Protective Marking OFFICIAL

[redacted]

By email to [redacted]

Human Tissue Authority
151 Buckingham Palace Road
London SW1W 9SZ

Tel 020 7269 1900
Email enquiries@hta.gov.uk
Web www.hta.gov.uk

Date 1 May 2019

Dear [redacted]

Freedom of Information request

Thank you for your request for information under the Freedom of Information Act (FOIA), which was received by the Human Tissue Authority (HTA) on 2 April 2019. Your email outlined the following request:

I am requesting any documentation, including letters, emails, reports, meeting minutes etc, related to concerns about the Wellcome Sanger Institute's compliance with the Human Tissue Act submitted to the authority in 2019. I'm seeking information and/ or documents relating to a complaint/ any concerns/ report of potential or alleged breaches of the act, any investigation that took place, any report that was published or details of any sanctions that were instigated?

Response

Information within the scope of the request – including emails, letters, reports and other relevant documents - are provided in the attachment to this letter, comprising a single PDF document.

Some information has been redacted (or not supplied) in line with the scope of the information request, in accordance with relevant (and absolute) exemptions set out in the Freedom of Information Act 2000 (FOIA) and following the redaction guidance set out in the HTA's applicable corporate document.

The lawful exemptions relied on in this response are section 40 and section 41 of the FOIA.

Section 40 provides an exemption for information, which constitutes the personal data of a third party and disclosure would breach any of the data protection principles. In this case, we have withheld information, which relates to identifiable individuals and so constitutes personal data as defined in the General Data

Protection Regulation (**GDPR**), and disclosing it would be unlawful and unfair, therefore breaching the data protection principles contained in the GDPR. Where possible, we have simply redacted the names of individuals to disguise their identities. However, we have also needed to redact additional information, which could be used to identify those individuals.

Section 41 provides an exemption for information which was provided to the HTA in confidence and which, if it were disclosed, would constitute an actionable breach of confidence. The information withheld in this case constitutes information which was provided to the HTA by third parties in circumstances placing a duty of confidentiality on the HTA, and in our view it would constitute a breach of that duty if the HTA were to disclose it.

Individuals are entitled to make anonymous or confidential allegations to the HTA in respect of organisations that we regulate. Whilst we do try to disclose as much information as possible in respect of our statutory activities, we are not able to disclose information where to do so would breach our duty of confidentiality. More information about how we treat allegations can be found at:

https://www.hta.gov.uk/policies/policy-handling-allegations-about-individuals-or-establishments-matters-within-htas-remit

The section 41 exemption is absolute and therefore not subject to a public interest test. However, we do recognise that there are occasions where there will be a public interest defence to a disclosure in breach of confidence. We do not consider that this is the case here, because the public interest in protecting individuals who wish to make confidential allegations outweighs the public interest in disclosure.

Further information

If you are unhappy with the way the HTA has handled your request for information in this case, you may in the first instance ask us for an internal review by writing to us at the above postal or email address.

If you remain dissatisfied with the handling of your request or complaint, you have the right to appeal directly to the Information Commissioner for a decision, at the address below. There is no charge for making an appeal.

Information Commissioner's Office
Wycliffe House
Water Lane
Wilmslow
Cheshire SK9 5AF

Telephone: 08456 30 60 60 or 01625 54 57 45
Website: www.ico.gov.uk

Yours sincerely

[redacted]

[redacted]

Regulatory Decisions

Investigation of the Wellc...

General

Title	Investigation of the Wellcome Sanger Institute		
Licence		**Created On**	07/03/2019 11:27
Meeting type	Case review meeting	**Sector**	Research
Date of meeting	07/03/2019 00:00	**Organisation**	Wellcome Sanger Institute
Owner	[redacted]		

Meeting Members

Decision maker [redacted]	**Chair person**	**Legal advisor**
RM 1 [redacted]	**RM 2**	**RM 3**
Observer - 1	**Regulation Officer**	

Decision Making Steps

Summary of concerns prior to meeting	See letter [redacted] (12 February 2019) and formal response dated 27 February 2019.
List of shortfalls and risks presented by these shortfalls	Unlicensed establishment
List of stakeholders and	For escalation to RDM (see relevant field below).

impact of decision, including impact on growth from April 2017

Rationale for decision	**Evidence suggests the following:** **Uncertainty about status of dried blood spots as relevant material** **Work had NHS REC approval** **Work focussed purely on malarial parasites and not on any human components** **Establishment considers the errors to be administrative, relating to the management of the REC approval; specifically, in relation to covering new donor cohorts** **Technical issues were resolved, involving the approving REC** **Imported samples had their own approvals** **Thorough audit [redacted] - no major non-conformities** **Corrective actions taken, including training relevant to human tissue research** **Cogent reasons for not liaising with us (not licensed by us/no mandatory requirement, considered a discrepancy in REC approved procedures, referred to our standards and guidance in addressing actions)**
Decision	Other
Decision if other	Escalate to RDM

Regulatory Actions

Name	Created On	Due Date	Own

There are no Regulatory Actions to show in this view. To get started, create one or more R

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Existing cases related with this report

Title	Status	Case Number

There are no Cases to show in this view. To get started, cre

0 - 0 of 0 (0 selected) Page 1

Documents

Sharepoint URL

Notes

Status	**Active**

Regulatory Decisions

Investigation of the Wellc...

General

Title	Investigation of the Wellcome Sanger Institute		
Licence		**Created On**	13/03/2019 16:56
Meeting type	Regulatory decision meeting	**Sector**	Research
Date of meeting	14/03/2019 12:30	**Organisation**	Wellcome Sanger Institute
Owner	[redacted]		

Meeting Members

Decision maker	**Chair person**	**Legal advisor**
Harrison, Nicolette	[redacted]	
RM 1	**RM 2**	**RM 3**
[redacted]		
Observer - 1	**Regulation Officer**	
	[redacted]	

Decision Making Steps

Summary of concerns prior to meeting

We acknowledged that SOP 26 is not intended for dealing with unlicensed establishments. However, we have followed the structure and approach as it provides a consistent, and useful framework for decision making.

We acknowledged that HTA does not have statutory powers to investigate allegations or complaints, but, given the facts of the case we decided we needed to at least establish the facts. Policy 029 makes it clear that HTA may refer matters to the Police, where they are so serious and involve an unlicensed establishment.

The evidence suggests the following:

Uncertainty about status of dried blood spots as relevant material
Work had NHS REC approval
Work focussed purely on malarial parasites and not on any human components
Establishment considers the errors to be administrative, relating to the management of the REC approval; specifically, in relation to covering new donor cohorts
Technical issues were resolved, involving the approving REC
Imported samples had their own approvals
Thorough audit [redacted] - no major non-conformities
Corrective actions taken, including training relevant to human tissue research
Cogent reasons for not liaising with us (not licensed by us/no mandatory requirement, considered a discrepancy in REC approved procedures, referred to our standards and guidance in addressing actions)

List of shortfalls and risks presented by these

Not applicable.

shortfalls

List of stakeholders and impact of decision, including impact on growth from April 2017	Not applicable.
Rationale for decision	**Irrespective of whether the material could be considered relevant material, the fact that the research work was approved by a Recognised NHS REC means that it falls outside the licensing remit of the HTA and is not a breach of the licensing requirements of the HT Act 2004. We agree with the establishment, that the errors were in relation to the administration of the research approval agreed with the REC. We note there are no residual matters within our remit.** **Actions:** **1. Inform and liaise with HTA comms.** **2. Write to [redacted] with our conclusions and confirmation that our investigation is over, and we will not be taking any regulatory actions. We will also explain our relationship with the HRA, which oversees the governance of RECs, and our intention to inform them of our decisions in this matter.** **3. Liaise to HRA, to raise awareness of these matters.** **4. Write to the [redacted] with our conclusions and confirmation that our investigation is over.** **5. Draft a summary for the Delivery Report.**
Decision	**Other**
Decision if other	**Take no further action (conclude investigation)**

Regulatory Actions

Name	Created On	Due Date	Own

There are no Regulatory Actions to show in this view. To get started, create one or more R

0 - 0 of 0 (0 selected) Page 1

Existing cases related with this report

Title	Status	Case Number

There are no Cases to show in this view. To get started, cre

0 - 0 of 0 (0 selected) Page 1

Documents

Sharepoint URL

Notes

Status Active

[redacted]

From: [redacted]
Sent: 25 March 2019 13:10
To: [redacted]
Subject: FW: Sharing information on a closed investigation
Attachments: Letter from the HTA to [redacted] 12 Feb 2019 - CONFIDENTIAL.pdf; DW Sanger letter 270219 (plus attachments) .pdf; Letter to [redacted] 15 March 2019.pdf

Hi [redacted]

Just FYI below re: concerns raised, looked into by HTA, no breach of H mT Act found.

[redacted]

Give me a call if you have any Qs!

[redacted]

From: [redacted]
Date: Monday, 25 Mar 2019, 11:02 am
To: Nicolette Harrison <Nicolette.Harrison@hta.gov.uk>, [redacted]
Subject: FW: Sharing information on a closed investigation

For information.
[redacted]

HTA [redacted]
Human Tissue Authority

Direct: [redacted]
General: 020 7269 1900
Mobile: [redacted]
Email: [redacted]
Web: www.hta.gov.uk

151 Buckingham Palace Road, London, SW1W 9SZ

From: [redacted]
Sent: 25 March 2019 11:01
To: [redacted]
Subject: Sharing information on a closed investigation

Dear [redacted]

Under the terms of the information-sharing agreement between HTA and HRA, I am writing to let you know of an investigation we have closed into concerns that were raised with us about research being undertaken at the Wellcome Sanger Institute.

I have attached our original letter to [redacted] (12 February), the formal response we received (by email on 1 March) and our closure letter (15 March).

Read together, they give the full picture of the matters that we investigated and what we have concluded.

As you will see, [redacted] was provided with the opportunity to raise concerns about us sharing the information with you and has not done so.

In summary, concerns were raised that the licensing requirements of the Human Tissue Act 2004 had been contravened. We have concluded they were not but it has been recognised that there were issues in the Institute's management of the ethical approval, which appear to have been satisfactorily resolved. We do not believe, therefore, that there are any urgent regulatory matters for you to deal with but you may take a different view.

Our [redacted] have liaised with your equivalent [redacted] at HRA in case of any media enquiries or other requests.

If it would be helpful to have a supplementary conversation, please do not hesitate to get in touch.

With best wishes

[redacted]

[redacted]

From: [redacted]
Sent: 26 March 2019 09:12
To: [redacted]; Nicolette Harrison
Cc: [redacted]
Subject: FW: Allegations about the Wellcome Sanger Institute

Hi [redacted]

Please be aware of the following FOI request, which I am sure we will want to discuss.

Thanks

[redacted]

From: [redacted]
Sent: 25 March 2019 17:28
To: [redacted]
Cc: [redacted]
Subject: Re: Allegations about the Wellcome Sanger Institute

Hi [redacted] I would also like to submit a formal freedom of information request pertaining to the investigation around the alleged breach of the HTA by the Wellcome Sanger Institute. Please let me know if you have any further questions regarding this.
Best wishes,
[redacted]

On Mon, Mar 25, 2019 at 5:23 PM [redacted] wrote:

> Hi [redacted]
>
> [redacted]
>
> Please can you confirm.
>
> Best wishes,
> [redacted]
>
> On Mon, Mar 25, 2019 at 4:28 PM [redacted] wrote:
>
> > Dear [redacted]

Thank you for your email, which arrived before we had contacted you formally with our final conclusions on the concerns you raised with us relating to the Wellcome Sanger Institute.

[redacted]

To confirm, we have concluded that there was no breach of the licensing requirements of the Human Tissue Act 2004 and we have closed our investigation.

We have reached this position following review of comprehensive information that we received from [redacted] in response to the questions we put to [redacted].

The malarial parasite research, involving dried blood spots, was exempted from HTA licensing by virtue of the work having received ethical approval from an NHS research ethics committee. We accept the Institute's conclusion that the delayed notifications to the research ethics committee (REC) of new imported sample cohorts constitute an error in the management of the REC approval that was given and we understand these matters were subsequently resolved with the approving REC.

Given that the matters are considered an administrative error in the handling of arrangements agreed with the approving REC, we have shared the information we have received from [redacted] with the Health Research Authority (HRA), with which we have a Joint Working Protocol within a Memorandum of Understanding (MoU). The MoU reinforces that exchange of information will be expected where either the HRA or the HTA identifies concerns about an organisation and those concerns are considered to be relevant to the other party's regulatory functions. Although we have no reason to believe that the matters in question were not dealt with appropriately between the Institute and the approving REC, the HRA has functions relating to RECs and we believe, therefore, that they should have access to the same information that was shared with us. Under the terms of the information-sharing agreement, we have apprised HRA of our decisions, conclusions and actions in relation to this case.

Finally, in your email to [redacted] on 18 January, you also raised a concern about the processing of HCV-infected material, about which I am aware we have not yet responded to you. I wanted to confirm that HTA cannot advise you on this matter outside our remit but I believe that applicable guidance from the Health and Safety Executive exists.

In your email from 21 March, you ask for information relating to this case. I am not sure if the scope of your request goes beyond what I have provided in this response - please do let me know if you have any further queries or requests.

With thanks and best wishes

[redacted]

From: [redacted]
Sent: 21 March 2019 13:25
To: [redacted]
Cc: [redacted]
Subject: Re: Allegations about the Wellcome Sanger Institute

Hi [redacted],

[redacted]

Please let me know.

Best wishes,

[redacted]

On Tue, Feb 5, 2019 at 4:47 PM [redacted] > wrote:

> Dear [redacted]
>
> **Allegations about the Wellcome Sanger Institute**
>
> I am writing to you following the concerns you have raised about the Wellcome Sanger Institute, and the information you have provided.
>
> You were previously in contact with [redacted] about these matters. While writing to you, I wanted to let you know that I will be your main point of contact from now on.
>
> For your information, I have provided a link to the HTA's 'Policy for handling allegations about individuals or establishments on matters within HTA's remit', which can be found on our website:
>
> https://www.hta.gov.uk/policies/policy-handling-allegations-about-individuals-or-establishments-matters-within-htas-remit
>
> The policy covers the definitions of terms used and summarises the next steps, including HTA investigation. I refer you specifically to the parts of the policy which outline the principles for managing allegations made confidentially, which you have done in this case. For your reference, a key principle is reproduced below:
>
> 'The HTA will explain to the individual that they will do their utmost to protect their confidentiality but may be required to disclose their identity to the establishment or to another investigating authority and can give no guarantee that their personal details will not be disclosed.'

If I require any further details, I shall write to you. I will also keep you updated on our findings and conclusions, as appropriate.

Please do not hesitate to contact me directly if you would like any further information.

Kind regards,

[redacted]

[redacted]
Human Tissue Authority

Direct: [redacted]
General: 020 7269 1900
Email: [redacted]
Web: www.hta.gov.uk

151 Buckingham Palace Road, London, SW1W 9SZ

[redacted]
Human Tissue Authority

Direct: [redacted]
General: 020 7269 1900
Mobile: [redacted]
Email: [redacted]
Web: www.hta.gov.uk

151 Buckingham Palace Road, London, SW1W 9SZ

[redacted]
Human Tissue Authority

[redacted]

From: [redacted]
Sent: 28 March 2019 16:34
To: Nicolette Harrison; [redacted]
Subject: FW: Allegations about the Wellcome Sanger Institute

For information

[redacted]

From: [redacted]
Sent: 28 March 2019 16:32
To: [redacted]
Cc: [redacted]
Subject: Re: Allegations about the Wellcome Sanger Institute

Hi [redacted]

Thanks for processing my FOI request. I will follow up with the HRA as well regarding this.

Best wishes,
[redacted]

On Thu, Mar 28, 2019 at 1:30 PM [redacted] wrote:

> Dear [redacted]
>
> I am sorry for the short delay in responding to your email.
>
> Please be assured that we are content that, based on the information we have received on these matters, there was no breach of the licensing requirements of the Human Tissue Act 2004.
>
> The information we received confirmed that the research was given qualifying ethical approval in 2015, thereby providing an exemption from the research storage licensing requirements of the Human Tissue Act 2004. The Institute accepts it made errors in the notification procedure regarding additional sample cohorts, which were subsequently resolved with the approving research ethics committee. [redacted]

[redacted]

From: [redacted]
Sent: 26 March 2019 09:10
To: Nicolette Harrison; [redacted]
Subject: FW: Allegations about the Wellcome Sanger Institute
Attachments: [redacted]

For information
[redacted]

From: [redacted]
Sent: 25 March 2019 17:24
To: [redacted]
Cc: [redacted]
Subject: Re: Allegations about the Wellcome Sanger Institute

Hi [redacted]

[redacted]

Please can you confirm.

Best wishes,
[redacted]

On Mon, Mar 25, 2019 at 4:28 PM [redacted] wrote:

> Dear [redacted]
>
> Thank you for your email, which arrived before we had contacted you formally with our final conclusions on the concerns you raised with us relating to the Wellcome Sanger Institute.
>
> [redacted]
>
> To confirm, we have concluded that there was no breach of the licensing requirements of the Human Tissue Act 2004 and we have closed our investigation.

We have reached this position following review of comprehensive information that we received from [redacted] in response to the questions we put to [redacted]

The malarial parasite research, involving dried blood spots, was exempted from HTA licensing by virtue of the work having received ethical approval from an NHS research ethics committee. We accept the Institute's conclusion that the delayed notifications to the research ethics committee (REC) of new imported sample cohorts constitute an error in the management of the REC approval that was given and we understand these matters were subsequently resolved with the approving REC.

Given that the matters are considered an administrative error in the handling of arrangements agreed with the approving REC, we have shared the information we have received from [redacted] with the Health Research Authority (HRA), with which we have a Joint Working Protocol within a Memorandum of Understanding (MoU). The MoU reinforces that exchange of information will be expected where either the HRA or the HTA identifies concerns about an organisation and those concerns are considered to be relevant to the other party's regulatory functions. Although we have no reason to believe that the matters in question were not dealt with appropriately between the Institute and the approving REC, the HRA has functions relating to RECs and we believe, therefore, that they should have access to the same information that was shared with us. Under the terms of the information-sharing agreement, we have apprised HRA of our decisions, conclusions and actions in relation to this case.

Finally, in your email to [redacted] on 18 January, you also raised a concern about the processing of HCV-infected material, about which I am aware we have not yet responded to you. I wanted to confirm that HTA cannot advise you on this matter outside our remit but I believe that applicable guidance from the Health and Safety Executive exists.

In your email from 21 March, you ask for information relating to this case. I am not sure if the scope of your request goes beyond what I have provided in this response - please do let me know if you have any further queries or requests.

With thanks and best wishes

[redacted]

From: [redacted]
Sent: 21 March 2019 13:25
To: [redacted]
Cc: [redacted]
Subject: Re: Allegations about the Wellcome Sanger Institute

Hi [redacted]

[redacted].

Please let me know.

Best wishes,

[redacted]

On Tue, Feb 5, 2019 at 4:47 PM [redacted] wrote:

Dear [redacted]

Allegations about the Wellcome Sanger Institute

I am writing to you following the concerns you have raised about the Wellcome Sanger Institute, and the information you have provided.

You were previously in contact with one of my colleagues, [redacted], about these matters. While writing to you, I wanted to let you know that I will be your main point of contact from now on.

For your information, I have provided a link to the HTA's 'Policy for handling allegations about individuals or establishments on matters within HTA's remit', which can be found on our website:

https://www.hta.gov.uk/policies/policy-handling-allegations-about-individuals-or-establishments-matters-within-htas-remit

The policy covers the definitions of terms used and summarises the next steps, including HTA investigation. I refer you specifically to the parts of the policy which outline the principles for managing allegations made confidentially, which you have done in this case. For your reference, a key principle is reproduced below:

'The HTA will explain to the individual that they will do their utmost to protect their confidentiality but may be required to disclose their identity to the establishment or to another investigating authority and can give no guarantee that their personal details will not be disclosed.'

If I require any further details, I shall write to you. I will also keep you updated on our findings and conclusions, as appropriate.

Please do not hesitate to contact me directly if you would like any further information.

Kind regards,

[redacted]

HTA [redacted]
Human Tissue Authority

[redacted]

From: [redacted]
Sent: 28 March 2019 16:34
To: Nicolette Harrison; [redacted]
Subject: FW: Allegations about the Wellcome Sanger Institute

For information

[redacted]

From: [redacted]
Sent: 28 March 2019 16:32
To: [redacted]
Cc: [redacted]
Subject: Re: Allegations about the Wellcome Sanger Institute

Hi [redacted],

[redacted]

Thanks for processing my FOI request. I will follow up with the HRA as well regarding this.

Best wishes,
[redacted]

On Thu, Mar 28, 2019 at 1:30 PM [redacted] wrote:

> Dear [redacted]
>
> I am sorry for the short delay in responding to your email.
>
> Please be assured that we are content that, based on the information we have received on these matters, there was no breach of the licensing requirements of the Human Tissue Act 2004.
>
> The information we received confirmed that the research was given qualifying ethical approval in 2015, thereby providing an exemption from the research storage licensing requirements of the Human Tissue Act 2004. The Institute accepts it made errors in the notification procedure regarding additional sample cohorts, which were subsequently resolved with the approving research ethics committee. [redacted]

If you have any concerns about research ethics approvals or processes, please contact the Health Research Authority, which has now been informed of this case.

Finally, please also be assured that your request for information under the Freedom of Information Act 2000 is currently being handled by our [redacted].

With best wishes,

[redacted]

From: [redacted]
Sent: 25 March 2019 17:24
To: [redacted]
Cc: [redacted]
Subject: Re: Allegations about the Wellcome Sanger Institute

Hi [redacted]

[redacted]

Please can you confirm.

Best wishes,

[redacted]

On Mon, Mar 25, 2019 at 4:28 PM [redacted] wrote:

> Dear [redacted]

[redacted]

From: [redacted]
Sent: 29 March 2019 15:35
To: [redacted]
Cc:
Subject: RE: Allegations about the Wellcome Sanger Institute

Dear [redacted]

I understand the queries you have raised about this case.

Our view remains that the work was ethically approved (such that the research licensing requirements under the Human Tissue Act 2004 were exempted) and we agree with the Institute that the delayed notifications to the REC were errors in the handling of the expected processes within an existing ethical approval, rather than a breach of the licensing requirements of the Human Tissue Act 2004.

We consider our involvement in these matters to be concluded unless any new concerns within our regulatory remit are brought to our attention.

With best wishes

[redacted]

From: [redacted]
Sent: 28 March 2019 16:32
To: [redacted]
Cc: [redacted]
Subject: Re: Allegations about the Wellcome Sanger Institute

Hi [redacted],

[redacted]

Thanks for processing my FOI request. I will follow up with the HRA as well regarding this.

Best wishes,
[redacted]

[redacted] Mar 28, 2019 at 1:30 PM [redacted] wrote:

> Dear [redacted]
>
> [redacted]
>
> [redacted]

[redacted]

From: [redacted]
Sent: 29 March 2019 11:13
To: Nicolette Harrison; [redacted]
Subject: Request for information under the Freedom of Information Act 2000 HTA365:0250110

For information

[redacted]
Human Tissue Authority

Direct: [redacted]
General: 020 7269 1900
Email: [redacted]
Web: www.hta.gov.uk

151 Buckingham Palace Road, London, SW1W 9SZ

From: [redacted]
Sent: 29 March 2019 11:05
To: [redacted]
Subject: Request for information under the Freedom of Information Act 2000 HTA365:0250109

Dear [redacted]

Thank you for your recent email requesting information under Freedom of Information Act 2000.

I am writing to ask if you could clarify the scope of your request, to ensure that we are providing you with the information that you require.

Currently, your request states the subject of the information ('information pertaining to the investigation around the alleged breach of the HTA by the Wellcome Sanger Institute'), but does not specify the actual type or format of information you would like to receive within this subject.

In order to respond appropriately to your request, please would you reply to clarify this detail.

If you are struggling to clarify the request, there is information on the Information Commissioner's Office website on *How to access information from a public body* that may be of use.

Kindest regards

T: +44 (0)1223 834244
W: www.sanger.ac.uk
E: [redacted]

27 February 2019

[redacted]
Human Tissue Authority
151 Buckingham Palace Road
LONDON
SW1W 9SZ

Dear [redacted]

Re.: Concerns about the Wellcome Sanger Institute

Thank you for your letter dated 12th February 2019 in which you state that it has been alleged that blood samples were stored at the Wellcome Sanger Institute without a suitable HTA storage licence or appropriate approval from a recognised REC.

We should like to put this matter in to some kind of context by explaining the nature of the study and the materials used. The samples in question were blood spot filter papers generated by a drop of blood from a donor being placed onto a piece of filter paper and left unsealed to dry. The blood spot filter papers were stored at ambient temperature and then shipped to the UK. Due to the uncertainty of whether any intact human cells remained on the filter papers, and as the Institute requires either documented evidence from the research team or reference to relevant published evidence obtained elsewhere to prove otherwise, the Institute treated the filter papers as HT Act defined 'relevant material'. The study had been given a favourable ethical opinion by an NHS REC, but a discrepancy had been noted in the procedure for notifying the REC regarding additional sample cohorts.

All the dried blood spots were to be used in one study of malarial parasites. Any human component from the blood spots was 'incidental' to the research question, as the focus was on the analysis of the parasites themselves.

All sample donors for the study were from non-EU countries and local ethical approval had been obtained in the countries in which the donors resided. Samples were fully anonymised at the level of the individual donor, but linked to geographical location.

Answers to each of the points you raised in your letter are as follows:

Wellcome Sanger Institute
Wellcome Genome Campus
Hinxton, Cambridge
CB10 1SA

Genome Research Limited
Registered Office:
215 Euston Road
London NW1 2BE

- **Please confirm whether it is correct or not that samples of relevant material have been stored at the Institute for 'research in connection with disorders, or the functioning, of the human body'. If so, given that the Institute is not licensed by the HTA, please also confirm whether it is correct or not that relevant material has been stored for research within the scope of the Act that has not been given a 'favourable opinion' by a UK-based recognised REC.**

  As it is uncertain as to whether dried blood spots on filter paper, unsealed and kept at ambient temperature, contain intact human cells, the Institute's opinion was that, if this was unknown, then the samples should be treated as 'relevant material' as defined by the HT Act. The filter papers were stored for research purposes [redacted] under their existing NHS REC-approved study entitled 'Natural History of Malaria', REC reference 15/EE/0253, which had received a favourable opinion granted by the Cambridge South NHS REC on 3rd August 2015 (approval letter attached). All the relevant material was stored for a research study which had been given a favourable opinion by an NHS REC.

- **If it is correct that samples of relevant material have been stored in breach of the licensing requirements of the Act, please provide full explanations of how this unlawful activity happened and how it was properly investigated within the Institute.**

  We believe that the samples had been stored correctly as the study in which they were to be used had received a favourable opinion from an NHS REC. The incident related to an administrative error in the sample acquisition process.

  The results of the investigation showed that the study details provided in the protocol and the IRAS application were broad and covered the use of samples from multiple donor cohorts around the world. However, in order to better track each sample cohort, it was stated in the application that Notices of Substantial Amendment (NoSAs) would be submitted to the REC each time it was known that a new donor cohort had been recruited to the study. [redacted] considered that the new cohort of blood spot filter papers were already covered by the existing NHS REC approval, and the filter papers were duly shipped to the Institute.

[redacted]

Wellcome Sanger Institute
Wellcome Genome Campus
Hinxton, Cambridge
CB10 1SA

Genome Research Limited
Registered Office:
215 Euston Road
London NW1 2BE

An initial NoSA to the existing REC approved study 'Natural History of Malaria' was drafted and submitted to the REC on 19th December 2017 to cover the majority of the samples. A second NoSA was submitted on 7th March 2018 to cover the smaller number of samples returned to overseas partners. The delay in the submission of the second NoSA was caused by waiting for copies of local REC approval letters from the overseas partners to be received. Once the second NoSA had been given a favourable opinion by the NHS REC, the filter papers held by the overseas partners were returned to the Institute. REC approval letters for these NoSAs are attached.

During investigations, the [redacted] noted that [redacted] had a good understanding of the regulations and Institute policy associated with the receipt, storage and use of human samples, and that the mis-understanding lay with how the NHS REC approved study should be administrated in terms of amendments for additional donor cohorts.

[redacted] involved have reviewed and improved their practices, and published new and amended procedures to prevent procedural issues relating to additional donor cohorts from happening again. The [redacted] at the Institute have continued to work closely with the research team.

As a follow-up, the [redacted] undertook an audit [redacted] using the HTA's Research Standards and Guidance as an audit template. No major areas of non-conformity were reported from the audit.

[redacted] had to answer to [redacted] that processes would change to ensure that this could not happen again.

A change in the role of the [redacted] means that [redacted]

[redacted] would like it noted that the [redacted]

- **If it is correct that samples of relevant material have been stored in breach of the licensing requirements of the Act, please confirm whether or not the Institute continues to be in breach of the Act.**

We confirm that the study is not in breach of the Act.

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CB10 1SA

Genome Research Limited
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- **If it is correct that samples of relevant material have been stored in breach of the licensing requirements of the Act, please provide full explanations and supporting evidence to demonstrate:**
  - **How the unlawful activity has since been made lawful (if that is the case), and;**
  - **How the risks of something similar happening again have been mitigated**

We believe that the samples had been stored correctly as the study had received a favourable opinion from an NHS REC, and the incident relates to an administrative error. As it was unknown as to whether or not intact human cells remain in dried blood spots on filter papers, the Institute took the opinion that the filter papers should be classed as 'relevant material' under the HT Act.

Although the samples had not been stored in breach of the licensing requirements of the Act, we would still like to take this opportunity to answer your supplementary questions to this bullet point below:

- Two NoSAs amending the existing NHS REC approved study 'Natural History of Malaria', REC reference 15/EE/0253, were submitted to the REC and given a favourable opinion (NoSA favourable opinion letters are attached). These amendments rectify the discrepancy in the procedures notified to the REC in the original submission.

- The [redacted] conducted a thorough audit of [redacted] on [redacted] using the HTA's Research Standards and Guidance as an audit template (audit report attached).

Research policies (including 'Ethical Guidelines on the Use of Human Materials') are made available to all teams on the Institute's intranet. The 'Research Policies Handbook' is sent as a paper copy to all new staff by HR in the new staff recruitment pack. New Faculty inductions, including an explanation of the requirements of the HT Act and internal policy and procedures relating to the use of human materials in research, are provided by the [redacted] PhD student inductions on research policy and regulations and associated 'ethics' seminars, ad hoc team talks, 'Local Coordinator' (lab manager) training, and many one-to-one meetings with researchers when setting-up their studies, are undertaken by the [redacted]

[redacted]

All members of the team involved in the handling of human relevant material have to attend mandatory training (both external and internal to the Institute).

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External training

Team members have to pass the following e-learning modules as developed by the Medical Research Council (MRC), which can be found at: https://byglearning.com/mrcrsc-lms/course/index.php?categoryid=1:

- Good Research Practice (unless individuals are able to show evidence that they have completed ICH-GCP training in the last 3 years)
- Research and human tissue legislation
- Research and human tissue legislation assessment – England, Wales and NI

[redacted]

Internal training

In addition to the external training, team members involved in the handling of human relevant materials receive training on internal Sanger SOPs:

- import and export of human samples and storage
- disposal and transfer of human samples

Team members also receive training in SOPs on current procedures in the context of specific projects.

[redacted]

[redacted]

[redacted]

- **If it is correct that samples of relevant material have been stored in breach of the licensing requirements of the Act, please provide an explanation for why the HTA was not contacted directly by the Institute to discuss these matters.**

  We believe that the samples have not been stored in breach of the HT Act as the research study had received a favourable opinion from an NHS REC. Even though the Sanger Institute is not licensed by the HTA, we referred to the HTA's Research Licensing Standards and Guidance document for

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guidance as to how to proceed. At section GQ5, part (b) the guidance states 'Although there is currently no requirement for establishments in the research sector to report adverse incidents to the HTA, if a DI has concerns about an adverse event, they are encouraged to contact us for further advice.' As a non-licensed establishment, and given that the incident related to a discrepancy in procedures purporting to a study which had received a favourable opinion by an NHS REC, and that there was no threat to human safety, and that the incident was neither major nor critical, we decided that reporting this incident to the HTA was not required. Whilst we believe that we were correct in our approach, it would be helpful to have the benefit of the guidance of the HTA on this matter if the position has changed since the guidance quoted above was published.

- **If it is correct that samples of relevant material were stored in breach of the licensing requirements of the Act and, to remedy the breach, samples were transferred to a HTA-licensed establishment, please provide the details for this establishment.**

  Filter papers associated with the second NoSA were returned to the overseas project partners. These filter papers have since been re-sent to the Sanger Institute for the study 'Natural History of Malaria', REC reference 15/EE/0253.

- **If it is correct that the Institute submitted two Notices of Substantial Amendment (NoSAs) to an NHS REC to cover all 13,000 samples, thereby exempting the need for an HTA storage licence to be in place, please provide the details of the NHS REC involved, including the REC Reference Number.**

  The study to which this letter refers is entitled 'Natural History of Malaria', REC reference number 15/EE/0253. Favourable opinion was granted by NHS Cambridge South REC. Favourable opinion letters from the REC relating to the original study approval (dated 3rd August 2015) and the two NoSAs (approval dates 26th January 2018 and 3rd April 2018) are attached.

  We do hope you have sufficient information to be able to carry out a complete review, and we look forward to your response.

[redacted]

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Enclosures:
Malaria 2015.08.03 REC Favourable Opinion Letter
161220 15.EE.0253 Substantial Amendment 5 Favourable Opinion
161220 15.EE.0253 Substantial Amendment 6 Favourable Opinion
Audit Human Materials 2018 Audit Report [redacted] final 05122018

Health Research Authority
NRES Committee East of England - Cambridge South
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Telephone: 0115 8839428

03 August 2015

[redacted]
Wellcome Trust Sanger Institute
Wellcome Trust Genome Campus
Hinxton
Cambridge
CB10 1SA

Dear [redacted]

Study title:	**The Natural History of Malaria - host, parasite and vector interactions**
REC reference:	**15/EE/0253**
IRAS project ID:	**161220**

The Research Ethics Committee reviewed the above application [redacted]

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, [redacted] Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below. .

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from NRES. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS Sites

The favourable opinion applies to all NHS sites taking part in the study taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Summary of discussion at the meeting

The Committee [redacted]

- **Social or scientific value; scientific design and conduct of the study**

  The Committee considered this to be important research and that the application was well prepared.

  The Committee noted the research will include whole genome sequencing which could reveal incidental findings not related to malaria however members considered this aspect had been appropriately addressed within the application at A6-2 (page 7) of the IRAS form.

  Members of the Committee noted that the response to A59 of the IRAS form states that the sample size is not known and queried how much blood / samples are likely to be collected.

  [redacted]

- **Informed consent process and the adequacy and completeness of participant information**

  The Committee noted that consent will have been given for all samples which will be used in the research.

  The Committee noted that that no generic consent forms had been supplied in the application for the samples obtained in Kenya or the United States and asked the applicant whether the samples complied with the ethical requirements for those particular countries.

  [redacted]

  The Committee was unclear what the 'Donor Consent – Components' document relates to.

  [redacted]

Other ethical issues were raised and resolved in preliminary discussion [redacted]

- **Care and protection of research participants; respect for potential and enrolled participants' welfare and dignity**

  The Committee noted that all DNA sequence and genotyping data will be held in either managed access or open access electronic archives. It was noted that there was a very small risk of possible identification but the Committee considered [redacted] had adequately reflected this within the application.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [AON Letter of Insurance (GRL)]		08 October 2014
IRAS Checklist XML [Checklist_08062015]		08 June 2015
Participant consent form [redacted] PIS & CF]		
Participant information sheet (PIS) [CTLS PIS & CF]		
REC Application Form [REC_Form_08062015]		08 June 2015
Research protocol or project proposal [Malaria Protocol]	V.1	
[redacted]		

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

[redacted]

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

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

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

15/EE/0253	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

[redacted]

[redacted]

E-mail: nrescommittee.eastofengland-cambridgesouth@nhs.net

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*

"After ethical review – guidance for researchers" [*SL-AR2 for other studies]*

Copy to: [redacted]

NRES Committee East of England - Cambridge South

Attendance at Committee meeting [redacted]

Committee Members:

Name	*Profession*	*Present*	*Notes*
[redacted]		[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]		[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	

Also in attendance:

Name	*Position (or reason for attending)*
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

NHS
Health Research Authority

East of England - Cambridge South Research Ethics Committee

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Royal Standard Place
Nottingham
NG1 6FS

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

26 January 2018

[redacted]
Wellcome Trust Sanger Institute
Wellcome Trust Genome Campus
Hinxton
Cambridge
CB10 1SA

[redacted]

Study title:	**The Natural History of Malaria - host, parasite and vector interactions**
REC reference:	**15/EE/0253**
Amendment number:	**5**
Amendment date:	**14 December 2017**
IRAS project ID:	**161220**

The above amendment was reviewed [redacted]

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering letter on headed paper [19122017 Covering letter.doc]		19 December 2017
Notice of Substantial Amendment (non-CTIMP) [Ethics approval letter_QEH_prospective study 2017.pdf]		21 August 2017
Notice of Substantial Amendment (non-CTIMP) [AmendmentForm_ReadyForSubmission.pdf]	5	14 December 2017
Other [KSPH_IRB Approval ACT with English translation.pdf]		21 April 2011
Other [Letter_Mali_IRB_May2013 with English translation.pdf]		31 May 2013
Other [MOLECULAR CHARACTERIZATION OF DRUG RESISTANCE IN PLASMODIUM FALCIPARUM.pdf]		02 November 2017
Other [NMRCD.2007.0004 AM# 14 approval.pdf]		18 September 2017
Other [NMRCD.2007.0004 CR# 11 approval.pdf]		14 July 2017
Other [Renewal approval ACT_Sept2013 plus english translation.pdf]		28 September 2012
Other [SCC 1476v2_[redacted] (with suggestion)_16May16.pdf]		16 May 2016
Other [SMART study_MREC approval letter_2012.pdf]		18 October 2012
Other [IRB [redacted] with English translation.pdf]		21 November 2016
Other [KL initial ethics approval_Aim 1_new.pdf]		25 March 2015
Other [AutorisationACT_MiniSanteProvincial[1] with English translation.pdf]		08 October 2011
Other [DFS-1134-1-Burkina Faso Mgen Ethics Approval_CP2 with English translation.pdf]		17 July 2007
Other [Ethical clearance - NMIMR.pdf]		08 March 2017
Other [Ethics_Approvals.pdf]		17 August 2015
Other [IRB 2015 with English translation.pdf]		15 October 2015
Other [Amendemnt_016_I_N033_July2017 with English translation.pdf]		20 July 2017
Other [Amendment 5 study cohorts.docx]	1.0	19 December 2017

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our Research Ethics Committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

15/EE/0253:	**Please quote this number on all correspondence**

Yours sincerely

[redacted]

E-mail: nrescommittee.eastofengland-cambridgesouth@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: [redacted]

East of England - Cambridge South Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 12 January 2018

Committee Members:

Name	*Profession*	*Present*
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Also in attendance:

Name	*Position (or reason for attending)*
[redacted]	[redacted]

NHS
Health Research Authority

East of England - Cambridge South Research Ethics Committee

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Royal Standard Place
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NG1 6FS

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

03 April 2018

[redacted]
Wellcome Trust Sanger Institute
Wellcome Trust Genome Campus
Hinxton
Cambridge
CB10 1SA

[redacted]

Study title:	**The Natural History of Malaria - host, parasite and vector interactions**
REC reference:	**15/EE/0253**
Amendment number:	**6**
Amendment date:	**21 February 2018**
IRAS project ID:	**161220**

The above amendment was reviewed [redacted]

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering letter on headed paper		21 February 2018
Notice of Substantial Amendment (non-CTIMP)	6	21 February 2018
Other [Ethical approval MDA_CNBS with English translation]		
Other [Ethical approval MiPMON with English translation]		
Other [Ethical clearance Vincent SpotMalaria Cameroon]		
Other [Ethics committee letter Colombia renewals and English translation]		
Other [Ethics MoH BP NT 2012-13 with English translation]		
Other [Ethics Vietnam artekin with English translation of Dutch ethics]		
Other [Papau New Guinea research permission letter]		
Other [Study approval letter]		
Other [Malian Ethics and English translation Committee approval for Consent #1 version 1 and Assent #1 version]		
Other [Malian Ethics and English translation Committee approval for Consent #1 version 2]		
Other [Study cohorts]		
Research protocol or project proposal [Protocol No NOnN-KEMRI 545]		
Research protocol or project proposal [Protocol No 545 Amendment]		

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our Research Ethics Committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

15/EE/0253: Please quote this number on all correspondence

Yours sincerely

[redacted]

[redacted]

[redacted]

[redacted]

Enclosures: *List of names and professions of members who took part in the review*

Copy to:

[redacted]

East of England - Cambridge South Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 29 March 2018

Committee Members:

Name	*Profession*	*Present*
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Also in attendance:

Name	*Position (or reason for attending)*
[redacted]	[redacted]

[redacted]

Human Materials Audit Plan/Report

[redacted]

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1. Audit specifications

Type of audit	Laboratory audit	
Date of the audit	[redacted]	
Date of the audit plan	15/8/2018	
Date of the audit report	[redacted]	**Final:** 5/12/2018
Team audited	[redacted]	
Audit Contact	[redacted]	[redacted]
Other contact for the audit	[redacted]	[redacted]
Objectives of the audit	To assess if the [redacted] are storing Human Tissue Act 'relevant material' in compliance with the Human Tissue Act, the HT Act Code of Practice (Research), Sanger Policy and Sanger SOPs and aspects of the HTA Research Licensing Standards and Guidance as listed in section 5 of this Plan below.	
Scope of the audit	• To determine compliance with the requirements of the Human Tissue Act, Code of Practice, Sanger Policy and SOPs. • To determine compliance against items within the HTA Research Licensing Standards and Guidance document (as listed in this Audit Plan). • To determine the effectiveness of the tracking of samples of 'relevant material' during sample acquisition into [redacted] laboratory areas and transfer between Sanger laboratories. • To assess the effectiveness of tracking sample usage and disposal.	

	• To assess training and communication of the legal and Sanger policy and SOP requirements and procedures across the [redacted]
References	• Human Tissue Act (2004) • Human Tissue Authority's Code of Practice (Research) • Human Tissue Authority's Research Licensing Standards and Guidance (as listed in this Audit Plan) • GRL Policy for the Use of Human Biological Material • Sanger SOP: Import and/or Export of Human Tissue (Human Tissue Act) • Sanger SOP: Storage, Disposal and Transfer of Human Tissue (Human Tissue Act) • Sanger human_materials_tracking information for [redacted]
Team of auditors	Auditors: [redacted]
Recipients of the report	**GRL Sponsor's Representative and HMDMC**
[redacted]	[redacted]

2. Context

[redacted] use genomic and genetic approaches to investigate the biology of malaria, with the goal of delivering new biological insights and improved strategies for disease prevention. [redacted]

The Sanger must comply with the requirements of the Human Tissue Act. The Institute has also set in place its own requirements through the adoption of a 'Policy for the Use of Human Biological Material', SOPs and a human relevant materials tracking spreadsheet.

The Sanger's Human Materials and Data Management Committee (HMDMC) has delegated authority from the Sanger's Board of Management to monitor compliance of projects with GRL's ethical and legal policies and procedures for the use of human biological material, and with all relevant legal and regulatory requirements.

An audit of the [redacted] was performed to assess compliance with relevant legislation and Institute policy and SOPs.

3. Methods utilised

The audit was conducted using the following methods:

- Discussion [redacted]
- An assessment of the laboratory and administrative processes relating to the acquisition, transfer and disposal of samples of 'relevant material'.
- Cross-checking information held centrally and locally against actual samples stored.
- Obtaining information about the communication of legal and policy requirements to, and within, [redacted]
- Reviewing evidence of training and project-specific standard operating procedures, to be provided on the day as examples.

4. Summary of the main positive and negative points

- **Positive points**

The auditors were very pleased to discover a very well co-ordinated approach to obtaining REC approvals and recording of sample receipt, use and disposal. The processes put in place are a significant improvement on previous sample and REC approval tracking [redacted]. [redacted] welcomed the audit and feedback, and the auditors welcomed the very positive and collaborative attitude of the [redacted] are keen to improve their knowledge which has been demonstrated by initiating the adoption of training in working with human materials, provided through e-learning.

Cross-referencing samples with the relevant HMDMC approval was complete.

Regular lab meetings will be held where samples can be discussed and there is good communication [redacted] about the human samples.

[redacted] feel strongly supported by the [redacted] communication is frequent and productive, and collaborative working is standard practice.

Pipettes are calibrated on a regular basis. [redacted] keep a record of the serial number of the pipette and the date of calibration. In addition to this a calibration sticker with the date of calibration is placed on the pipette.

There are good processes set up with the suppliers of the samples to Sanger [redacted] to ensure no samples are received to site with identifiable information associated with them or in advance of UK REC approval being obtained.

There are detailed contingency plans in place, with regularly updated contact information should any of the sample storage fail.

- **Negative points**

No negative points were documented.

- **Comments**

An annual revision of SOPs needs to be implemented to ensure they are kept up to date.

Some samples for functional studies are transferred [redacted], using specialised equipment not available at Sanger. [redacted] is registered with the HTA, and this arrangement has been approved by HMDMC, but there is no formal written agreement between the [redacted]

[redacted] have read the associated REC application and protocol, [redacted] The parameters of what the REC approval covers are summarised in the SOPs.

5. Items seen during the audit

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
Consent			
1	*HMDMC applications are in place for all studies which use human materials* [redacted] [redacted] Ethical approval is sought from the host country [redacted]	PP	Positive Finding: there are a number of different HMDMCs in place for different REC approvals. [redacted] are aware of the different HMDMCs and reference them appropriately.
2	*Linked or fully anonymised samples only are received, or an HMDMC Data Protection Form has been completed for Level 4 (identifiable) data* No identifiable data has ever been received. A SOP is in place for the receipt of samples. This process for receipt of samples includes sending the partners a sample collection kit, which includes anonymized bar codes to be used for each sample. The partner study form and protocol indicates no identifiable information is to be sent to Sanger.	PP	Positive Finding: No identifiable data has ever been received.
3	*Conditions of use and disposal listed in legal agreements, such as MTAs, are known and complied with* A partner study form replaces a traditional MTA in most cases. [redacted] There are different agreements for samples coming from other collaborators [redacted]	PP	Positive finding: there are different agreements in place for different collaborators. [redacted] have a clear understanding of the differences and where the documents can be obtained.

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
4	*Processes are in place that allow the identification and destruction of an individual sample and derivatives upon withdrawal of donor consent* [redacted]	PP	Positive Finding: All samples can be traced back to source
5	*Other observations* All sample cohorts are UK REC approved. These documents along with SOPs are stored within [redacted]	PP	Positive Finding: there is a clear document management system in place with all documents accessible to [redacted]
Governance and Quality Systems			
6	*Clear and controlled relevant documentation, including revision history and version number, 'effective from' date, review date, pagination, author and reviewer names.* [redacted] have clear SOPs associated with all their working practices. These have revision history, version numbers, effective from dates, pagination and author names.	AFI	Area For Improvement: [redacted] There is a need to set a revision date; an annual revision was agreed with [redacted] being appropriate.
7	*Qualifications of staff and relevant training are recorded, including recording that staff have read and understood SOPs* [redacted]	PP	Positive Point: [redacted]
8	*Documented induction training programme for new staff, including visiting staff* [redacted]	PP	Positive Finding: there is a clear and documented training programme in place

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
	[redacted]		for working in the labs with the human materials.
9	*Systems to ensure data protection and donor confidentiality (if relevant)* Partners are sent a sample collection kit including bar codes. In the protocol accompanying this it indicates no sample identification information is to be sent to Sanger. If any identifiable information was to arrive there is a SOP detailing what should be done. No identifiable information has ever been received.	PP	Positive finding: Systems are in place to prevent any identifiable data coming to Sanger.
10	*System for creation, review, amendment, retention and destruction of records* No information is ever destroyed, all details are kept within the electronic systems to allow for tracking of DNA samples back to original blood sample. [redacted]	PP	Positive finding: All information is appropriately stored
11	*Staff have appraisals and personal development plans* Staff have annual appraisals which include personal development plans	PP	Positive finding: Staff are regularly appraised.
12	*Clear SOP(s) for collection (including requirement for HMDMC approval), receipt, sample labelling, sample preparation/preservation, storage, transport to ensure integrity of the tissue and disposal* There are clear SOPs which include a summary of the REC approval.	PP	Positive finding: There are clear SOPs that align with the REC approval for the receipt, use and destruction of the samples.
13	*Regular review of SOPs*	AFI	A revision date needs adding to the SOPs.

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
	The SOPS are not currently reviewed on a regular basis		
14	*Organised record-keeping* All records associated with samples are organised [redacted] and also on the sample tracking system. All samples are labelled with barcodes and sample derivatives can also be traced using the sample management systems	PP	Positive finding: There are very clear records for the many thousands of samples. [redacted] are able to navigate their systems well.
15	*Systems to deal with adverse events* There is an incident/near miss form. [redacted]	PP	Positive finding: There is a clear line of communication for any adverse events.
16	*Appropriate cleaning and decontamination of equipment* There is a 6 monthly service of all the cabinets; this includes a full decontamination before service [redacted] The date of the last service is documented on a sticker on the cabinet. The process of decontamination is covered in the CL2 handbooks, discussed during the new staff induction process, on [redacted]	PP	Positive finding: the equipment is appropriately cleaned and decontaminated on a regular basis.
17	*Transfer of material takes place under an appropriate MTA* All samples are transferred under an agreed partner study form, these replace MTAs in most cases. Prior to receipt of sample form existing collaborators the local approvals associated with the samples are checked, if these have expired then there is a need for a local approval extension before samples can be received at Sanger. [redacted]	PP	Positive finding: The traffic light system makes it really clear what stage of the approval process a partner sample cohort has reached. This system should ensure no samples arrive at Sanger until all appropriate approvals are in place. [redacted] have worked hard to develop an easy to use clear system.
18	*Change control mechanisms for the implementation and review of new operational procedures* [redacted]	PP	Positive Finding: there are regular meetings to discuss implementation of new operational processes.

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
	[redacted]		
19	*Matters relating to activities involving the use of human materials are discussed at regular meetings involving staff, and formal meetings are minuted* [redacted]	PP	Positive finding: The implementation of new quarterly review meetings is a positive finding.
20	*Clear reporting lines and accountability, documented roles and responsibilities* [redacted].	PP	Positive finding: [redacted] have a clear management structure and clear lines of responsibility.
21	*Incident reporting systems and SOPs are in place, and effective corrective and preventive actions are taken* Incident forms and SOPs are in place. Copies of any previous incident forms are kept and used to learn from for the future. Not all issues are escalated depending on the severity of the incident, no need to escalate unnecessarily.	PP	Positive Finding: Appropriate systems are in place for incident reporting.
22	*Other observations*		
Traceability			
23	*Identification system which assigns a unique code to each sample and to each of the products associated with it* All samples are assigned a unique barcode and labelled in a clear standardised way. All sample labelling and collection equipment, including the standardised barcode labels, are sent to partners in sample collection	PP	Positive finding: Each collaborator sample cohort is assigned a unique set of bar codes, appropriate for the sample size. These printed bar codes are shipped to the partners as part of a sample collection kit. No sample

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
	kits. In this way, the [redacted] ensure no samples are labelled with the same number and also ensure identifiable information is not received at Sanger. [redacted]		collection kits are shipped until after both local and UK NHS REC approvals are in place. In this way there are additional assurances in place to prevent receipt of samples for which there is not appropriate ethical approval in place. This measure is to be commended.
24	*A register of the samples and the associated products* All samples and the barcodes associated with them are logged [redacted]	PP	Positive finding: All samples are appropriately registered
25	*Records of: when and where tissue was acquired and received; associated HMDMC approval number; sample location, uses to which sample was put; when and where samples were transferred and to whom* Transfer of samples to [redacted]: samples are given an internal ID which is registered in the sample drive. The date of transfer to sample management is recorded, as is the date the sample is returned [redacted] All samples received are sent to sample management even if there are duplicates to save logistical challenges of trying to pair up duplicate samples upon their return to the [redacted]	PP	Positive finding: All records are up to date and clear.
26	*Records of transportation and delivery are kept* Delivery of samples from external partners are recorded onto the tracker system. The sample manifest arrives with the samples [redacted]	PP	Positive finding: the different paper trails associated with different sample types are clearly know within the [redacted] and documented appropriately.

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
27	*Records of any agreements with courier or transport companies are kept* All records of courier agreements are kept within purchasing. [redacted]	PP	Positive finding: the record keeping of courier and transportation is outwith the [redacted] remit
28	*Records of any agreements with recipients of relevant material are kept* [redacted] Upon checking the status of the agreements in place between the two departments [redacted]	Note	Note: [redacted]
29	*Track ethical approval expiry dates and relevant conditional agreements, such as, consent opt-outs* All local and UK ethical approvals are covered in the partner study form. No samples can be shipped to Sanger without both local and UK NHS REC approval. In order to ensure this the sample collection kits are not sent until after UK NHS REC approval is obtained.	PP	Positive Finding: the processes in place to monitor and track all local and UK ethical approvals are excellent. There have been significant improvements in the monitoring and tracking

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
			of human samples within [redacted] over the last 12 months.
30	*Other observations* The auditors identified 4 samples chosen at random [redacted] on the tracker sheet, all were dried blood spots. The sample barcode was checked [redacted] to identify the barcode number for the samples. Three of the samples were identified as having been disposed of and a search in the storage cupboard confirmed they were no longer available. The fourth sample was easily found in the DBS storage cupboard [redacted] The [redacted] drive had accurate storage information for all samples randomly selected, including sample type, storage location and HMDMC number. Three further samples were identified in the DBS storage cupboard, the barcode number was used to identify the internal sample ID. All three samples were found in the tracker drive with accurate information on their storage location, sample type, sample cohort and HMDMC number.	PP	Positive Finding: Good traceability of all samples
Premises, Facilities and Equipment			
31	*Premises and facilities are appropriate* Yes, premises are appropriate	PP	Positive Finding
32	*Premises and facilities are safe, secure, well maintained and clean* Yes, premises are clean	PP	Positive Finding
33	*Equipment is appropriate, clean, regularly maintained, and upgraded or re-furbished when necessary* The -80C freezer is on the BMS system. The lab and building managers maintain the equipment.	PP	Positive finding
34	*Users have access to instructions for equipment and are aware of how to report an equipment problem* There is an online facilities management system (CAFM) and all issues are reported [redacted]	PP	Positive finding
35	*Environmental controls prevent potential contamination* [redacted]	PP	Positive finding
36	*Staff are provided with suitable PPE*	PP	Positive finding

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
	All staff are provided with appropriate lab coats, eye protection and gloves. All lab staff are required to wear their PPE to work in the labs.		
37	*Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept* [redacted]	PP	Positive finding: Pipettes and equipment are regularly maintained, monitored and calibrated and records are maintained
38	*There is sufficient storage capacity* [redacted]	PP	Positive finding: although the storage facilities are running out the [redacted] have already implemented plans to obtain more.
39	*Storage conditions are monitored, recorded and acted on when required, including temperature monitoring and temperature alarms which are regularly tested and periodically manually challenged* Dried blood spots are stored at ambient temperature in dedicated storage cabinets, which are labelled as containing human relevant material. Fresh blood is stored in aliquots at 4C. Other relevant materials are stored at -80C in a BMS monitored alarmed freezer. [redacted].	PP	Positive finding: Storage conditions are appropriate
40	*Signs on freezers to define alarm set-points for temperature ranges* The -80C freezers are monitored in the building management system (BMS) for out of hours use. [redacted]	PP	Positive finding: Freezers are appropriately labelled.
41	*Freezers have a remote temperature monitoring alarm and callout system* -80C freezers are managed in the BMS.	PP	Positive finding: Freezers storing human relevant materials are appropriately monitored

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
42	*Documented contingency plans in place in case of failure in storage area* Regarding failure of storage areas, all the -80°C and liquid nitrogen tanks are networked, as are a few of the fridges and freezers. [redacted] This means that if alarms occur or accidents are found out of hours the appropriate person is contacted alongside service engineers.	PP	Positive Finding: There are detailed contingency plans in place, with updated contact information should any of the sample storage fail.
43	*Fridges, freezers and other vessels which contain human tissue should be appropriately labelled and prevent mix-ups with other tissues* Fridges are labelled appropriately. Serum is stored as relevant material	PP	Positive finding: There is appropriate labelling in place.
44	*Other observations* [redacted]	PP	Positive finding
Disposal			
45	*Disposal is carried out in accordance with the HTA's Codes of Practice* [redacted]	PP	Positive Finding: Samples are disposed of appropriately and in line with REC approvals.
46	*Date, reason for disposal and the method used are documented* All disposals of human materials are recorded. This is either directly on the human materials tracker or more	PP	Positive finding: Sample disposal is appropriately documented.

Item	Observations (grouped under HTA Standards headings)	Label *	Recommendations from the audit team
	routinely for dried blood spots there is a link to the team drive.		
47	*Supporting procedures should detail requirements for records, for example, of disposal* This is covered in the lab SOPs named 112_SOP_ lab03 and use of human blood products and [redacted]	AFI	Area For Improvement: There are a number of SOPs associated with the group. The auditors suggest giving each SOP a revision date.
48	*Records of disposal should be kept* Records of disposal include autoclaving via a validated route. The date of disposal is recorded in the tracker.	PP	Positive finding: Records of disposal are appropriate.
49	*Other observations*		

*

PP	Positive Point
Note	Note
AFI	Area For Improvement, Minor non-conformity
NC	Major non-Conformity

6. People audited/seen (to be completed following the audit)

Name	Position
[redacted]	[redacted]

Date of the report (draft): 1st October 2018

Date of the report (final): 5th December 2018

Agreed Follow-up Actions

Action	Responsible Person	Time-frame
[redacted]	[redacted]	May 2019
[redacted]	[redacted]	May 2019

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Human Tissue Authority
151 Buckingham Palace Road
London SW1W 9SZ

Tel 020 7269 1900
Email [redacted]
Web www.hta.gov.uk

Date 12 February 2019

[redacted]
[redacted]
Resolution Foundation
2 Queen Anne's Gate
LONDON SW1H 9AA

Dear [redacted],

Concerns about the Wellcome Sanger Institute

My name is [redacted] and I am a [redacted] at the Human Tissue Authority (HTA) which, in general terms, was set up in 2005 to regulate the removal, storage and use of cellular human material for a broad set of 'scheduled purposes'. I am writing to you, [redacted] with concerns relating to the Wellcome Sanger Institute (the 'Institute') that have been brought to our attention.

Since the 1 September 2006, the Human Tissue Act 2004 ('the Act') has mandated that the storage of 'relevant material' (such as blood samples containing human cells) for 'Research in connection with disorders, or the functioning, of the human body' must take place on premises suitably licensed by the HTA, unless an exemption applies. In relation to research within the scope of the Act, there is an important exemption to the need for a HTA storage licence, which applies where the cellular material is being stored for research for which approval has been given by a 'recognised' Research Ethics Committee (REC) or is pending. Should it be helpful, our code of practice on research provides information and guidance on the statutory requirements of the Act and our regulatory expectations with regard to human tissue research matters within our remit, including the relationship between licensing and ethical approval.

The concerns in this case relate to the alleged storage of at least 13,000 blood samples, for research within the scope of the Act, without a suitable storage licence or the appropriate approvals from recognised UK RECs. If these allegations are correct, the Institute has been responsible for a breach of the licensing requirements of the Act.

Although we have never received any direct report or communication from the Institute about these matters, I understand the samples were received by the Institute in the 12 months leading up to March 2018. I understand that the samples were imported from outside the UK and may have been subject to ethical review in their source countries.

After its discovery, I understand [redacted] at the Institute sought to resolve the unlawful storage activity by arranging for the transfer of the samples to a HTA-licensed facility, thereby meeting the licensing requirements of the Act. In addition, I also understand that the Institute submitted two Notices of Substantial Amendment (NoSAs) to an NHS REC to cover all 13,000 samples, thereby exempting the need for a HTA storage licence to be in place.

Given the seriousness of these matters, I would be grateful if you could provide written responses to each of the following points.

- Please confirm whether it is correct or not that samples of relevant material have been stored at the Institute for 'research in connection with disorders, or the functioning, of the human body'. If so, given that the Institute is not licensed by the HTA, please also confirm whether it is correct or not that relevant material has been stored for research within the scope of the Act that has not been given a 'favourable opinion' by a UK-based recognised REC.
- If it is correct that samples of relevant material have been stored in breach of the licensing requirements of the Act, please provide full explanations of how this unlawful activity happened and how it was properly investigated within the Institute.
- If it is correct that samples of relevant material have been stored in breach of the licensing requirements of the Act, please confirm whether or not the Institute continues to be in breach of the Act.
- If it is correct that samples of relevant material have been stored in breach of the licensing requirements of the Act, please provide full explanations and supporting evidence to demonstrate:
    - how the unlawful activity has since been made lawful (if that is the case), and;
    - how the risks of something similar happening again have been mitigated
- If it is correct that samples of relevant material have been stored in breach of the licensing requirements of the Act, please provide an explanation for why the HTA was not contacted directly by the Institute to discuss these matters.
- If it is correct that samples of relevant material were stored in breach of the licensing requirements of the Act and, to remedy the breach, samples were transferred to a HTA-licensed establishment, please provide the details for this establishment.
- If it is correct that the Institute submitted two Notices of Substantial Amendment (NoSAs) to an NHS REC to cover all 13,000 samples, thereby exempting the need for a HTA storage licence to be in place, please provide the details of the NHS REC involved, including the REC Reference Number.

Please provide your formal response to me by close of business on **Friday 1 March 2019**. I understand that you might need to work with [redacted] to answer the points in this letter. Following receipt of your formal response, I will review the information and contact you again with the next steps or a request for further information. I should make you aware that, after we are satisfied that we have enough information, the next steps may include consideration of whether to refer this case for investigation by the police. I, therefore, request your full cooperation while we investigate the circumstances which led to unlicensed activity.

Please do not hesitate to contact me should you require further information.

Yours sincerely,

[redacted]

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Human Tissue Authority
151 Buckingham Palace Road
London SW1W 9SZ

Tel 020 7269 1900
Email [redacted]
Web www.hta.gov.uk

[redacted]
Resolution Foundation
2 Queen Anne's Gate
London
SW1H 9AA

Date 15 March 2019

Dear [redacted]

Re: concerns about the Wellcome Sanger Institute

Thank you again for the information you supplied to us, dated 27 February 2019.

We have concluded that there was no breach of the licensing requirements of the Human Tissue Act 2004 and we do not intend to make any more requests for further information.

Given that the matters are considered an administrative error in the handling of arrangements agreed with the approving research ethics committee, we intend to share the information you have sent to us with the Health Research Authority (HRA), with which we have a Joint Working Protocol within a Memorandum of Understanding (MoU). The MoU reinforces that exchange of information will be expected where either the HRA or the HTA identifies concerns about an organisation and those concerns are considered to be relevant to the other party's regulatory functions. Although we have no reason to believe that the matters in question were not dealt with appropriately between Wellcome Sanger Institute and the approving research ethics committee, the HRA has functions relating to research ethics committees and we believe, therefore, that they should have access to the same information you have shared with us. Under the terms of the information-sharing agreement, we also intend to apprise HRA of our decisions, conclusions and actions in relation to this case. If you have any concerns that you would like us to consider in relation to the sharing of information with HRA, please contact me directly by **close of business on 22 March 2019**.

Yours sincerely,

[redacted]