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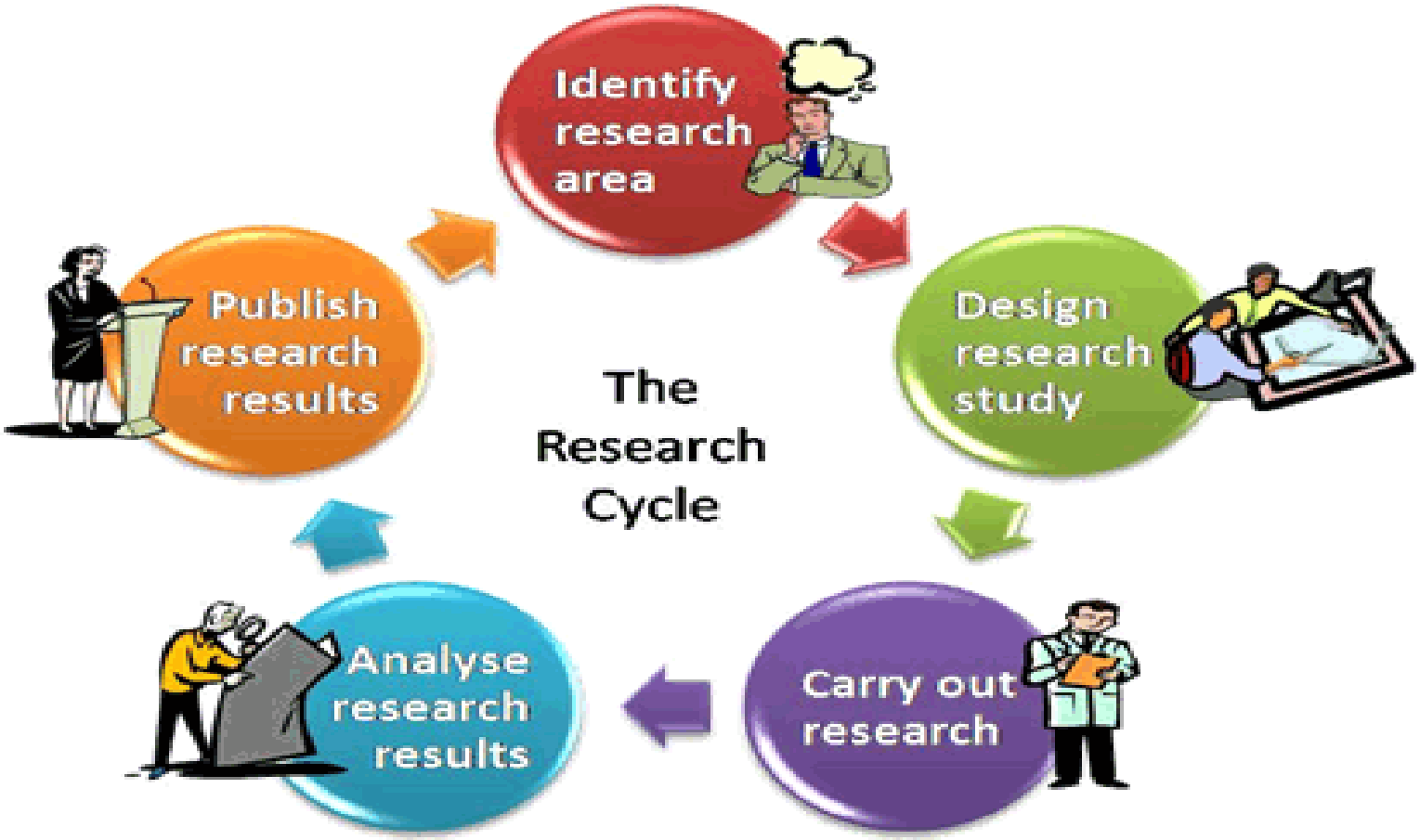
Regulations and Ethical Challenges in Research

RCSI DEVELOPING HEALTHCARE LEADERS WHO MAKE A DIFFERENCE WORLDWIDE

Why Research?



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Principals of Ethical Conduct

- **Integrity:** a commitment to the search for knowledge, honest, ethical conduct of research and dissemination and communication of results

- **Respect for Persons:** regard for the welfare, rights, beliefs, perceptions and customs of the person involved in research

- **Beneficence:** researcher's responsibility to minimise risk of harm or discomfort to research participants

- **Justice:** fair distribution of the benefits and burdens of participation in research for any research participant

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Fundamental Concerns for Ethical Research

- While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects. (Helsinki 2013, No. 8)
- Medical research should be conducted in a manner that minimises possible harm to the environment. (Helsinki 2013, No. 11)

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Fundamental Concerns for Ethical Research

- Medical research involving human subjects must be conducted only by individuals with the appropriate ethics and scientific education, training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional. (Helsinki 2013, No. 12)

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Governance of Clinical Trials

- REGULATIONS REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC

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History of Ethical Review (RECs)

- The 1975 amended version of the Declaration of Helsinki referred to the basic principle that the protocol of a proposed research project should be submitted to an independent body for “consideration, comment, and guidance”.
- 2001 Clinical Trial Directive instructed Member States to take the measures necessary for establishment and operation of Ethics Committees … (Article 6).
- Clinical Trials Regulation (EU) No 536/2014

  “The ethical review shall be performed by an ethics committee in accordance with the law of the Member State concerned”. (Article 4)

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NEW REGULATIONS REGULATION (EU) No 536/2014

- Single electronic submission through the EU portal, both for national and multinational studies.
- All communication between sponsor and reporting member state (MS) as well as between all stakeholders (sponsor, drug authority, ethics committee) via EU portal only.
- One national contact point per MS to facilitate the authorisation procedure.

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REGULATIONS REGULATION (EU) No 536/2014

- **Part I:** Trial protocol, scientific background, risk (harm) – benefit assessment, IB, details specified in Article 6 and Annex I

- **Part II:** Informed Consent material, qualification of investigators and suitability of study sites (centres) etc., details specified in Article 7 and Annex I

Part I: Evaluated by all MS concerned, reporting MS coordinates the assessment and provides ‘single decision’

Part II: Evaluated by all MS concerned, each MS provides its decision

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Benefits

- Innovate and lead
  - in clinical trial regulation and
  - in innovation of new medicines and better use of existing medicines.
- Streamlined, coordinated, proportionate and transparent
- Modification, registration and results reporting
- Streamlined and coordinated clinical trial between and within MS, using best expertise in the MS concerned
  - Streamlined safety reporting,
  - Proportionate supervision of clinical trials,
  - Transparency supporting public confidence, participation and critique and enabling

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Challenges

- Scientific and ethical review by Research Ethics Committees.
- Harmonization of ethical review!
- Attempts to limit the role of Research Ethics Committees
- What about ethical audit of research?
- Access to the EU Portal?

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EU proposals to revise data protection rules

"We have some facts about you that you don't remember, some that you thought were really secret, and some that never even happened."

On 14 April 2016, after the final European Parliament vote, the EU reached an informal agreement on new laws on data protection, which will set out new European rules on privacy in the digital age. *Position of the Council at first reading with a view to the adoption of a Regulation of the European Parliament and of the Council of on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC) 2016*

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EU proposals to revise data protection rules

- It appears that EU legislators have removed a controversial amendment to new data privacy law which would have imperilled efforts to use personal data for large studies
- EU negotiators in Strasbourg signed off on the new European Data Protection regulation.
- The rules are expected to take effect from 2018.

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EU proposals to revise data protection rules

- Concern that specific consent each time an individual's data was used in research, would be unworkable.
- Provisions in the new rules which say if it's truly impossible to inform someone of personal data use, then it is permissible to use it.
- This will legally protect a researcher whose makes use of thousands or millions of health records. In cases like this it would be impractical to seek consent for each and every one, it could also risk biasing results.

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EU proposals to revise data protection rules

- Consent is already an important principle of research.
- Safeguards and governance structures are already in place to ensure personal information is used safely and ethically.
- Member states will have to introduce or adapt their legal basis to the new regulation and ensure that proper exemptions apply to research.

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Health Information and Safety Bill – Revised Scheme

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HSE Guidelines (2013)
Categories of research
Research involving archival material

- Where archival biological material or data was obtained from persons for research or clinical purposes, where the material or data is not individually identifiable (i.e. anonymous), and where there are no potential harms to the person from whom the material or data was obtained, consent requirements may be waived.

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HSE Guidelines (2013)
Categories of research
Research involving archival material

- Where existing material or data is individually identifiable, researchers should make every reasonable effort to obtain consent from individuals for the use of their archival biological material or data.
- A REC may waive the consent requirement subject to conditions outlined below.
- Researchers who have not obtained consent from participants for secondary use of their archival material or data should only use such material or data if they can satisfy a REC that:

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HSE Guidelines (2013)
Categories of research
Research involving archival material

- The use of the material/data without the participants' consent is unlikely to adversely affect the welfare of individuals involved
- The researchers will take appropriate measures to protect the privacy of individuals, and to safeguard the material/data
- The researchers will comply with any known preferences previously expressed by individuals about any use of their material/data
- It is impossible or impracticable to seek consent from individuals to whom the material/data relates; and

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HSE Guidelines (2013)
Categories of research
Research involving archival material

- “Impracticable" refers to excessive difficulty or onerousness that jeopardises the conduct of the research as opposed to inconvenience.
- As a condition of access, archival biological material or data should be de-identified by the data controller.

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Health Information and Safety Bill – Revised Scheme

- Explicit consent for the processing of health information, which is classed as sensitive personal data, is a key part of current data protection law.

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Health Information and Safety Bill – Revised Scheme

- The Data Protection Commissioner is now the person who will have a pre-approving role in research projects that rely on this so-called consent exemption or waiver.
- The office would charge a fee for such approvals, which it is envisaged would only be granted in certain “strict and limited” circumstances.
- A request for a decision from the Data Protection Commissioner permitting “the collection and use...of personal data that relate to one or more individuals without the consent of those individuals”.

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Health Information and Safety Bill – Revised Scheme

- The person making the proposal will have to demonstrate that:
  - Their research requires access to the personal data they are asking for, rather than anonymised or 'de-identified' data.
  - Be of "sufficient importance that the public interest in it outweighs to a substantial degree the public interest in protecting the confidentiality of the personal data concerned".
  - Guarantee the personal data will not be used in such a way that damage or distress is, or is likely to be, caused to those individuals.

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Health Information and Safety Bill – Revised Scheme

- The Bill also sets out proposals for “data matching” programmes, which would require certain parties to provide the health information of individuals for use in a national programme.
- The Health Information and Patient Safety Bill, in tandem with legislation to introduce individual health identifiers to track people through the system from cradle to grave, is a key component of the Government’s health strategy.

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Challenges

- The role of RECs
- “audit” versus “research”
- Recourse to the Data Protection Commissioner
- Costs and time frames.
- Student Research
- With regards data matching concern around the information given and whether patients were given adequate opportunity to opt out of having their data transferred.

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Biobanks

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Biobank Dilemmas

- Broad Consent vs. Specific Consent
- Privacy, Confidentiality (Data Security) vs. Data Sharing
- Feedback vs. Right not to know
- Access policies and procedures
- Control v Ownership
- Withdrawal

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Importance of Consent in Biobanking

- Demonstrates respect for donors
- Allows people to control whether their samples and data are used for research purposes (voluntariness)
- Allows them to decide if the risks and burdens of research are acceptable to them
- Allows people to protect and potentially promote their values and interests
- Allows for transparency which can promote/earn public trust; important for sustainability

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Consent Models

- **Specific**- Deemed unsuitable for biobanks as it allows the use of biological specimens and related data only in immediate research; precludes any future study that is not foreseen at the time of the original consent.
- **Layered**- Several options given to the research subject about future uses.
- **Broad**- permission for a broad range of research purposes. When does broad consent become blanket consent?
- **Dynamic**-interactive relationship between custodians of biobanks and donors of material using web technologies.

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Broad Consent

- At the time of data and sample collection, future research use may be difficult to anticipate or may only be describable in very broad general terms, for example, for ‘cancer research’, ‘rare disease research’ or ‘medical research’.
- Consensus emerging: broad consent with ethics approval, with the right to withdraw from the study, is acceptable if there is a continuous flow of information on project developments and the necessary governance framework is in place.
- Is this always possible or desirable?

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Re-consent

- Respect for autonomy involves re-consent where the REC deem the scope of the original consent may preclude the proposed research use.
- Where legal requirement for consent was in place at time of sample/data collection, re-consent or notification with an opt-out option should be pursued.
- In case of minors (or where samples/data collected when person was a minor) re-consent or notification with opt-out should always be pursued.
- Where re-contact not feasible or small sample numbers are of utmost importance, or samples from an older collection with no consent, a waiver could be considered in accordance with legal system.

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Governance of Biobanks

EC Report 2012 Biobanks for Europe: A Challenge for Governance

Recommendation 1

Member states and European institutions should develop a consistent and coherent legal framework for biobanking that should protect participants' fundamental rights, in particular in the areas of privacy, data protection and the use of human tissue in research.

Recommendation 3

For European biobanks to operate successfully there need to be sustainable governance mechanisms to involve and engage the public, and in doing so ensure their continual participation, trust and support.

Recommendation 4

Sustainable governance mechanisms for creating a relationship of reciprocity between biobanks and European society need to be encouraged so that Europeans can understand and obtain the benefits from biobank research.

Recommendation 8

The potential to use web 2.0 technologies to involve patients, research participants and the wider public, in the governance of biobanks should be supported to ensure that Europeans can have trust in biobank research and those organizations that establish and maintain biobanks.

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Role of RECs

- Important role for RECs in ensuring ethical standards and the scientific merit of research involving humans.
- Ongoing advances in biotechnology and continued growth of biomedical research.
- The role of RECs has become more complex – particularly regarding genomic and biobank-based research.
- Scope and size of biobanks is increasing; samples, data and results are crossing borders – These issues require international guidance and a uniformity of approach.
- Question arises whether RECs have the appropriate competencies to deal with such issues.
- Are RECs “fit for purpose” in the governance of biobanking?
- Is another mechanism of oversight required?

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Incidental Findings: To tell or not to Tell?

- Incidental findings: unanticipated discoveries made in the course of research that are outside the scope of the research but are clinically relevant and actionable.
- Growing body of empirical research suggests that many individuals want and even expect to receive their IFs, especially if researchers find something serious
- As part of the consent process, prospective research participants should be provided with the option of whether or not they wish to have medically relevant incidental findings disclosed to them.
- “Right not to Know” should be respected

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Withdrawal

- A fundamental tenet of consent: Individual should be free to withdraw his/her consent at any time without penalty.
- Large-scale biobanks recognise the importance of facilitating such withdrawal - however, the complete withdrawal of all samples and data may not always be possible.
- Different methods of graded withdrawal are employed by different national biobanks:
    - "No further use"– deletion of samples and data
    - Deletion of identifiable data but samples still retained and used
    - Destruction of samples but not any data already obtained
    - "No further contact"
- Essential that any limitations on withdrawal are clearly outlined as part of the informed consent process.

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Payment Research Participation

Existing Situation CIOMS Guideline 7 (2002)

- Subjects may be reimbursed for lost earnings, travel costs and other expenses incurred in taking part in a study; they may also receive free medical services. Subjects, particularly those who receive no direct benefit from research, may also be paid or otherwise compensated for inconvenience and time spent. The payments should not be so large, however, or the medical services so extensive as to induce prospective subjects to consent to participate in the research against their better judgment

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Payment Models

- **Free Market:** paid for service, rules of supply & demand, no upper wage limit, more risk-more money
- **Wage Payment:** research a form of labour, wage set equivalent to unskilled labourer
- **Reimbursement:** research form of public service, compensated for cost of participation
- **Appreciation:** gifts or small amounts of money as sign of appreciation
- **Fair Share:** partners in research, should share in financial benefits

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Health Information and Safety Bill – Revised Scheme

- A system of Approved RECs by HIQA

Health Information and Safety Bill – Revised Scheme

- **PART 3: RESEARCH ETHICS APPROVAL**
- Provides for a voluntary, national, streamlined research ethics approval structure for health research not already governed by other legislation.
- This Part does not apply to clinical trials of medicinal products or medical devices as these are already governed under other legislation.

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Health Information and Safety Bill – Revised Scheme

- A major benefit for health researchers will be the creation of a single point of contact via HIQA as well as obtaining a single ethical approval for national or regional health research.
- HIQA will be the supervisory body for approved research ethics committees (ARECs)
- It will also provide an avenue for researchers to apply for a data protection consent exemption in certain limited and restricted circumstances.

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Health Information and Safety Bill – Revised Scheme

- Membership of approved research ethics committee. Provide that:

(1) An approved research ethics committee shall consist of expert members and lay members to be appointed by its appointing authority.

(2) There shall be no more than 21 persons and no less than 12 persons appointed to be members of an approved research ethics committee and at least one quarter of members shall be lay members.

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Health Information and Safety Bill – Revised Scheme

(3) The appointing authority shall appoint an expert member as chairperson and a lay member as deputy chairperson of the approved research ethics committee.

(4) A person is not eligible for appointment as a member of an approved research ethics committee if the person is not a fit and proper person.

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Expert Members

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Health Information and Safety Bill – Revised Scheme

- Expert member is:

(a) is a practising or retired health practitioner,

(b) has qualifications or experience relating to the conduct of health research (other than as a member of a research ethics committee),

(c) has qualifications or experience in the area of ethics, statistics, social sciences, philosophy or theology,

(d) is a practising or retired barrister or solicitor, or

(e) belongs to a class or category of persons prescribed by the Minister for the purposes of this definition;

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Challenges

- Voluntary Approved REC?
- Problem with the definition of “expert members”

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THANK YOU

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