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The Health Research Regulations 2018
A research perspective

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Response of the Research Community to the HRR 2018 Regulations - IAMS

- Concerns re GDPR requirement for explicit consent
- Challenges in implementations, including:

(a) Differences in interpretation of the legislation between institutions leading to huge site to site variation

(b) Impact of (a) on clinical trials;

(c) Slowing up of research due to protracted decision-making, resource implications, difficulties navigating a new regulatory system for research.

National survey of researcher opinions

Mee et al, 2021

Additional concerns highlighted:

(a) absence of meaningful consultation when drafting the HRRs

(b) difficulty comprehending the HRRs and confusion regarding their impact on clinical trials

(c) requirement for Ireland only amendments to international clinical trial documentation, to reach the threshold of “explicit consent”

(d) future of non-interventional clinical trials and critical care research in Ireland

(e) negative impact on PhD (Doctor of Philosophy), MD (Doctor of Medicine) and ICAT (Irish Clinical Academic Training) programmes

(f) Ireland’s capacity to contribute to large international collaborative research projects

(g) reports that the increased bureaucratic burden (ethical and HRRs related) had slowed and in some cases halted research

Requirement for explicit consent

Identified or identifiable personal data cannot be included in health research unless (a) GDPR “explicit consent” exists or (b) a consent declaration has been granted

Explicit consent means that the data subject must give an express statement of consent.

An explicit consent statement should specifically refer to:

- the particular data set that is to be processed,
- the precise purpose of processing (including any automated decision-making),
- should identify any risks and/or implications that might arise for the data subject as a result of the data processing, and
- Should provide any other relevant and specific information that might influence the decision of a data subject to give or not give their consent.

Impact of GDPR explicit consent in research

Kirwan et al, 2020

HRRs' mandatory GDPR explicit consent requirement adds an additional layer of consent, on top of the pre- existing legal and ethical requirement of informed consent.

This raised uncertainties in relation to:

- retrospective chart reviews
- pre-screening
- emergency research
- capacity
- bio-banks
- the need to re-consent previously obtained consent in order to achieve the new legal standards of GDPR explicit consent.

Amendments to Health Research Regulations

Address five substantive areas:

- Processing of personal data to establish suitability or eligibility for inclusion in health research (pre-screening)
- Carrying out low risk retrospective chart reviews
- Deferred consent for the processing of personal data for health research in exceptional situations
- Informed consent for health research obtained during the time of the EU Data Protection Directive
- Explicit consent for processing personal data in a health research context.

Case study - prescreening

- Study of rare genetic variants in families with multiple individuals with autism and other neurodevelopmental difficulties (Autism Family Study)
- PI: Geneticist
- Co-PI: Child psychiatrist

- Inclusion criteria - > 2 first degree relatives with autism + one other relative with another NDD

- Pre-screening – Child Psychiatrist can ask members of the MDT if there are families in the clinical service on their caseloads there are up to 3 affected individuals
- MDT members highlight families from their caseloads meeting the criteria
- Child psychiatrist can check file to ensure eligibility
- Child Psychiatrist contacts the family to seek their involvement in the study and for their agreement to be contacted by the research team

Lack of consensus on interpretation of HRR between two HEIs

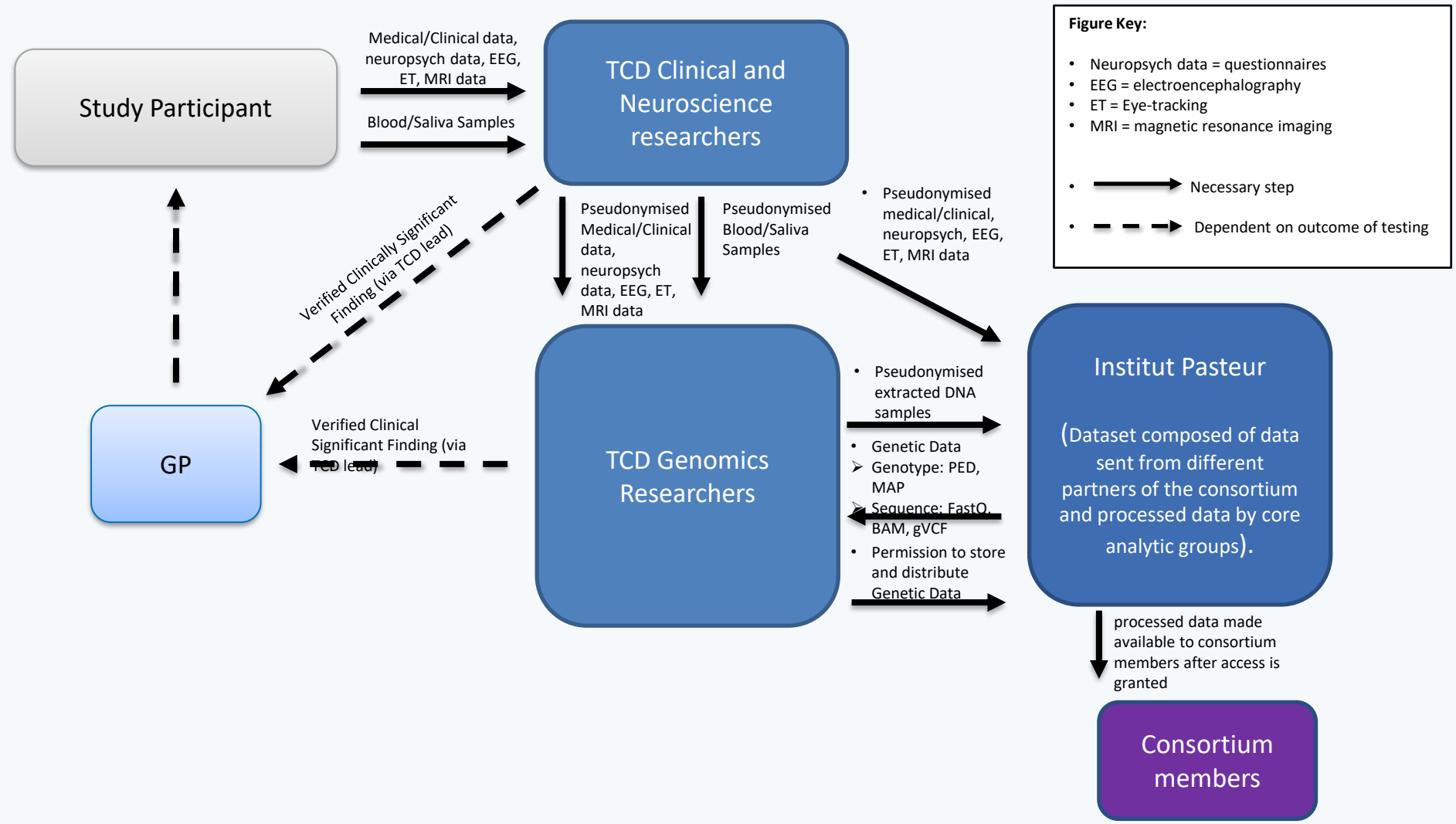
- Genomic analysis of samples recruited to the Autism Family Study
- Consent in place for genomics research and data sharing
- Co-investigator moved to another Irish HEI mid-project
- That HEI would not accept the existing REC approval and consent forms for study subjects recruited because MU not explicitly named on the consent form (although data sharing is)

"…….. re-consent should be sought for "new HEI" involvement in the project. This consent must be explicit giving full details of the project, "new HEI" role who we will be sharing it with, the right to withdraw etc. Information sheets and consent forms should be submitted and approved by "new HEI" Ethics Committee."

Is explicit consent truly 'informed consent'

- Need for transparency – unbundled consent require to clarify what data processing will occur with someone's data.
- Explicit consent means that the data subject must give an express statement of consent.
  - An explicit consent statement should specifically refer to:
  - the particular data set that is to be processed,
  - the precise purpose of processing (including any automated decision-making),
  - should identify any risks and/or implications that might arise for the data subject as a result of the data processing, and
  - Should provide any other relevant and specific information that might influence the decision of a data subject to give or not give their consent.

Example PIL from multisite study involving genomics, behavioural, psychiatric, neuroimaging data and audio/video recording


Study Participant
Medical/Clinical data, neuropsych data, EEG, ET, MRI data
Blood/Saliva Samples
TCD Clinical and Neuroscience researchers
Figure Key:
Neuropsych data = questionnaires
EEG = electroencephalography
ET = Eye-tracking
MRI = magnetic resonance imaging
Necessary step
Dependent on outcome of testing
Verified Clinically Significant Finding (via TCD lead)
Pseudonymised Medical/Clinical data, neuropsych data, EEG, ET, MRI data
Pseudonymised Blood/Saliva Samples
Pseudonymised medical/clinical, neuropsych, EEG, ET, MRI data
GP
Verified Clinical Significant Finding (via TCD lead)
TCD Genomics Researchers
Pseudonymised extracted DNA samples
Genetic Data
Genotype: PED, MAP
Sequence: FastQ, BAM, gVCF
Permission to store and distribute Genetic Data
Institut Pasteur
(Dataset composed of data sent from different partners of the consortium and processed data by core analytic groups).
processed data made available to consortium members after access is granted
Consortium members

PARENTAL/CAREGIVER GENERAL CONSENT FORM

If you are agreeable to both you and your child's participation in the overall study and assessments being recorded, please complete the consent form below.

	Yes	No
I have read (or been read to) the information about the study. I have had the opportunity to ask questions and all my questions have been answered to my satisfaction		
I understand the information and what taking part in this study involves.		
I am willing for my child to participate in the project, but I feel under no obligation to allow this participation		
I am willing to participate in the project, but I feel under no obligation to do so.		
I understand that the information collected in the study will be kept strictly confidential and will only be made available to the research team at Trinity College Dublin, and researchers within the AIMS-2-TRIALS consortium.		
I understand that I can withdraw my child from the study at any stage without giving an explanation, and withdrawal will not affect my/my family's medical care.		
I freely and voluntarily agree for my child to be a part of this research study, having been made fully aware of the risks and benefits.		

Consent to the use of personal data		
I consent to the use of the information collected about me (personal data) for this study.		
I consent to the use of the information collected about my child (personal data) for this study.		
Consent to video/ audiotaping of interviews or assessment	**Yes**	**No**
I consent to the video or audio-recording of my interview with the research clinician if required.		
I consent to the video or audio-recording of my child's assessments with the research clinician if required.		
I agree to these audio or video recordings being shared with other authorised researchers for research reliability.		
I agree to these audio or video recordings being used to train clinician's in autism assessment.		

Incidental findings	**Yes**	**No**
I consent to being informed if any genetic variant of clinical significance is discovered from the biological sample I provide.		
I consent to being informed if any genetic variant of clinical significance is discovered from the biological sample my child provides.		
I consent to providing my family doctor's contact details, and I understand that if I do not provide these details, my child will not be able to participate in the MRI component of the study.		

My data retention and sharing/future research*	**Yes**	**No**
*As explained in the information leaflet, future research will use your data to explore new questions that arise from the results of this study, relating to rare genetic variants and neurodevelopmental disorders. The purposes of data sharing for future research are to speed up the search for impactful findings in autism research. Any future research projects using your data will have approval from the relevant research ethics committee.		
I consent to my anonymised cognitive and behavioural data being retained following completion of this study for the purposes of further ethically approved research.		
I consent to my anonymised cognitive and behavioural data being shared with research collaborators for future ethically approved research.		
I consent to my child's anonymised cognitive and behavioural data being retained following completion of this study for the purposes of further ethically approved research.		
I consent to my biological samples being retained following completion of this study for the purposes of further ethically approved research.		
I consent to my pseudonymised biological samples being shared with research collaborators for future ethically approved research.		
I consent to my pseudonymised biological samples being shared with publicly available databases for the scientific community for the purposes of ethically approved research. I understand that if data will be shared in this way that the research team will contact the ethics committee to request permission for data sharing.		
I consent to my data being fully (irrevocably) anonymised after project completion should the Principal Investigator of the study wish to do so.		

My child's data retention and sharing/future research	Yes	No
I consent to my child's anonymised cognitive and behavioural data being retained following completion of this study for the purposes of further ethically approved research.		
I consent to my child's anonymised cognitive and behavioural data being shared with research collaborators for future ethically approved research.		
I consent to my child's anonymised cognitive and behavioural data being retained following completion of this study for the purposes of further ethically approved research.		
I consent to my child's anonymised neuroimaging data, including EEG and MRI data, being retained following completion of this study for the purposes of further ethically approved research.		
I consent to my child's anonymised neuroimaging data being shared with research collaborators for future ethically approved research.		
I consent to my child's biological samples being retained following completion of this study for the purposes of further ethically approved research.		
I consent to my child's pseudonymised biological samples being shared with research collaborators for future ethically approved research.		
I consent to my child's anonymised cognitive and behavioural data being shared with publicly available databases for the scientific community for the purposes of ethically approved research. I understand that if data will be shared in this way that the research team will contact the ethics committee to request permission for data sharing.		
I consent to my child's anonymised neuroimaging data being shared with publicly available databases for the scientific community for the purposes of ethically approved research. I understand that if data will be shared in this way that the research team will contact the ethics committee to request permission for data sharing.		
I consent to my child's pseudonymised biological samples being shared with publicly available databases for the scientific community for the purposes of ethically approved research. I understand that if data will be shared in this way that the research team will contact the ethics committee to request permission for data sharing.		
I consent to my child's data being fully (irrevocably) anonymised after project completion should the Principal Investigator of the study wish to do so.		

Future Contact	Yes	No
I consent to being contacted by a member of the research team after 10 years to ask for consent to continue to retain my data for future research.		

Participant's Name (Printed):.....

Participant's parent/legal guardian Name (Printed):.....

Participant's parent/legal guardian Signature:.....

Date:.....

To be completed by the researcher	Yes	No
I have fully explained the purposes and nature of this research to the participant's parent/legal guardian in a way that s/he can comprehend, and I have invited him/her to ask questions about the study.		
I have explained the potential for risks and benefits to the participant's parent/legal guardian in a way that s/he can comprehend.		
I confirm that I have provided the participant' with copies of the information leaflets and consent forms.		

Name of researcher:.....

Signature:.....

Date:.....

Some reflections on the broader impacts of the HRR on the process of research

- Heavy administrative load
- Multiple ethical amendments in the past two years – average of 1-2 per study.
- DPIA and DMP required for each study that is ongoing.
- New studies have been easier to manage due to the availability of pre-existing applications but during COVID predominantly survey-based research.
- E.g. *"Over the past year, we have diverted most of our resources to aligning with the health research regulations. Research has had to take a back seat. We could not have re-booted a HRRs compliant registry and biobank without close and ongoing support from our local Clinical Research Facility (CRF) regulatory affairs team; this cost us €17,000 and counting, money which has been diverted away from research".*