

European Translational Information and Knowledge Management Services

eTRIKS Deliverable Report

Grant agreement no. 115446

Deliverable 7.5.2

ESAB Advisory Report:

Report of the eTRIKS Ethics and Security Advisory Board part 2

Due date of deliverable: Month 48

Actual submission date: Month 52

Dissemination Level				
PU	Public	Х		
РР	Restricted to other programme participants (including Commission Services)			
RE	Restricted to a group specified by the consortium (including Commission Services)			
СО	Confidential, only for members of the consortium (including Commission Services)			

DELIVERABLE INFORMATION

Project				
Project acronym:	eTRIKS			
Project full title:	European Translational Information and			
	Knowledge Management Services			
Grant agreement no.:	115446			
Document				
Deliverable number:	D7.5.2			
Deliverable title:	ESAB Advisory report:			
	Report of eTRIKS Ethics and Security Advisory			
	Board			
Deliverable version:	1			
Due date of deliverable:	Month 48			
Actual submission date:	Month 52			
Leader:	Charles Auffray; David Henderson			
Editors:	Robert Irmisch Fabien Richard,			
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Authors:	Neil Fitch			
Reviewers:	Fabien Richard, ESAB members			
Participating beneficiaries:	CNRS, BioSci Consulting			
Work Package no.:	WP7			
Work Package title:	Ethics for eTRIKS platform data			
Work Package leader:	Charles Auffray, David Henderson			
Work Package participants:	Robert Irmisch Fabien Richard,			
	Chris Marshall, Neil Fitch			
Estimated person-months for deliverable:	2			
Nature:	PU			
Version:	1			
Draft/Final:	Final			
No of pages (including cover):	14			
Keywords:	Ethics, Data Security, Federated Data Model			

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1. Introduction

1.1. Purpose

This deliverable is part 2 of D7.5 and forms the evidence base of the (much wider) dialogue and input of the Ethics and Security Advisory Board (ESAB) to eTRIKS ethics activities.

As set out in the Description of Work, WP7 aims to identify and implement the legal and privacy requirements of the eTRIKS project (and oversee the implementation of the information security requirements), to ensure compliance with national (European) and international legislation and requirements. In order to achieve these aims, WP7 works to:

- 1) Identify and document all necessary ethics requirements (legal, information security and data privacy) for the eTRIKS platform and services; monitor and audit the implementation of the requirements made by other work packages.
- 2) Establish, document and develop the eTRIKS process guidelines (including review, approvals and authorization mechanisms) that need to be implemented so as to conform to the necessary legal, information security and data privacy requirements.
- 3) Coordinate the deployment of the necessary tools and mechanisms that ensure that storage, access and processing of data in eTRIKS is in compliance with national (European) and international legislation and requirements.
- 4) Conduct training programmes to ensure that users of the system are aware of their ethical and legal responsibilities prior to being granted access to the eTRIKS platform.
- 5) Establish an eTRIKS Ethics and Security Advisory Board (ESAB) to provide accurate guidance on ethics matters that arise and to ensure close coordination with the ethics workgroups of other IMI and non-IMI projects using the eTRIKS platform.

This Deliverable provides a summary of the discussion between members of WP7, the eTRIKS Executive Committee and the members of the ESAB during the Second Annual Meeting of eTRIKS, on December 7th 2016.

1.1. Intended audience

The readership of this document is assumed to be familiar with eTRIKS and its overall aims, including being aware of the progress to date with respect to achieving the deliverables of WP7.

1.2. Scope

This Deliverable documents the discussion and recommendations arising from an all-day meeting with the members of the ESAB. In addition to providing the ESAB members with background information on the eTRIKS project and an update on the work of WP7, presentations were made summarizing the security aspects of the project dealt with by WP1 and WP2. The summary and data protection challenges of the client IMI projects ABIRISK and OncoTrack were presented. The security and data privacy issues inherent in providing eTRIKS service to a pan-European consortium were highlighted using the OncoTrack project as a Use Case. The members of the ESAB provided insight and recommendations on dealing with these problems and also provided recommendations on other matters raised during the meeting, as summarized in sections 9 and 10 of the Deliverable.

2. Final ESAB Meeting – December 7th, 2016 Minutes of the Meeting

Attendance:

Charles Auffray (CNRS-EISBM), David Henderson (Bayer), Emmanuel Rial-Sebbag (INSERM), Fabien Richard (CNRS-EISBM), Neil Fitch (BioSci Consulting), Pim de Boer (HuMedSci Consultancy), Susanna Palkonen (EFA), Bartha Knoppers (McGill University), Annamaria Carusi (University of Copenhagen).

Remote attendance:

Chris Marshall (BioSci Consulting) Robert Irmisch (Sanofi)

ESAB members:

Pim de Boer (HuMedSci Consultancy), Susanna Palkonen (EFA), Bartha Knoppers (McGill University), Annamaria Carusi (University of Copenhagen), Emmanuel Rial-Sebbag (INSERM),

3. Introduction to the Meeting

Thanks are due to Bayer for supporting this meeting.

This will be the Final ESAB FtF meeting. Further meetings can be planned as needed for further iterations of the core documents or papers.

The main aim of meeting is to review the document D7.9 and review the publication plans.

There remain gaps to fill in the WP7 resourcing. Y.A. Montjoye from ICL will be joining WP7 in 2017 to partly fill this gap. Bayer will also be supporting additional contributions from F. Richard. This resource may be used to publish and update the documents.

4. Background discussion

An update of the significant impact of the *Genome Medicine* paper by Auffray et al was provided. This is an opinion article resulting from a one day workshop held in Luxembourg in October 2015 with the participation of several eTRIKS partners. The objective of this opinion paper was to provide the European Commission with a review of the state of the art, and proposals for an action plan to make sense of big data in health research, including the harmonisation of the legal and regulatory aspects and privacy issues discussed in WP7.

In measuring the impact of this paper, not only classical metrics are used, but a new approach using an attention score, which takes into account social media impact. An attention score of >100 is reached, placing this publication in the top 1% of over 7 million papers. This score reflects how timely this work is in the current environment.

The Global Alliance for Genomics and Health (http://genomicsandhealth.org) - a intensive data sharing project, is worth noting. Documents have been translated into 13 languages with

3 policies formed on consent, accountability and later on mutual recognition. A Task Team has been set up to look at the requirements for a code of conduct relating to the EU regulations. A data protection board will be set up. This approach is also reflected in the *Genome Medicine* paper.

The topics introduced and the new duties relating to these topics - which are also reflected in the eTRIKS WP7 work - also need to be considered in the wider framework of eTRIKS. More data sharing, not less is the aim, but then standards, including security standards, are needed to facilitate this.

eTRIKS will complete the IMI funded period in September 2017. The focus in this final period is on completing the already planned work.

The eTRIKS Network aims to continue the exploitation of the outputs beyond the funded period.

Understanding how the ethical aspects tie together and tie in with the wider objectives could be another avenue for further work. John Mattison can be connected with to discuss this further.

5. Definitions and terminology

Definitions of GDPR and of data itself are used in this work. However, only the data sharing and data re-use aspects are covered by this document, reflecting the aims and concerns of the eTRIKS project.

The term, 'data subject' is used in the EU regulation, rather than study participants. This term can be clarified in the document, both what this means and add our preferred terminology.

Emmanuelle related an experience of a session where the term 'data subject' was felt to be necessary as it relates to the legal phrasing. However, the terms need clarifying. In Canada the term 'subject' is no longer used. Some discussion of this terminology can be included in the related paper.

Different regions also use different terms, e.g. Precision Medicine in US vs Personal Medicine in Europe or Translational Medicine in China. However our documents speak globally and therefore we can determine the right terminology.

6. Challenges in data sharing

The lack of harmonisation of data sharing laws is the first challenge. The anonymisation of the data and issues around the volume and richness is the second challenge. Data noise is a key issue.

The move towards personalised medicine has issues around aggregate data and the need to link back to source data. A link to contact the patient may also be needed, and how to maintain this while ensuring privacy needs thought and discussion in relation to

each dataset. In the EU General Data Protection Regulation (GDPR) (Regulation (EU) 2016/679) there is an exception - if it is too difficult to contact a study participant then this is disallowed.

Improved participation in research may be seen through ensuring robust processes, which are transparent and build trust. It may also change how study participants are involved as partners in research.

The broad reluctance of data providers/owners to engage in data sharing needs to accounted for. There are reasonable concerns which need to be recognised, foremost having results scooped by others (see ownership in the next section).

FAIR principles are used to define how data should be shared. Availability of the data itself is not enough. The resource needed to bring data up to FAIR standards is significant and usually is not recognised. This reflects the culture in the research community. However, attitudes and requirements from certain institutions are changing.

Nonetheless there is a wide spectrum of data sharing practices seen in different research areas. The difficulty and resource demand of the task of both approving and making data shareable should also be recognised. In some cases there are concerns that sharing data can sometimes lead to unnecessary work. To balance this, the resource input should be weighed against a degree of accountability, when performing the 'act' of not sharing data.

We cannot oblige a study participant to share data, but if the option to share their data is chosen, it should be clear that their data could be used in the general use (the 'scientific purpose' has a broad meaning as explained in the recital 159 of the GDPR). We should bring into the context of why this is an issue within this project. The data for secondary use purposes needs to be defined in the document. The right to object is sacrosanct. This does mean that contact with the study participant needs to be maintained. How to do this both technically (traceability) and practically (time, resource) are major issues. The secondary use of data, the data sharing procedure beyond the initial study, and the portability of patient data' are should be added in the consent form whatever the initial study is (clinical trial or research study).

To scale up data sharing is challenging but has been done in cancer. Controlling the process is key. Work is underway to determine how to internationally facilitate data sharing. A model that can be globally applied is necessary.

As shown in the model, a 'data broker' is likely needed, or several of these within a country, who would need to meet the safe haven requirements. This should be a functional entity rather than a legal entity, with certification from national authorities if required. Regional or national hubs/brokers/connector may be needed, depending on the legal context. This concept may facilitate sharing of data with institutions who do not want their data being shared outside their firewall, forming a trusted third party model.

The wording around data sharing and the proposed model needs to be carefully formed - to avoiding implying that data sharing is risky in itself, and to include the patient perspective. Data breach by a third party is seen as a risk. There is no way of controlling what a third party does with the data. However, there is no evidence that sharing data leads to a data breach.

(Data) Enclaves may become a challenge, rather than something to leverage on.

A further source is the 12 attributes of data protection by Paul Burton to enable a safe haven. (Ps: Paul Burton provides the following definition noting that the origins and evolution of the term have made its use unclear: 'a repository in which useful but potentially sensitive data may be kept securely under governance and informatics systems that are fit-for-purpose and appropriately tailored to the nature of the data being maintained, and may be accessed and utilized by legitimate users undertaking work and research contributing to biomedicine, health and/or to ongoing development of healthcare systems'. Bioinformatics (2015)doi:10.1093/bioinformatics/btv279First published online: June 25, 2015))

Decision/Next Action:

Fabien: Include a footnote explaining the term 'data subject' in the paper and report

Fabien: Define Secondary data in the document

Fabien: Include a more active model of roles rather than a purely education approach for study participants

7. Challenges in data sharing – ownership and publication issues

The concept of ownership is deep rooted.

Clinicians need to be part of the sharing culture and move away from feeling ownership of paper. Genomics England have a traditional way of data sharing - researchers need to go to the site to view data. This reduces the risks of misuse but the enclave approach is also controlling and has a negative on the impact of the sharing of the data. H index lead concerns relating to ownership of data also has a significant impact. Reflected is the fact that sometimes data owners are also not even aware of papers published in their name.

Current structures which reward publications mean we cannot expect researchers to change without some change in the framework or compensation by some means for their effort. Reward structures are key in solving this issue. This framework also has a global context in terms of the dynamics of data sharing and national permutations of the global environment.

Recognition of the data sharing is often lacking with a lack of a system to reward the data sharer. Quality data is also essential - there are many ways of sharing data that bring little value. Funders of course do push for data to be shared.

The long list of co-authorship is another issue. However a publication policy would need to be a separate paper, although a simple recognition can be made.

8. Communication and education in relation to data re-use

Phrasing around data sharing should be in the Informed Consent forms. This should also be explained to study participants. Study participants need to understand what is being signed - true informed consent is necessary. Who will do this, with what resources is a question that will need to be answered.

Training - including of students - is essential is delivering a change in attitude to data sharing. The authorship culture may also need to be completely revised, and this includes the framework within which researchers work.

Rather than using the term education, more active roles for people could be better approach. This could be part of the model with defined roles including those from other things people are involved in in their lives. This can be highlighted in the document. More active information on benefits including actual benefits (blood example in UK).

It is necessary to inform patients that narrow purposes for research severely limits the value of your contribution. In some countries a domain has to be specified but is usually for approved research.

9. The concept and approach of the data sharing model

Data Protection Authorities are listed as secondary simply because they sit outside of the immediate processes concerned in the model. The virtuous circle shows how the benefits can be used to leverage greater data sharing.

TRUST principles are outlined¹. These are seen together with the FAIR² principles in the model. The data subject (SP) is seen as the ultimate authorizer.

The right to be forgotten is not included in D7.8 and needs to be in the revised version. The right to be respected (ongoing consent provided even after death) is in many cases not respected - the data is often pulled out when someone dies, despite the Informed consent.

The national level situation determines the approach in a number of cases. Competent adults rights though should be respected from the time of the signature - with Alzheimer's Disease or not. The user case of the process of consenting for children is used for other cases where authorisation is needed.

¹ <u>https://www.whitehouse.gov/sites/default/files/microsites/finalpmiprivacyandtrustprinciples.pdf</u>

http://www.sidley.com/~/media/update-pdfs/2015/07/20150715-us-healthcare-and-privacy-update.pdf ² https://www.force11.org/group/fairgroup/fairprinciples

http://www.nature.com/articles/sdata201618

However, if someone gives consent and their genetic data (or other familial data) could affect other family members the situation is less clear. The family may have the right to request withdrawal. Other health data may be equally sensitive - and how would one set of health data be defined as more sensitive than another? Genetic data should in this case be health data - genetics should be normalised and therefore integrated into the general approach to data privacy.

Decision/Next Action:

Bartha Knoppers to provide articles that support the TRUST principles.

10. Review of proposed data sharing model

The information flow is shown. The platform could have two types of data in relation to the study participants. This would lead to two different data types, one for broad approved use and one for more specific uses or where the study participant has opted to be contacted every time their data is to be re-used for a non-specific purpose. The platform would have different classes or levels of data use.³

The proposed model would be an active platform - dynamic in some ways. People may change their minds as well, particularly after the first treatment phases. Dynamic information may be more a requirement than dynamic consent. However some global information would need to be provided.

An issue is that re-consent will not work with people who do not want to be contacted. They will effectively not participate in most cases additional up research.

Narrow consent can be used to opt in (one click) without re-consent via an ethics board, but simply asking via a notification to the study participant. This would allow a dual platform to run. Narrow = dynamic consent.

Any use that is compatible with informed consent is accepted for secondary use. In Germany the legal framework means that there is respect for the restriction of the extent of the informed consent, but only for the same (disease) area. In France one purpose needs to be defined, but then research in this area does not require re-consent.

When presenting the model, the starting point can be from the bottom up, so from the study participant perspective, rather than the from the computer/Data brokers downwards.

The interpretation of the initial purpose of the data use needs to be clear - this may be the first use of the data.

The general sharing of data rule does not override the specific re-use of data rule. However if the use of the data is not incompatible then it is acceptable following the EU regulation. 3 categories can be considered.

- 1. Broad consent for continued use
- 2. Specific re-use of data consent only and on notification.
- 3. Re-consent process for requesting broad consent put in place

 $^{^{3}}$ See slideset – slides 29-32 – for a full explanation which was not able to be provided in the meeting

In all cases people have the right to withdraw at any time. Anonymised data is not considered here as this only relates to personal data.

The platforms could have the ability to host all re-usable data plus the consent permissions, but only the data with consent would be visible to the data broker.

Personalised medicine cannot be achieved without personal data positions translated into an operable process.

The relationship between the public and the data sharing federation would need to be defined. The ICGC is an example of how to do this.

A registered user of the data facility would have to follow their local (regional or national) law, even when working on data from other countries. The person accessing the data would be doing the processing. An international database is difficult due to conflicting regulations. In reality the restrictions may not be overwhelming, except for genetic data.

Original broad consent remains the key to opening up re-use of data use. The consent code would be used to categorise the type of consent. If local law and consent allow for data sharing then direct communication with platforms can be made. The federations can go directly to all the data brokers. The federation would have a co-ordinating function and would know what each broker can offer.⁴

The proposed structure is felt to be workable in unitary countries. The international element brings challenges. Data brokers will need to be connected if a federation is to be formed. The function of the broker can also help to prevent duplication of work.

Project platforms may want their data to be used, but then with the enriched data returned to the platform. The platform then evolves. Enriched data is not tackled in D7.8 due to eTRIKS priority on data re-use.

Every time new information is produced it should be collected - this is the reciprocity principle. This should be the case for both primary and secondary data purposes. This also means that further findings with medically actionable results are fed back to clinicians/patients.

Priority rights for analysing the data can be granted for one year. Thereafter there would be an obligation to return the enriched data and an allowance for others to publish or analyse the data.

Decision/Next Action:

Emmanuel - send numerical law article to Fabien

⁴ A unique point/data broker is needed to collect all the data and analyse them. The portal has no computing power to do that because this is not its role.

11. Publications

D7.9: There is broad support for the model presented in today's meeting. Further comments can be made by Bartha and Emmanuelle on the next version, once the deliverable report is submitted. Target journal: Nature Review Genetics. Nature Biotech is considered too far from the subject area. The Nature Scientific Data Journal could be a reserve option.

D7.6: The paper relating to this deliverable report has not yet been submitted due time pressures. The new lecturer or resource at ICL can take this paper forward. They would be a co-author on the paper. Target journal: IT of security journal - WP2 can also contribute - as a co-production.

ESAB members would be co-authors on the publications. Fabien would be first author.

D7.8: This needs to be updated according to the regulation before it can be published. This can be separated from D7.9. The report itself will not be re-submitted, but the paper can be sent to the IMI. Target journal: BMC Medical Ethics first choice, also open access. Bioethical journal would be too slow. BMJ could be an option but with a lower chance of success. Emmanuelle is willing to help. Fabien to lead.

Additional ideas: **Post:** A post or article can also be written based on Fabien's poster.

Letter: Building translation projects - the eTRIKS challenges - a 800 word letter could be worthwhile. ESAB members may be able to assist in forming a letter. Specific resource for this would need to be determined after progress is made with the above items.

Decision/Next Action:

Bartha and Emmanuelle to send further comments on D7.9 to help form the publication

12. Reporting and resource

There is recognition of the need for the type of skills involved in this work. Recruiting people with the right experience is challenging.

Bayer is utilizing their WP7 resource commitment to sub-contract to Fabien Richard which will help ensure the achieved outputs are exploited.

Decision/Next Action:

Decision: The D7.9 deliverable report can be submitted after a few key changes. These include comments sent to Fabien by ESAB members

13. Future ESAB input

A conference call can be set up for beginning of next year to run through changes and the reshaping for publications.

Other entities will also want to work on the code of conduct. The model and the standards for implementing the model will need a wider societal engagement.

Decision/Next Action:

Neil to arrange a conference call in Q1 2017 to look at the revised document and publication progress.

14. Close out of meeting

The ESAB members are thanked for their significant and valuable input. Fabien Richard is congratulated on forming these documents discussed, together with the WP7 team.

15. Signed attendees list



eTRIKS ESAB Meeting

December 7th 2016

Marriot Hotel, Charles De Gaulle Airport, France

Attendance list

4

Name	Institution	Signature
Auffray Charles	EISBM	Charles Ht
Carusi Anna Maria	University of Copenhagen	Aburi
De Boer Pim	HuMedSci Consultancy, VUmc	R
Fitch Neil	BioSci Consulting	day
Henderson David	Bayer	Diffente
Knoppers Bartha Maria	McGill University	B 1. Know
Palkonen Susanna	EFA	Juran Pan
Rial-Sebbag Emmanuelle	Université de Toulouse	Ma.
Richard Fabien	EISBM	