

The NHS Needs More Regulation Not Less

In 'Bureaucracy Busting'

A DeNDRoN Workshop

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Bureaucracy: The Name of the Beast

- *'Management or administration marked by hierarchical authority among numerous offices and by fixed procedures'*
- *'An administrative system in which the need or inclination to follow rigid or complex procedures impedes effective action'*
- So Regulation is not Bureaucracy.
- Bureaucracy may derive from a mistaken management or administrative function but not a legal one
- Bureaucracy is what happens when a NHS body attempts to operate in a regulatory environment but without a regulatory system that is fitted to the task.
- Good Regulation should be pro-active to facilitate good Research and Research Governance.
- Legislative frameworks can be either:
 - Permissive (2001 CT Directive), (EC Regulation for legal framework of ERI)
 - Mandatory in effect (Regulation on Medicines for Paediatric Use)
 - Non-legislative legal solutions: self-governance by contractual undertakings 'from the bottom up'

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

As it was meant to be:

- Lisbon Strategy March 2000
- To create an EU 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

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The European Research Area Re-Launch: Towards a full realisation of the ERA

As it is now:

- Lisbon and Barcelona Targets for S&T spend as a % of GDP are not being met
- EU loses pace to US and Far East in S&T
- De-Linkage between EU Researchers and Industry, 'The European Paradox'
- Industry bias to US and Japan because of EU competition law?
- Fragmentation in S&T initiatives in funding and research priorities

The New Strategy:

- ERA must embrace globalisation with global S&T priorities
- ERA to forge links with OECD and non-OECD partner states in bi-regional or bloc coalitions
- ERA relations with blocs on a technological par with EU and with blocs that are not at par
- New policy initiatives and new ethical approaches to Developing World, Russia, China, India
- EU to South-South Alliance of Developing Countries to compete with Northern economies?
- EU as an exporter of tailored training and expertise in R&D, Research Governance, Statistical and Data Management to support global research objectives

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The European Research Area Re-Launch: New Instruments to achieve the New Strategy in S&T by 'Soft Law'

Ljubljana Process - launched 16th May 2008

- Universities, RPO, Researcher Mobility and access to world class RI are main pillars of the ERA
- Enhanced governance based on a *long term* vision of ERA developed in partnership between member states and the European Commission with stakeholder, business and citizen support.
- Open Method of Coordination (OMC) to set monitoring and evaluation criteria by national level initiatives to a common goal with political level guidance from start to finish
- Avoid unnecessary complexity and improves coherence: see the use of 'soft law' in OMC by use of national reform plans as an alternative to the use of Directives or Regulations and without EU Parliament or ECJ intervention

Instruments:

- ERA-NET, ERA-NET+, ERA-Clusters, JTI, Art. 169 Initiatives e.g. EDCTP: return for international aims
- Specific International Cooperation Actions (SICA) for use with non-associated states and ENP
- Enhanced RI in context of allowing access to European Neighbourhood Policy (ENP), tailored to suit
- FP7 Science and Society, strengthen dialogue on research ethics to support EDCTP and science education
- European Strategic Forum for International Cooperation (ESFIC) as a permanent focal point
- European Research Council to channel bottom-up research proposals for priority and funding

Q. Are prevalence of business interests responsible for the avoidance of 'hard law' regulatory solutions to S&T priorities in ERA?

Q. Will a 'bottom up approach' to R&D priorities serve to diminish 'bureaucracy' or increase it?

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The Future Regulatory Framework of the ERA: Governance for Bio-Medical Research

Q. Is Bio-medical Research a special case for 'Hard Law' because of patient rights//market forces?

EMA Conference October 2007

- More direct regulation of key areas of research activity, c.f. The Regulation on Medicines for Paediatric Use.
- Extend the regulatory structure to include other forms of bio-medical research by direct regulation rather than Directive, e.g. non intervention studies
- Single European Research Passport with a single + local ethics opinion
- New legislation to clarify and demarcate the role of NCA and REC to preserve rights and integrity of trial subjects
- Give RECs direct access to EudraCT and EudraVigilance databases and a power of suspension on safety grounds
- Harmonise the Insurance and Indemnity arrangements for multi-national CTIMP through law
- Promote harmonisation in GCP and the elimination of double standards in EU States

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The Future Regulatory Framework for ERA: 'Clinical Trials Dumping' and EPAR

O. A special case for urgency in a global ERA? Can dumping outside ERA be reduced by regulation?

Opinion 17 EGE:

- Clinical research in Developing World countries cannot be assimilated to 'Market Forces' economic activity
- Clinical trials in Developing World countries cannot be avoided for convenience

EMEA Conference 2007:

- EDCTP has development aims for capacity building with EU member states and pharma sector and EDCTP will not be funded if these aims are not achieved
- Recital 8 of Directive 2003/63/EC requires a systematic test of the GCP and ethical equivalence of all CTIMP performed outside EU, especially where there is no mutual recognition agreement between countries
- European Public Assessment Report for Marketing Authorisation should contain a clear statement of ethical standards achieved in the CTIMP
- Evaluate and consolidate provisions in 2001 CT and 2005 GCP Directives for protection of trials subjects inside and outside EU to avoid Clinical Trials Dumping
- Increase GCP inspections in Developing World countries to increase compliance

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'Hard Law' or 'Soft Law' approaches in Drug Safety: GSK Seroxat and a Clinical Trials Database

EMEA Conference 2007 on the Operation of 2001 Clinical Trials Directive (2001/20/EC)

- 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

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'Hard Law' or 'Soft Law' approaches in Drug Safety: GSK Seroxat and a Clinical Trials Database

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?

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'Hard Law' or 'Soft Law' approaches in Drug Safety: GSK Seroxat and a Clinical Trials Database

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 Agreement Art.39 and the public protection override for trade secrets

Practical issues in mandatory registration:

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

Solutions 'Hard' or 'Soft':

- ABPI industry-led undertakings to register voluntarily
- Improve guidance on information access under current legislation
- RG-led solutions based on REC requirements for applicants to search the literature and registers so as to avoid allegations of failure to get proper consent and 'medical assault'
- Governmental action at national and EU level for new legislation?

ABPI Best Practice Model for Disclosure of Results and Transparent Information on CTs June 2008

- Access to PHRMA database and IFPMA portal is difficult
- Re-configure searchability and web presentation for optimal patient and service-user-friendliness

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'Hard Law' Solutions in Drug Safety: Rationalised EU Pharmacovigilance [1]

EC Strategy to Better Protect Public Health by Strengthening and Rationalising EU Pharmacovigilance
5th December 2007

Purpose of the reform of the Legal Framework for EU Medicinal Products for Human Use under Directive 2001/83/EC:

- Minimise duplication of effort between NCA and EMEA
- Strengthen rules on transparency for pharmacovigilance data
- Simplify reporting of Adverse Drug Reactions and optimising use of EudraVigilance database via electronic submission
- Rationalise rules on decision making across all markets - cost saving for industry
- Stimulate innovation to meet unmet need by use of Post Authorisation Safety Studies
- Establish clear standards in Good Vigilance Practices by use of Guidelines (not 'soft law' because part of a legislative solution)

Adverse Drug Reaction redefined:

- 'Conditions of Normal Use' does not feature in the new definition.
- 'Unexpected adverse reaction' is removed and subsumed within ADR definition (ADR is unintended)
- 'Abuse of medicinal product' removed from definition
- EMEA to monitor signals for EU-authorized drugs via EudraVigilance
- MA holder has wider duty to record ADR if reasonable possibility of causal relationship/causal relationship cannot be excluded

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'Hard Law' Solutions in Drug Safety: Rationalised EU Pharmacovigilance [2]

EC Strategy to Better Protect Public Health by Strengthening and Rationalising EU Pharmacovigilance
5th December 2007

Marketing Authorisation:

- Only key elements of PVS to be submitted at MA; holder to keep a Pharmacovigilance System Master File - simpler MA application
- Clear legal basis for inspections and access to the PVS Master File
- Clear legal basis at MA submission for Risk Management Plan
- Clear legal basis for Post Authorisation Safety Studies where there is a public health concern
- Periodic Safety Update Reports to be simplified and made proportionate to risk, to reduce routine reporting
- Clarify/emphasise the duty of MA holders to report changes in the risk-benefit balance and to update product information
- Therapeutic Efficacy for MA is now subsumed into criterion of risk-benefit balance

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'Hard Law' Solutions in Drug Safety: Rationalised EU Pharmacovigilance [3]

EC Strategy to Better Protect Public Health by Strengthening and Rationalising EU Pharmacovigilance
5th December 2007

Simplified Safety Reporting:

- All serious Third Country reports to go to the EU EudraVigilance database only
- All EU domestic reports to EudraVigilance and from there to EU member states
- EMA (not Industry) to undertake literature review and submit literature case reports to EudraVigilance, to reduce duplication of effort and reporting from multiple industry sources
- This is to reduce the incidence of case reporting between MA holders and NCAs and EMA
- Clear legal basis for Patient Self Reporting via new PIL form to MA (intensively monitored drugs) or else to NCA via web portal (other drugs)
- EU web portal on drug safety with links to NCA, legal provision for an EU Drug Dictionary
- SPCh and PIL to contain defined section on Key Safety Information for patients
- Public access to EudraVigilance for individual adverse reaction reports subject to privacy(!)

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Advanced Therapy: Market Stimulus through Regulation

EC Regulation on Advanced Therapy Medicinal Products
Commencement 30th December 2008

- Products based on tissues/cells + principal mode of action pharmacological/ immunological/metabolic
- Products containing viable tissue/cells as combination products
- Applies to products made by industrial process, not non-routine individual prescription
- Centralised Authorisation Procedure with new EMA Committee for AT to CHMP
- Procurement for AT should be by voluntary or unpaid subscription (!)
- SPCh and PIL should enable tracing of origin of tissue/cell product components (privacy)
- MA application to detail need for follow-up procedures, risk management system
- Evaluation/certification of SME output, on a non-MA basis, to facilitate R&D and later MA
- Fees for EMA scientific advice for AT reduced by 90% for SME and 65% for others
- Fees for MA reduced by 50% for hospitals and SME on proof of EC special relevance

Q. Will 'hard law' requirements work better than 'soft law' initiatives?

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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
- PiMA 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

Q. Will 'hard law' requirements work better than 'soft law' initiatives?

- See Inventory of Steps as at July 2008: some states have not contributed to the current inventory of national measures
- UK Establishment of NIHR MCRN

**Q. Consider the scope for regulation of stem cell 'patent thickets':
What other examples of potential market regulation are there?**

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The Reform of NHS Information Governance: Joined-Up Working under a new Legal Framework [1]

Q. RECs must engage in Privacy issues and must collaborate with PIAG/NIGB in a joined-up decision making process.

Q. A new legal framework is needed to replace DPA 1998 and common law with a specific legal code for Bio-Medical Research

The current function of PIAG as part of NIGB under HSCA 2008:

- Statutory approval under section 60 HSCA 2001/ section 252 NHA 2006 (pending HSCA)
- To override common law duty of confidentiality in database research without consent
- Where neither practicable nor desirable to seek consent or to anonymise the data
- PIAG considered by some to be temporary expedient until NHS SUS can achieve Anonymisation for patient data
- PIAG merged with NIGB and will enable consolidated NHS R&D approvals for registry use
- PIAG approval may currently be optional for researchers and if so REC may be main arbiter of confidentiality issues for research applicants

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The Reform of NHS Information Governance: Joined-Up Working under a new Legal Framework [2]

Academy of Medical Sciences Report *Personal data for public good: using health information in medical research* January 2006

- PIAG strategy of 'consent or anonymise' is flawed. More emphasis on public interest/benefit.
- Lack of joined up working between PIAG and REC compromises research
- A new defence that research has public funding and REC approval on ground of necessity and proportionality.
- More use needed of the section 33 DPA 1998 exemption for research
- Harmonisation of approvals process for ICO, PIAG, REC, NHS R&D.
- 'Privacy Culture' prevents quick fix
- If these proposals fail then reform the legal framework to consolidate and simplify common law and Data Protection rules and NHS Act 2006

Q. How far does IRAS improve this situation? The cases are possibly too few to decide the matter.

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The Reform of NHS Information Governance: Joined-Up Working under a new Legal Framework [3]

PIAG *Response to the Data Sharing Review* February 2008

- DPA 1998 lacks specificity for the health sector and is hard to apply
- Section 33 research exemption is probably incompatible with EU Directive. Is it?
- PIAG approval with time limited data retention is better than section 33 exemption.

Speaker's Observations:

- There is dissonance in the current NHS IG Framework
- If NHS *Connecting for Health* fails then so too does the rationale of PIAG- if PIAG is meant to be a temporary expedient pending Anonymisation through SUS
- Also, what if Anonymisation does not negate the common law duty of confidentiality- what hope for SUS?
- There will be a need for a new type of IG regulator for the Health Sector in the long term because:
- There is too much functional separation between R&D Departments, NIGB and the ICO
- DPA and common law duties are not co-terminous and have different exclusions: anonymity/public interest
- DPA is not suited to the age of ambient or ubiquitous computing
- DPA might be challenged by other EU member states in any event, see Germany and the 'Greens'

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The Reform of NHS Information Governance: Joined-Up Working under a new Legal Framework [4]

MOJ Data Sharing Review (July 2008)

- Data Protection Act 1998 is not optimised for ease of application
- Fast Track Legislation for 'clear need' data sharing requirements
- 'Safe Havens' to facilitate secure data exchange for research and statistical applications

PIAG Response to the MOJ Data Sharing Review

- Current legal powers under NHS Act 2006/HSCA 2008 could be used to create a legal basis for Safe Havens

Speaker's Observations:

- Data Protection Act and Duty of Confidence are not co-terminous.
- NIGB is not the regulator for data protection duties
- Special legislation for Cancer Registries and other bodies for exemption from patient right of opt out based on public interest test?

*Q. So how can the existing powers under HSCA 2008 alone be adequate for safe havens?
New law is needed to facilitate Bio-Medical Research.*

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The Reform of NHS Information Governance: Joined-Up Working under a new Legal Framework [5]

The Long Term 'Fix'

- A new legal code for the health sector to replace DPA and common law
- A single composite test for information use without consent
- Enhanced public interest test measured against necessity and proportionality
- Supported by a Privacy Impact Assessment and ISO data security standards for the bio-medical research sector
- A new EU Information Directive to achieve harmonisation?
- A single IG regulator for the medical research sector with clear demarcation of function and cooperation between REC and NHS R&D Departments and ICO for all research with a clear basis for general or specific approvals.
- There should be an appeals mechanism from this regulator. No appeal from PIAG or NIGB
- Should the regulator be independent and if so how?

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The Reform of NHS Information Governance: Joined-Up Working under a new Legal Framework [6]

The Short Term 'Fix'

- Reconstitute PIAG as a specialist REC?
- Better coordinated working between PIAG/NIGB and REC
- Common legal protocols and common rules of working for researchers, PIAG/NIGB, REC, R&D
- PIAG/NIGB to consult REC before making a statutory approval/refusal
- Common timeline for IRAS submissions to enable PIAG/NIGB advice/approval to be given before REC final opinion
- Common timeline to allow REC to dispute with PIAG on each application
- PIAG/NIGB is final arbiter but clear written reasons to be recorded by PIAG/NIGB and REC
- ICO remains final arbiter in Data Protection Issues. Consolidation is therefore needed

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The Future for Research Ethics Committees

- RECs must facilitate scientific research within a globalised ERA
- RECs must therefore expect to deal with issues in third countries
- RECs will require joined-up cooperation with local ethics boards
- RECs must protect the rights and legal rights of the research subject
- RECs must deal with protocol illegality
- RECs must adopt and apply legal solutions in the course of ethical review
- RECs must deal with insurance and indemnity issues with a legal scrutiny
- RECs may in time require powers of investigation
- Smaller numbers of RECs
- Specialist RECs to facilitate ERA objectives, e.g. GTAC
- De-linkage from the DH?
- Reconstitution as a regulatory ethics authority under legal code for Patient Rights?

Cf. *Research Ethics Review (2008) Vol 4, No 3, 111-116: C.L. Roy-Toole: Illegality in the Research protocol: the Duties of RECs under the 2001 Clinical Trials Directive*

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Mind How You Go...



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