Royal College of Surgeons in Ireland
Coláiste Ríoga na Máinleá in Éirinn

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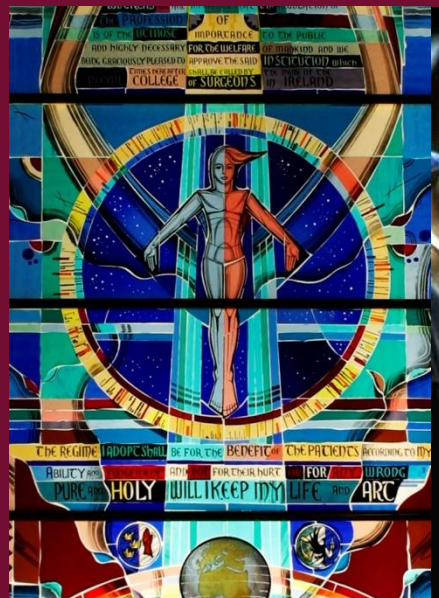
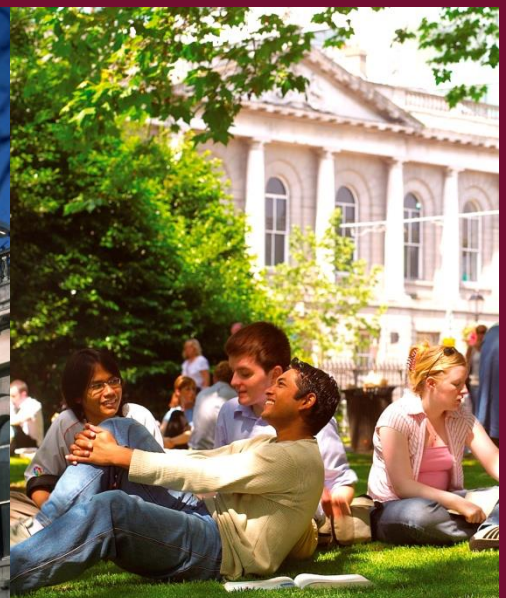
Federation of European Academies of Medicine

Ethics Committees: Looking Forward

Prof David Smith





OUTLINE

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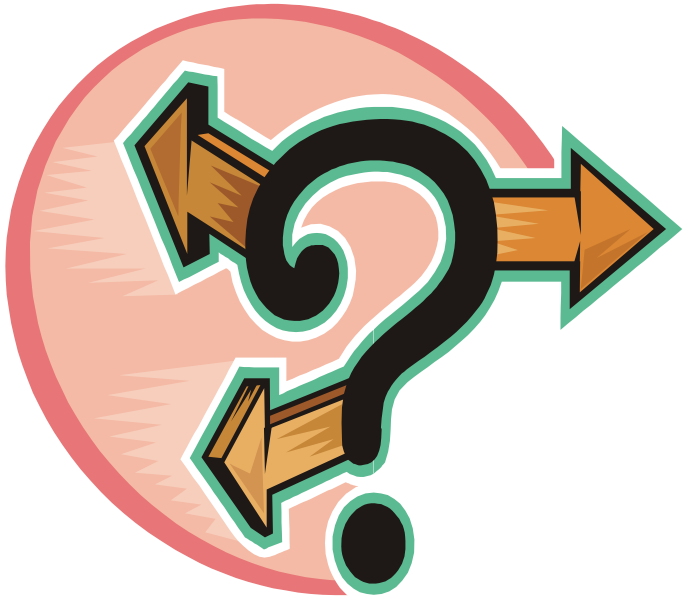
1. What is the Role of Research Ethics Committees?
2. Regulation of the European Parliament and the Council on Clinical Trials on Medicinal Products for Human Use and repealing Directive 2001/20/EC (COM 2012)
3. Expansion of the remit of RECs to now include monitoring and auditing of research
4. The RECs responsibility to uphold integrity in Research.
5. Composition of RECs – Specialised membership – Specialised Committees
6. Effectiveness of RECs in achieving their objectives.



Distinctions

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- Clinical Trials
- Human Related Research
- This situation in Ireland

I would like to thank Dr Siobhan O'Sullivan for her assistance in developing this presentation.

Recognised Research Ethics Committees, Ireland

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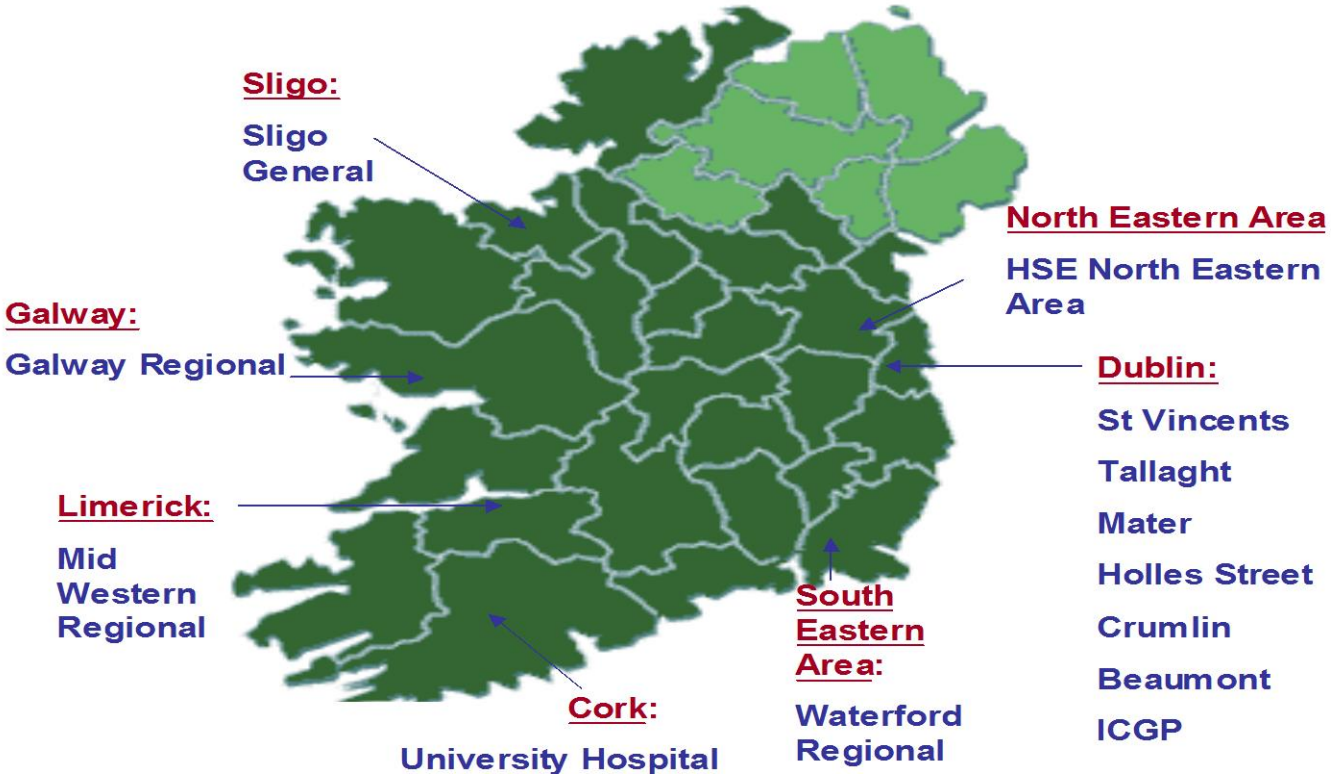

Research Ethics Committees, Ireland

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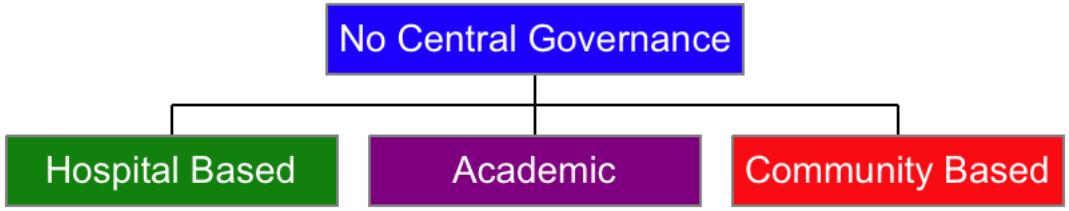

AMNCH Tallaght Hospital
Beaumont Hospital
Bon Secours Hospital
C.U.H. Temple Street
Cappagh National Orthopaedic Hospital
Coombe Women's Hospital
Cork Clinical Teaching Hospitals
Galway Regional Hospital
Limerick Regional Hospital
HSE North East
Waterford Regional Hospital
James Connolly Memorial Hospital
Letterkenny General Hospital
Mater Misericordiae University Hospital
Mayo General Hospital
National Maternity Hospital
National Rehabilitation Hospital
Rotunda Maternity Hospital
Royal Victoria Eye & Ear Hospital
Sligo General Hospital
St Francis Hospice
St Patrick's Hospital
St Vincent's Healthcare Group
St Vincent's Hospital
St. Lukes Hospital
Our Lady's Children Hospital

Carlow Institute of Technology
Waterford Institute of Technology
Dublin Institute of Technology
St Patrick's College of Education
NUI Galway
NUI Maynooth
Dublin City University
RCD School of Social Work and Social Policy REC
Royal College of Physicians of Ireland
Royal College of Surgeons of Ireland
Trinity College Dublin Children's Research
Trinity College Dublin Medical Faculty
Trinity College Dublin Nursing and Midwifery
Trinity College Dublin Social Work & Social Policy
Trinity College Dublin School of Psychology
University College Cork Applied Psychology Postgraduate
University College Cork Social Research
University College Dublin - Humanities
University College Dublin Research
University College Dublin School of Psychology Undergraduate
University of Limerick
University of Limerick College of Education
University of Limerick College of Humanities
University of Limerick College of Informatics and Electronics
University of Limerick Kemmy Business School
University of Limerick Physical Education and Sports Science

Cheeverstown Intellectual Disability
Children's Sunshine Home
COPE Foundation Intellectual Disability
Daughters of Charity
Enable Ireland
HSE Autism Services
HSE Midland Area
Irish Prison Service
KARE Intellectual Disability
National Disability Authority
Sisters of Charity
St Michael's House Intellectual Disability
Travellers
Irish College of General Practitioners
Stewarts Hospital Services Ltd
Health Research Board
St. John of God Services
Economic Social Research Institute

History of Research Ethics Committees

- 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”. This was an important step in the evolution of what are now known as “Research Ethics Committees”. This repeated in 2008.
- 2001 Directive Member States shall take the measures necessary for establishment and operation of Ethics Committees … (Article 6)

Function of Research Ethics Committees

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- ***Protection***: to protect the rights and welfare of human subjects of research from any physical and mental discomfort, harm and danger from research procedures; to protect your rights as a researcher to carry out legitimate investigation; and the University's/hospital's reputation for research conducted and sponsored by it
- ***Advice***: can advise individual researchers on whether a project is likely to be harmful or offensive to subjects or the broader community
- ***Education***: has the task of increasing knowledge and awareness of ethical issues and regulations/directives
- ***Research Quality***: For research to be ethical, it must be scientifically sound
- ***Conciliation***: conciliation and adjudication of conflicts between investigators and participants

FUNDAMENTAL CONCERNS FOR ETHICAL RESEARCH

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- ***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

Regulation of the European Parliament and the Council on Clinical trials on Medicinal Products for Human Use and repealing Directive 2001/20/EC (COM 2012)

- The Report of the European Group on Ethics in Science and New Technologies made the following points:
- Aim to harmonise and fast-track the clinical trial process with a view to bringing new medicines to the market

1. **The marginalization of Research Ethics Committees.**
   - Assessment of trial split into two parts:
   - Part II – dealing directly with issues of ethical concerns including informed consent, compensation and rewarding issues, recruitment of research participants, data protection, and competence of research personnel, suitability of trial sites, use of samples – traditionally areas for the member states.

Regulation of the European Parliament and the Council on Clinical trials on Medicinal Products for Human Use and repealing Directive 2001/20/EC (COM 2012)

- Part I – sample size, randomization, comparator, its clinical and statistical evidence
- Evaluation of these aspects is crucial for the protection of research participants from harm and unnecessary risks, aspects that are at the core of ethical evaluation of medical research.
- This would be transferred from the Member State (MS) to the Reporting Member State.

2. **Regulation does not specially refer to ethics committees but leaves it up to member states to decide which bodies should be involved in the assessment.**
   - This would appear to be in contradiction with Helsinki 1975 and 2008 and the Council of Europe Convention on Biomedicine and its Additional Protocol on Biomedical Research
3. **Changing the structure of ethical evaluation might hamper the marketing authorisation process of new medicines.**
   - The FDA of the United States require that “the (Foreign clinical) studies be conducted in accordance with good clinical practice including review and approval by an independent ethics committee.
   - The European Medicine Agency has also set similar requirements for trials conducted outside the EU/EEA

4. **Assessment time of 10 days is too short.**
5. **The possibility of ethics shopping**
   - Sponsor of the trial is vested with the task of identifying which MS should act as the Reporting MS for the assessment of Part I. Other MS may only comment on the issues relating to Part I to the Reporting MS before it gives the assessment report of the trial.

Monitoring and Auditing of Research

- Expansion of RECs original remit of reviewing research proposals prior to their commencement.
- This is connected to the related theme of the involvement of RECs in upholding research integrity
- The inadequacy of current systems of monitoring research projects by ethics committees, widely recognized in the literature.

Monitoring and Auditing of Research

- Possible resistance amongst researchers.
- Monitoring programmes must be accompanied by adequate information and explanations to researchers highlighting the importance of participant feedback and emphasising its importance for improving the research process.
- An obstacle to more comprehensive monitoring procedures often cited is lack of resources.

Monitoring and Auditing of Research

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- **ESRC Framework for Research Ethics (FRE) 2010 Updated September 2012 stated that sh**ould be designed, reviewed and undertaken to ensure integrity, quality and transparency.
- But how do we define Integrity?

Monitoring and Auditing of Research

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- ***Honesty*** in presenting research goals and intentions, precise and nuanced reporting on research methods/procedures, and in conveying valid interpretations & justifiable claims with respect to possible applications of results.
- ***Reliability*** in performing research (meticulous, careful and attentive to detail), and in communication of the results (fair and full and unbiased reporting).
- ***Objectivity:*** interpretations/conclusions must be founded on facts and data capable of proof and secondary review; transparency in collection, analysis and interpretation of data, and verifiability of the scientific reasoning.

Monitoring and Auditing of Research

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- ***Impartiality*** and independence from commissioning/ interested parties, from ideological or political pressure groups, and from economic or financial interests.
- ***Open communication***, discussing work with other scientists, contributing to public knowledge through publication of findings, honest communication with general public.
- ***Duty of care*** for participants in and the subjects of research, be they human beings, animals, the environment or cultural objects. Research on human subjects and animals should always rest on the principles of respect and duty of care.
- ***Fairness***, in providing proper references and giving due credits to the work of others, in treating colleagues with integrity and honesty

Monitoring and Auditing of Research

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- **A Way Forward? A report from the European Forum for Good Clinical Practice Drafted by the Research Integrity Subgroup of the EFGCP Ethics Working Party (June 2010)**

1. **Definitions** of 'fraud' and, particularly, 'misconduct', were needed with clear demarcation between them, across Europe and the rest of the World.
2. Follow Denmark and the Nordic Countries and in the USA (with the ORI) for a **National Body on Research Integrity**. The case now had to be made for establishing such a body in other countries.

Monitoring and Auditing of Research

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3. **Training** stakeholders in clinical research projects in the principles of research integrity and the prevention of fraud and misconduct could not be over-emphasised.
4. Support needed for **research into research misconduct.**
5. Guidelines were urgently needed on encouragement for, and the protection of, the genuine **whistle-blower**.
6. **Guidelines** and examples of standard operating procedures for the monitoring of research projects to include integrity and detection of misconduct.

Monitoring and Auditing of Research

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7. An agreed protocol on the **value of audit** in the management of research misconduct.
8. The role of the **statistician** in confirming or denying a suspicion that data have been fabricated or falsified.
9. The ways in which an **enquiry** into suspected research misconduct should or should not be conducted needs to be clarified and harmonised.

Composition and Effectiveness of RECs

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- The increased complexity of data sets and advances in data-mining capabilities have serious data protection implications - this raises questions around the composition of RECs and whether RECs require members with specific professional expertise (e.g. in data protection).
- General RECs or Specialised RECs

Composition and Effectiveness of RECs

- **RESEARCH – AUDIT**
- Ethical considerations should apply to all medical practice, but many people act as if they apply only to research.
- For example, all research studies have to be scrutinised by an ethics committee, but most ethics committees specifically exclude audit studies from their remit.
- Consequently, the distinction between audit and research can have important implications, and the temptation to label research as audit is considerable.

Composition and Effectiveness of RECs

- In contrast to the intention of the Directive to centralise and harmonise the work of RECs, the number of RECs, the appointment of members to RECs, the timelines for obtaining research permission from them, and the procedures for obtaining informed consent from vulnerable persons are all varied across Europe.
- There is no uniform method of implementing European legislation in the different countries. This situation raises doubts about the feasibility of international multicentre studies in the EU.
- Therefore, harmonisation should be considered as regards legislation on clinical drug trials and also on other types of research, and should cover the working principles of RECs.

Composition and Effectiveness of RECs

- **Membership**
- Members with clinical practice experience (physicians and nurses) are mandatory for all surveyed ethics committees, together with specialists in activities related to medical research (epidemiologists, pharmacists, pharmacologists and/or biostatisticians).
- This is a legal requirement in Austria, Germany, Italy and Spain.
- Lawyers and other lay members (ethicists, social workers and religious leaders) are the second group of mandated representatives.
- One of the biggest differences among the target countries is the representation number of those experts.

Composition and Effectiveness of RECs

- The same is true for the participation of lay persons.
- In Denmark they represent the majority of all committees
- In Austria, France, Sweden and the UK they represent half of the membership
- In Hungary, Ireland, Italy and Spain one third or less.
- Representation of patients or patient groups is unevenly perceived as an ethical requirement.

Composition and Effectiveness of RECs

- These differences have resulted in immense variations regarding ethics committee working practices and workload.
- The efficiency of a review system depends on a clear regulatory framework.
- There is a need for a common regulatory framework on other categories of research not involving medicinal products.
- There is a need for formal training of ethics committee members.

Composition and Effectiveness of RECs

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- In several countries, regulatory legislation applied only to clinical trials on drugs and medical devices, in other states various types of research is also regulated but by laws which are different from those concerning trials, and in many countries, some research areas were not controlled by legislation at all.
- Who are these Committees responsible to?
- In many countries there is no appeal mechanism after a negative decision by an REC.

Composition and Effectiveness of RECs

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- There is a need for a fundamental debate regarding whether and which kinds of changes are needed for the further harmonisation of medical research governance in the EU and how cross-country medical research could be facilitated in the future.
- Key members of the medical research community have expressed the opinion that changes should be made at the European level and not by national governments.

THE FUTURE!!

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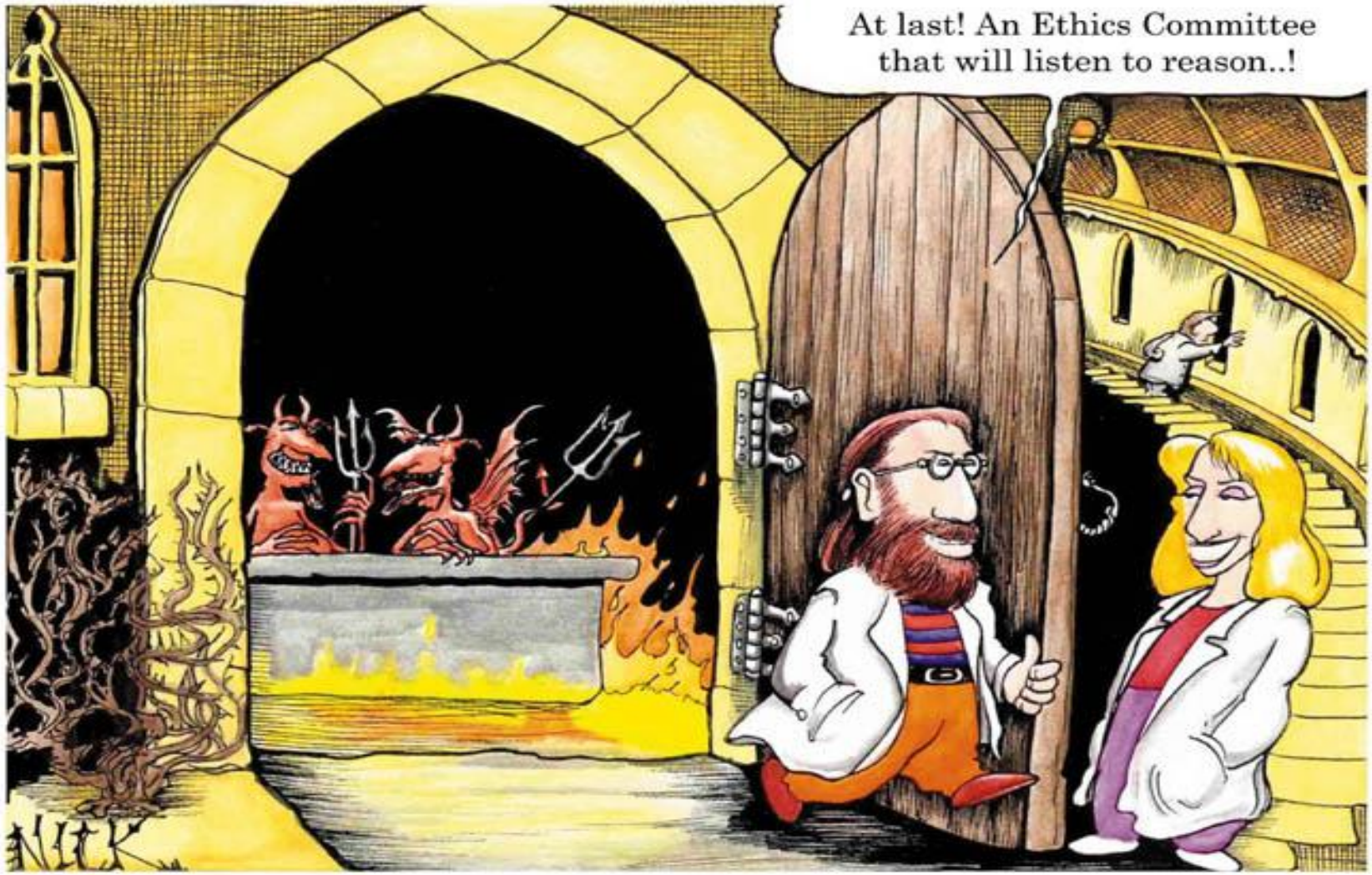

THANK YOU