIA that further clarification about the benefits and risks of the study will be provided to the participant by either the research team or an independent senior physician. The HRCDC commented that drawing upon the expertise of a senior physician was a positive approach to implement.
HRCDC Decision:	The consensus of the HRCDC was that a Conditional Consent Declaration should be made.
Duration of Declaration:	The Declaration is made on 13th April 2021 and is valid until deferred consent is obtained from participants who regain decision-making capacity. Where participants do not regain capacity, the declaration shall be valid until 31st December 2024 and for 15 years thereafter (until March 2039) or upon confirmation that the data has been rendered anonymised or destroyed, or whichever occurs sooner. The declaration shall not however be effective until full REC approval is granted.
Conditions Attached:	**Condition 1.** Where a participant continues to lack decision-making capacity for a prolonged period of time and where proxy assent remains in place, the HRCDC requests that the Applicant should seek confirmation from the individual who provided assent, that they wish for the participant's personal data to continue to be processed as part of the research study. Confirmation of proxy assent should be obtained at an appropriate stage of the study that does not cause undue distress or harm to the individuals concerned. The Applicant must report on this as part of the Annual Review including the number of participants where deferred consent has and has not been obtained. **Condition 2.** The Applicant must ensure that the appropriate legal agreement setting out the terms and conditions governing the transfer and use of data collected in Ireland, is executed between St. Vincent's University Hospital and the data controller MRINZ and including arrangements with other study parties where relevant. **Condition 3:** Considering the principle of data minimisation, the Applicant is requested to examine the length of the data archiving period of 15-years and whether this timeframe can be reduced. The Applicant is requested to report on this condition as part of the Annual Review. **Condition 4.** Confirmation of full research ethics approval from St. Vincent's University Hospital must be provided to the HRCDC, once granted. The conditional declaration shall not be in effect until this condition is met.

HRCDC Recommendations:	**Recommendation 1.** The HRCDC notes that proxy assent will be obtained after the participant has been assessed for study eligibility and randomisation. Where possible to do so, the HRCDC requests the Applicant to attempt to obtain proxy assent prior to these steps. **Recommendation 2.** As a reporting requirement of the Annual Review, the Applicant is requested to report on the PPI activities that will be carried out for this study. **Recommendation 3.** The HRCDC requests that the study information leaflets, and assent/consent forms are reviewed and amended as appropriate to ensure clarity, transparency, and consistency of information for participants and/or individuals providing assent. In this context the following specific observations were made by the HRCDC: - It should be more clearly set out within the assent/consent documents how participants can practicably withdraw from the study, including what will happen the personal data, biological samples and results, if assent or deferred consent is not provided or withdrawn, - It should be examined how clear and concise information on data protection rights could be provided in an easy to read and understandable format, in consultation the DPO. - The use of the term 'your responsible person' in the deferred consent documents may not be an appropriate description. Consideration should be given to an alternative descriptor, such as 'proxy', - The term 'assent' rather than 'consent' should be used study documents when referring to proxy assent. - Reference should also be made to the HRCDC consent declaration when referring to deferred assent as standard practice in ICU research, - The statement '*If there is no known objection by your relative to be included'* should be reframed more positively to ask the proxy individual if they believe their relative would wish to participate in this study, - Reference to the future use of data/samples in the assent documents should be amended to reflect that this consent declaration is for the Mega-Rox study only and does not extend to the processing of personal data in unknown, future research. As a general point the Applicant should also ensure that any consent obtained for the future use of data from the participant is compliant with data protection legislation.

Reference ID:	21-004-AF1
Lead Applicant:	Alistair Nichol
Lead Data Controller:	AM-Pharma B.V.
Title:	AP-recAP-AKI-03-01 (REVIVAL)
Research Objective:	This study is a Randomized, Double-Blind, Placebo-Controlled, Two-Arm Parallel Group, Multi-Center Phase 3 Pivotal Trial to Investigate

	the Efficacy and Safety of Recombinant Human Alkaline Phosphatase for Treatment of Patients with Sepsis-Associated Acute Kidney Injury (SA-AKI). Sepsis is the leading cause of acute kidney injury (AKI) and a major cause of death. Patients with SA-AKI have a high mortality and morbidity and are at risk of developing chronic kidney disease (CKD). AM-Pharma B.V. is developing Alkaline phosphatase (AP) which is a compound normally present in many human tissues. AP has many functions including helping the body fight infection and reducing organ injury during sepsis, as a novel AP medicinal product, called recAP, to be used as an intravenous (IV) infusion for the treatment of SA-AKI. The Phase 3 trial based on the significant survival benefit observed in Phase 2 trials and favourable safety profile observed in the Phase 1 and Phase 2 studies.
Reason for Declaration:	A declaration is sought for the purpose of processing personal data of individuals who lack decision-making capacity for this study, until such time deferred consent can be obtained from the individuals. Where the participant lacks decision-making capacity, proxy assent will be obtained. Data processing activities for which a declaration is required is for processing personal data for the purpose of the above referenced REVIVAL study (accessing, collecting, pseudonymising, transferring, analysing) as well as the storage/archiving only of personal data.
HRCDC Comments:	The HRCDC noted that provisional ethics approval had been granted by the Research Ethics Committee (REC) for the study where the design, methodology and ethical aspects of the study, including consent protocols are considered. Only studies that have ethical approval, or provisional ethical approval, can be considered by the HRCDC to consider if the public interest outweighs the requirement for explicit consent. The Chair requested each HRCDC member to indicate whether a consent declaration should be made. After discussing the application, and based on the information provided by the Applicant, it was the consensus of the HRCDC that a decision should be deferred pending receipt of further information. **Public Interest** • The HRCDC discussed and agreed that while there is a strong degree of public interest in this study, further information should be requested from the Applicant on important data protection areas. **International Data Controller** • It was discussed that while a consent declaration can be made to a non-Irish controller, it is effective within Ireland and therefore it must be clear that there will be an entity in the State that can be jointly responsible and accountable for compliance with the declaration. • The HRCDC commented that the Applicant did not directly address the query as to whether St. Vincent's University Hospital, or another

	Irish site, will be jointly responsible with AM-Pharma to ensure compliance with a consent declaration, if made. **Data Sharing** • It was discussed that the study is a multi-national clinical trial involving several research sites in Ireland, where data and biological samples collected in Ireland will be shared with various third parties outside of the State, in a pseudonymised/de-identified manner. The HRCDC commented that the scale of the study and the number of parties involved makes the application form and data flow relatively complex and challenging to follow, including identifying all the third parties to whom data will be transferred to for the purpose of the trial. • Considering the extent of data being collected and shared, the HRCDC emphasised that only the minimal amount of data required should be collected and transferred to third parties involved in the trial and with the appropriate terms and conditions in place to govern the transfer and use of data, including outside of Ireland or the EEA by the use of standard contractual clauses, where relevant. • The HRCDC noted that while the master list which holds identifiable data remains at the Irish sites, identifiable data will be shared with the Illingworth Research Group, a third-party UK nursing vendor, for the purpose of arranging the follow-up study assessments at the participant's home should they not be able to attend hospital. It was also noted that personal data collected during the home visits will also be shared with the Illingworth Research Group for quality control purposes. The Secretariat informed the HRCDC that these home visits will be conducted by research nurses located in Ireland. It was commented that the sharing of personal data for this purpose is reasonable given that many participants may not be able to attend hospital. The HRCDC discussed the potential data protection risks given how the data is transferred between the parties for this activity. It was noted that data is shared for this purpose by various means such as by paper and email transfers. The HRCDC queried if such an approach was necessary and whether it could be simplified to further protect the participant's data, for example by the use of a data management system. • The HRCDC also queried what data on Irish-based participants is shared and discussed with the Sponsor's nominated study physicians as part of the study's eligibility assessment process. • It was also noted that remote access to medical records and study documents will be provided for necessary monitoring and data verification purposes. The HRCDC noted that this remote access was not referenced in the application form and queried who will be given access, the extent of the data they will access and what security measures will be in place. **Bio-samples** • The HRCDC queried what happens to the bio-samples that are collected as part of this trial. Reference was made to the Applicant's response that bio-samples are stored and transferred to named data

processors and laboratories for analysis as part of the study. Bio-samples are stored for up to 5-years after the final clinical trial report is published for the determination of biomarkers. It was highlighted that the use of bio-samples for biomarkers is noted in the study protocol document and information leaflets.

Deletion of data and data protection rights

- The HRCDC discussed the Applicant's response with regard to the participant's data protection rights. It was noted that while data protection rights are outlined in the study information leaflets, the Applicant states that it may not be possible to delete certain data if requested to do so, for example in order to comply with clinical trial regulations.

Study Information Leaflets

- The HRCDC was of the view that the study information leaflets are lengthy and overly technical in nature and therefore maybe challenging to read. Furthermore, the HRCDC discussed that the proxy individual providing assent should be asked if their relative would wish to participate in this study as opposed to asking if they know of any objections that the participant may have.
- In addition, the HRCDC was of the view that the proxy information leaflet and assent form appear to place substantial responsibilities on the individual providing assent to activities beyond agreeing to inclusion in the study and data processing. For example, the information leaflet places the onus on the proxy individual to inform the study investigators if the participant is pregnant or participating in other trials as well as any changes to their health and medications. It was queried if such expectations and requirements from the proxy is suitable or applicable for the Irish arm of the study or whether a more tailored leaflet should be developed that reflects practices in Irish clinical sites.

Public and Patient Involvement (PPI)

- The HRCDC noted from the Applicant's response that no PPI activities have or will be undertaken. The HRCDC was therefore of the view that the Applicant should be requested to strongly consider what PPI activities can be undertaken during the lifetime of this study.

Data Collection Sites

- The Applicant outlined the 7 hospital sites in Ireland where the trial will be undertaken and that a single REC approval is being sought for these sites. However, the HRCDC noted from the study information leaflet that if the participant is transferred or re-admitted to another hospital, other than the trial site hospital, that data will continue to be collected. It was queried if this means that data will be collected from hospitals not outlined in the application form and if REC approval covers this activity.

	Deferred Consent • The HRCDC commented that more information could have been provided with regards the follow-up assessment visits at day 28 and day 90 in situations where the participant has not regained capacity and the visits are organised on the basis of proxy assent. It was discussed whether deferred consent would be obtained at the follow-up study assessments should the participant have regained decision-making capacity by this point. **Other** • It was commented that further efforts, beyond current reporting requirements, could be made to make this research and the findings more visible in the wider public domain.
HRCDC Decision:	The consensus of the HRCDC was that a decision should be deferred pending receipt of further information.
Further Information Requested:	**Query 1.** The data controller organisation and Applicant are requested to confirm that St. Vincent's University Hospital, or another Irish hospital site, will be jointly responsible with the data controller AM-Pharma for ensuring the implementation of and compliance with the consent declaration, if made. **Query 2.** It is noted that identifiable information is shared with the Illingworth Research Group for the purpose of arranging follow up home research visits where the participant is unable to attend hospital and that personal data collated from these visits, will also be shared for quality control purposes. The HRCDC are of the view that the scale of, and process by which, the data is transferred between the Irish sites and Illingworth involves various steps that may inadvertently increase the data protection risk to the participant's data. For example, it is noted that data is transferred and accessed by email, One Drive and paper copies. Given the scale of data being collated and subsequently shared, the Applicant is requested to examine and comment as to whether an alternative, more secure and streamlined data transfer process can be implemented between the Irish sites and Illingworth, including for example the use of a single data management system or portal. **Query 3**. The HRCDC note that the study information leaflets state that '*AM-Pharma or AM-Pharma authorised representatives'* may be provided with remote access to the medical records for review of the informed consent and verification of trial data points. The Applicant's responses in the application form only reference on-site monitoring visits, where the monitors are provided by Covance and confidentiality will be maintained by the monitors. Please confirm: (i) If remote access to the medical records of Irish participants will be provided for monitoring and verification purpose, (ii) if remote access is provided to non-Covance personnel/monitors for this purpose, including AM-Pharma or other representatives and

	(iii) what measures will be in place to ensure that remote access is provided in a secure manner and to protect data confidentiality. **Query 4.** The HRCDC wish to receive clarity on the Eligibility Assessment process: (i) Please confirm if the data shared/discussed with the nominated study physicians is limited to that entered onto the Medpoint Investigator portal or if additional data, including identifiable data, is shared/discussed, and (ii) Please comment on how data protection and confidentiality is maintained at this step of the study. **Query 5**. The HRCDC requests information on how public and patient involvement (PPI) activities can be undertaken during the lifetime of this study. A timeline and roadmap for PPI activity should be considered as part of the response. **Query 6.** It is noted that Section 5 of the proxy information leaflet requests the assenting individual to agree to several points beyond their relative's participation in the study and data processing, for example informing the trial about changes to the participant's health status. The HRCDC had queried if the level of responsibility and expectations placed on the assenting individual's role in the study, as described in the study information leaflet was appropriate or correct in an Irish context even if suitable in other jurisdictions. The Applicant is requested to examine and clarify for the HRCDC if the information leaflets and assent forms can be further tailored to reflect more accurately the role expected of assenting individuals in Ireland. **Query 7.** Further to Query 6, the Applicant is requested to examine and comment on whether the study information leaflets can be further simplified to make them less technical. **Query 8**. For participants who regain decision-making capacity, please comment as to whether the study will seek their deferred consent to continue in the study at the follow-up study assessments, including during the home-visits conducted by Illingworth. **Query 9.** The study information leaflet states that if the participant is transferred or re-admitted to another hospital, other than the trial hospital, that data will continue to be collected. Please clarify if data for the study trial will be collected from other hospital sites that are in addition to the 7 sites outlined in the Application form, if such a scenario where to occur. If so, i) describe how this data is to be collected and transferred for the purpose of the trial and ii) confirm that REC approval covers this activity.

Reference ID:	21-003-AF1
Lead Applicant:	Tom Rogers
Lead Data Controller:	St. James's Hospital, Dublin

Title:	Investigating the Epidemiology of *Mycobacterium bovis* Infection in Humans
Research Objective:	Bovine Tuberculosis, a form of TB caused by *Mycobacterium bovis*, was a common disease in Ireland prior to pasteurization of milk and programmes to eliminate this infection in cattle herds. The aim of this study is to investigate whether a recent rise in human *M. bovis* infection is due to reactivation of latent bovine TB infection with *M. bovis* that had been acquired years earlier - prior to widespread milk pasteurisation - or whether it is due to new infection transmitted to humans from infected cattle. The study will also review the potential role of recently licenced immunomodulatory medications in the development of *M. bovis.* This study plans to carry out a retrospective review of the healthcare records of patients who attended St James's Hospital (SJH) for investigation or treatment of their *M. bovis* infection. In parallel to this, it will perform whole genome sequencing (WGS) on DNA extracted from approximately 100 *M. bovis* isolates. These microorganisms are originally from patients attending SJH or other Irish hospitals, and a small number of domestic animals, that have been collected by the Irish Mycobacteria Reference Laboratory (IMRL; SJH) and stored over the last 20 years as part of routine clinical care, diagnosis, and national reference work. The study will compare its genome sequenced isolates to genome sequences that are already in the public domain in peer-reviewed journals and from genome sequences of *M. bovis* from infected cattle herds across Ireland and internationally. This may enable the study to identify clusters or possible transmission events between animals and humans and the timelines involved. Finally, it will link the available patient metadata collected by reviewing patient charts to their corresponding sequenced *M. bovis* isolates to hopefully give a better understanding of risk factors for and epidemiology of *M. bovis* in Ireland.
Reason for Declaration:	The Applicant states that it is not feasible to obtain explicit consent from participants. A consent declaration is required to process personal data, including personal data associated with bio-samples, for the purpose of this research study which involves the following activities: (i) Identifying eligible patients, accessing patient records/charts and collecting, pseudonymising and analysing the personal data from these sources, (ii) The processing of personal data associated with the existing *M. bovis* isolates from the Irish Mycobacteria Reference Laboratory (IMRL); the isolates will either be further analysed (i.e whole genome sequencing), or, where available, already have undergone whole genome sequence by the IMRL, (iii) Where possible, linking the personal data collected in point (i) with the whole genome sequencing in point (ii) for the purpose of analysis. Subsequent publication of results will be on anonymised data.
HRCDC Comments:	The HRCDC noted that provisional ethics approval had been granted by the Research Ethics Committee (REC) for the study where the design, methodology and ethical aspects of the study, including consent protocols are considered. Only studies that have ethical

approval, or provisional ethical approval, can be considered by the HRCDC to consider if the public interest outweighs the requirement for explicit consent.

The Chair requested each HRCDC member to indicate whether a consent declaration should be made. After discussing the application, and based on the information provided by the Applicant, it was the consensus of the HRCDC that a decision should be deferred pending receipt of further information.

Public Interest

- The HRCDC discussed whether the retrospective chart review study design and the corresponding data to be collected via this process, would sufficiently answer the research questions and if some of the data required, for example participant occupation, would be available from the sources outlined in the application form.
- While the consensus of the HRCDC was that there is a degree of public interest in this study due to the nature of the study, it was also of the view that more information on how the study design will help to address the research question, and other information, should be requested from the Applicant before determining if a consent declaration should be made.

Consent

- It was noted that 100 participants will be included in the study, with all having their laboratory microbiology records reviewed from the '*Telepath*' electronic records system, and 35-40 participants who attended St. James's Hospital for the management of their infection would also have their medical records reviewed. It was also discussed that patients from January 2000 until December 2020 will be included in the study. Considering the small number of participants, the HRCDC discussed if attempts to obtain consent should be made by the data controller, in particular consent from patients who were more recently diagnosed and treated.
- The HRCDC also queried if information was provided to, or consent had been obtained from the patient, for the storage and use of their bio-samples and data for purposes outside of care and treatment, at the time their bio-sample was collected. It was discussed that information on what previous consent was obtained from, or information provided to patients, if any, should be requested from the Applicant.

Data Collection Sites

- The HRCDC queried if non-SJH medical records will be accessed where participants who are included in the study did not attend SJH for treatment, or if the data collected for this cohort is limited to the 'Telepath' electronic records system only.
- It was also noted that the DPIA states that '*An application to the Ethics Committee in Tallaght hospital will be submitted after the application to the HRCDC has been reviewed'*. It was not clear to the

	HRCDC if the study plans to extend to other sites outside of St. James's Hospital. **Transparency** • The Applicant's response that information on the study will be provided on the St. James's Hospital website was noted. However, the HRCDC was of the view that further efforts to inform participants about the study, the use of their data and bio-samples and their data protection rights should be undertaken. The HRCDC discussed that more information on how transparency measures could be further enhanced should therefore be requested from the Applicant. It was commented that enhanced transparency measures could include contacting participants directly, information notices on relevant partner websites and notices in TB clinics. **Public and Patient Involvement (PPI)** • The HRCDC commented that the level of PPI should be enhanced for this study. This could include ensuring that a PPI study representative is recruited for the study as referenced by the Applicant, as well as engagement with relevant advocacy groups such as the Irish Thoracic Society. **Anonymisation** • The HRCDC queried whether the data can be anonymised before May 2023. **Other** • The HRCDC commented that the study generally appears low-risk and noted that no human DNA will be analysed.
HRCDC Decision:	The consensus of the HRCDC was that a decision should be deferred pending receipt of further information.
Further Information Requested:	**Query 1.** For the purpose of determining the public interest case, the Applicant is requested to comment further on how the study design and the use of data available and collected through this process, would sufficiently address the research questions. In answering this query, the Applicant is also asked to comment on whether the personal data used in the study, is likely to be available via a chart review, including for example participant occupation. **Query 2.** The HRCDC request information and clarity as to whether consent was obtained from, or information provided to patients at the time the bio-samples and data were initially collected from the patient. Specifically, it should be clarified if the bio-samples and data were consented for future storage and research use at the IMRL at that time. The original consent documentation should be provided, if available. **Query 3.** The HRCDC notes that 100 participants will be included in the study. All will have their laboratory microbiology records from the 'Telepath' records system reviewed, with 35-40 participants who

	attended St. James's Hospital for the management of their *M. bovis* infection also having their full medical records reviewed. Please confirm that medical records from other hospital sites for those who did not attend St. James's Hospital, but whose bio-samples are included in the study, will not be reviewed and that the data collected for this cohort is limited to what is on the 'Telepath' records system. **Query 4.** The DPIA states '*An application to the Ethics Committee in Tallaght hospital will be submitted after the application to the HRCDC has been reviewed'*. Please confirm if the study will or plans to extend to other sites outside of St. James's Hospital. **Query 5**. The HRCDC requests further detailed information from the Applicant as to what other transparency measures can be implemented in advance of the study commencing and throughout the lifetime of the study, to ensure there is public and patient awareness regarding the existence of and subsequent outputs of the study and their data protection rights. Consideration should be given to transparency measures beyond a project specific privacy notice on the St. James's Hospital website to include for example the use of other appropriate websites, notices in clinics and any relevant groups/platforms to promote and disseminate the outputs of the study. Consideration should also be given to how it may be possible to sign-post individuals to such notices. It is advisable to consult with the Data Controller's DPO on this matter and provide substantiating documentation to the HRCDC, where relevant, when responding to this query. **Query 6.** In line with the principle of data minimisation, can the data collected for this study be anonymised prior to May 2023?

8. Annual Reviews of Declarations

The Secretariat received and reviewed 2 Annual Reviews in advance of the meeting of which all were deemed to be complete:

- 19-018-AF2: COMBINE Study
- 19-019-AF2: IMPROVED Study

9. Any other Business

- The Secretariat highlighted that the term 'Public and Patient Involvement' could also encompass 'carer' i.e. 'Public, Patient and Carer Involvement'.

- The HRCDC were informed that the National Research Ethics Committee (NREC) will be launching 3 NRECs in May.

- The Secretariat highlighted an upcoming event that may be of interest to the HRCDC and that a link to the event will be circulated:
  - Irish Health Research Forum – *Advancing Genomics Research in Ireland: Part 2.*

The Secretariat provided an update regarding a guest speaker to discuss the topic of biobanking. The HRCDC were informed that further updates on this speaker will follow when available.

10. The HRCDC were reminded that a presentation by John Dunne from the Central Statistics Office would be delivered on the topic 'COVID-19 Data Research Hub', following the meeting. This forms part of a series information sessions for the HRCDC on topics of interest.

*** The Chair closed the meeting***