



How Legal and Regulatory Solutions can promote Clinical Research

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The European Research Area: The strategic objective for UK Bio-Medical Research

- Lisbon Strategy March 2000
- To create an internal market in Science and Technology
- To become the most competitive knowledge based economy in the world in key areas and in the medium term
- To promote economic growth jobs and social cohesion
- To exploit genome research in living organisms
- To increase competitiveness in European Bio-Tech Industry
- To bring basic knowledge through to the application stage to achieve real progress in medicine and life quality



Implementing the ERA


- 6th Framework Programme and Bio-Technology Platform
- 7th Framework Programme and Science and Society Platform
- FP6 Thematic Priority Life Sciences Bio-Tech for Health EUR 2514 million
- FP7 Competitiveness and Innovation Framework Programme EUR 4.21 billion (est.)
- Integrated Projects
- Networks of Excellence
- Art. 169 Treaty of Nice



Future Development Strategy for ERA

ERA Green Paper New Perspectives SEC (2007) 412

- Adequate flow of researchers in a single labour market
- Research and innovation clusters both real and virtual and in PPP
- Effective knowledge sharing with easy access to knowledge base and IPR
- Broader borderless ERA with EU neighbours and beyond
- The right mix of competition and cooperation to address common concerns



Centralise or de-centralise? Regulate or de-regulate?

Green Paper Questions

- Is a European legal framework needed to boost research and encourage investment?
- Is a European regulatory initiative needed to facilitate PPP?
- Do we need common principles for Peer Review, Quality Assurance and research evaluation?



Answering the Green Paper

- Centralism or Pluralism: the EU and US experience
- Regulated or permissive research environments
- Inter-governmental initiatives or researcher self-help

- Fit the legal solution to the problem
- Consider the examples to decide how:
 - Type 1 cases: legislation achieves a result
 - Type 2 cases: future legislation could achieve a result
 - Type 3 cases: legal frameworks fail now so take remedial action



The Clinical Trials Directive: its Present and Future

EMA London Conference 2007

Interesting results:

- Patient representatives approve of the CT Directive
- Extend GCP principles to all Bio-Medical Research by specific regulation
- CRO want regulation for a common research passport for multi-state trials
- Harmonise insurance and indemnity schemes across EU member states
- Enhancement of REC powers
- Verdict: A Type 1 example



Drug Safety: GSK Seroxat and a Clinical Trials Database [1]

EMA Conference 2007


- Mandatory reporting of SUSAR per IMP not per CT
- Eudravigilance Database to be common repository for SSAR and SUSAR
- Work sharing between NCAs and RECs to evaluate SSAR/SUSAR
- Provide a clear legal basis for a EU database for publication of CT data in Eudravigilance Database
- Configure a EU CT Database to optimize re-analysis and meta-analysis



Drug Safety: GSK Seroxat and a Clinical Trials Database [2]

MHRA GSK *Seroxat* Investigation supervenes:

- 2001 EU Medicines Directives did not apply to CT outside MA
- 2002 Directive applies post authorisation but not outside CNU
- EU Directives do not regulate CT outside EEA
- MHRA seeks legislative overhaul for maximum clarity in reporting
- UK Government supports stricter rules on reporting of SAR
- UK Government backs away from mandatory registration/publication
- What are the issues here?



Drug Safety: GSK Seroxat and a Clinical Trials Database

[3]

Legal obstacles to mandatory registration/publication of CT data:

- EudraCT is based on CTs that are proceeding to MA
- EudraVigilance is based on SSARs/SUSARs reported to the MA holder and then to NCA
- WTO TRIPS Art.39 and the public protection override

Practical Issues in mandatory registration:

- Effective databases or 'raw data soup'?
- Is a database a poor substitute for systematic review?

Solutions 'Hard' or 'Soft':

- ABPI industry-led undertakings to register voluntarily
 - RG-led solutions based on REC requirements for applicants to search the literature and registers
 - Improve guidance on information access under current legislation
 - Governmental action at national and EU level for new legislation
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- Verdict: A Type 2 or 3 example



Paediatric Medicine: market stimulus through regulation

Regulation on Medicines for Paediatric Use (EC) No 1901/2006, (EC) No 1902/2006


Regulatory intervention might stimulate markets and research by;

- Protection of new IP for qualifying products
- Manipulation of IP field to free up R&D for qualifying products
- Boosting quality assurance in patient safety and treatment

- New applications for MA need PIP
- 6 months extra patent protection through SPC for authorised products
- 2+10 years data protection/market exclusivity for orphan products
- PUMA to stimulate off-patent products with 10 years market exclusivity
- MA transference or else facilitate application for MA

- Paediatric Research Network to coordinate and reduce duplication of research
- Paediatric Clinical Trials Database with retrospective requirement to submit data and Public Access
- SPCh and PIS must reflect +ve and –ve study results

- Verdict: The Jury's still out.



Stem Cell Patents: market stimulus by collaborative action [1]

Arts. 52, 53 EPC and Arts. 5, 6 EU Bio-Tech Directive

- No patent for the human body in its un-isolated form
 - No patent for industrial or commercial use of a human embryo
 - Patent override where exploitation contrary to ordre public or morality
 - Patent permissible for diagnostic and treatment purposes
-
- No uniform legal consensus on embryo definition or protection across EU Member States
 - No current basis in EU law for prohibition of hESC patents resulting from embryo destruction on grounds of morality or ordre public
 - No prohibition for pluripotent hESC patent unless it involves ‘the direct, repetitive use of a human embryo as a raw material in a mechanical, chemical or technical process and/or any uses involving a trade in human embryos per se’
-
- UKPO differentiates between totipotent and pluripotent hESC patents



Stem Cell Patents: market stimulus by collaborative action [2]

US patent landscape

- WARF strong patent claim and a complex IP field
- 44/56% split in stem cell patents between public and private sector
- Fragmented ownership

Global patent landscape

- Dominant patents with multiple assignees
- Pre-dominance of government, academic and not for profit owners
- Fragmented ownership across multiple organisations
- Risk of 'Patent Thicket' in the stem cell patent field in US and rest of world

Market Effect

- EU stem cell research loses incentive because of lack of moral or legal uniformity or central co-ordinating strategy
- US research risks slow-down because of patent proliferation in a de-centralised research environment



Stem Cell Patents: market stimulus by collaborative action [3]

Law-based Solutions from Regulation to Self-Help

- Lack of EU moral consensus enables patent initiatives by UK researchers
- EU Member States are free to challenge patents and to allow morality issues to be determined by ECJ preliminary ruling
- UK or EU governmental legislative initiative to alter, reduce or eliminate elements of the Patent Thicket
- Political support will be necessary for this in face of acquired rights
- Market-oriented solutions using existing rights: directed and compulsory licensing, open source, patent pools
- 'Intellectual Property Clearing House' with universal listing and voluntary industry participation?
See PIPRA
- A Type 3 Case- but which route is best?

Sources:

Stem Cell Patents: European patent law and ethics report: FP6 28th July 2006 (Nottingham);

The global stem cell patent landscape: implications for efficient technology transfer and commercial development:
Karl Bergman & Gregory D. Graff: *Nature Biotechnology* 25, 419 - 424 (2007)



Legal Frameworks for Research Infrastructures

ESFRI
e-IRG

European Roadmap,

Source: ERA EG report: *Developing World-class Research Infrastructures for the European Research Area (ERA)*

- Inter-governmental initiatives with custom-built legal framework?
- New 'Off the shelf' legal structure for research groups to adopt?
- Art. 171 EU Treaty

- New structures to have limited or unlimited liability of members?

Existing structures:

- SE company model
- has EU-wide recognition, two types of governance, but rigid set-up

- EEIG
- Set up for cross-border activity, not set up for profit, lacking management control of its members, unlimited joint and several liability

- A Type 3 example



The Future of Research Ethics Committees

EMA Conference 2007

- Demarcate the role of NCA and RECs
- REC to have direct access to EudraCT and EudraVigilance
- REC to have powers to suspend CT pending resolution of safety issues

- The CT Directive makes a REC an independent regulatory body. Restructure it accordingly.
- REC should provide a legal expertise and legal assessment as do many EU ethics boards
- REC should deal with illegality in the protocol and legal 'Privacy' rights
- REC approval should be needed for research database usage without consent
- Do we therefore need a new IG Legal Framework for research that all governance bodies can use?
- What then is the role for PIAG, NIGB, and NRES in such a framework?

- Sources: PRIVIREAL, EUROSOCAP, Draft Revision of the Helsinki Declaration



Proposed 'Flag of Convenience' for EU Integrated Research Networks



From an original design for the European Union Flag by Rem Koolhaas
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