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EU Hot Topics Update

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4 June 2013

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Overview

- General Data Protection Regulation Proposal
- Medical Devices Regulation Proposal
- IVD Regulation Proposal
- Transparency of clinical data

Overview of Proposed Regulations

Data Protection Regulation

- Pervasive impact: pharma, med dev, biobanks, e-health, diagnostics etc
- Intent to significantly increase the rights of data subjects and toughen existing rules
- Fines up to 2% of global turnover
- Leading biomedical research organizations express concern that this will prevent or seriously impair scientific research. Similar concerns have been expressed by multiple the pharmaceutical, medical device, IVD and e-health industry bodies.

Clinical Trials Regulation

- All clinical trial data would "not be considered commercially confidential" once a marketing authorization is granted.
- On 25 April 2013, Court issued injunctions preventing the EMA from disclosing information re AbbVie's blockbuster Humira and InterMune's product Esbriet

The IVD Regulation

- Diagnostic services provided to European patients remotely would be regulated even if the IVD device is not physically in Europe.
- Intent to significantly increase the number of software programs that are regulated
- Dramatic expansion of the number of products that might be considered IVDs

The Bad, the Better and the Ugly

- To address national inconsistencies, each of the new laws will be a Regulation rather than a Directive. While this is intended to harmonise the approach to these issues, it will increase the compliance burden and may increase uncertainty.
- Initial drafts of the proposed legislation were tabled in 2012, with rev
- In case case, the legislation proceeded as follows:
  - ***The Bad*** : the initial drafts were disconcerting and reactions to perceived abuse
  - ***The Better***: the second drafts were improved/clarified with industry input
  - ***The Ugly:*** the Rapporteur's proposals were disconcertingly broad and unclear

Data Protection

Data Protection: Dynamic Test

- European DP law focuses on the *processing* of the data not the ultimate use
- This requires a dynamic test and a continual reassessment of:
  - Data itself and the need to use the data
  - Whether it is still necessary to process data
  - Ability to ensure that data subjects have a right of access and right to be forgotten
  - Where key-coding is used, the state of the art as regards the likelihood of identification of a data subject
    - The current encryption technology regarding the possibility of someone cracking the code
    - The information in the public domain as regards the likelihood of identification ("mosaicing")

Ignorance x Fear = Inertia

- Will the increased rights of data subjects increase or decrease certainty?
  - Right of access and right to be forgotten
  - High standard for consent
- Will the increased punishments for breaches of data protection laws (and to a lesser extent, breaches of privacy) increase compliance or fear?
  - Fines up to 2% of global turnover
- Will increased uncertainty increase compliance or restrict the development of biomedical products and services in Europe?

Proposal re Consent

- Difficult to be certain that the consent obtained in a clinical context will satisfy data protection requirements
  - Must be freely given, genuine, explicit, specific and informed
  - Consent should be given independently from other matters
    - consent to processing of data protection vs consent to treatment
  - Consent is not valid where there is a clear imbalance between the data subject and the controller
  - No consent by silence or inactivity (opt-out)
  - Consent should cover all processing activities carried out
  - Controller bears onus of proving consent
- Liese suggests a special category of consent for genetic testing
- Note: consent ceases once the processing is no longer necessary

Scenarios re Consent

- What is the status of valid consent given under the existing Directive?
- Is consent valid:
  - when given by a patient to a doctor?
  - where the consent was a condition of entry into a clinical investigation?
  - if given in a clinical investigation of product X be valid if it leads to a new product Y?
    - What if X was a HPV diagnostic and Y a new "morning after" pill?
  - if given in the same consultation as the consent to treatment?
  - when recorded in a single document with the consent to treatment?
- What if consent will skew (or invalidate) the results of the study?

Derogations: Articles 81 and 83

- The rigor required for *Consent* means that the following derogations become more important:
  - Medical treatment privilege - Article 81(1)(a)
  - Public health purposes – Article 81(1)(b)
  - Research Purposes - Article 81(2) and 83
- However, Albrecht proposes dramatic changes to these derogations

Article 81: Commission Draft

81(1): … processing of personal data concerning health must be … necessary for:

*(a) the purposes of preventive or occupational medicine, medi diagnosis, the provision of care or **treatment** or the management of health-care services, and where those data are processed by a **health professional** subject to the obligation of professional secrecy or another person also subject to an equivalent obligation of confidentiality under Member State law or rules established by national competent bodies; or*

*(b) reasons of **public interest in the area of public health**, such protecting against serious cross-border threats to health or ensuring high standards of quality and safety, inter alia for medicinal products or medical devices; or*

*81(2): Processing of personal data concerning health which is necessary for historical, statistical or scientific research purposes, such as **patient registries** set up for improving diagnoses and differentiating between similar types of diseases and preparing studies for therapies, is subject to the conditions and safeguards referred to in Article 83.*

Article 83: Commission Draft

*Art 83: … personal data may be processed for historical, statistical or **scientific research purposes** only if:*

*(a) these **purposes cannot be otherwise fulfilled** by process data which does not permit or not any longer permit the identification of the data subject;*

*(b) **data enabling the attribution** of information to an identified identifiable data subject is **kept separately** from the other information **as long as** these purposes can be fulfilled in this manner.*

Albrecht proposals re *research*

- Reinstates the requirement for *consent* except for research that:
  - serves an *exceptionally high public interest*; and
  - *cannot possibly be carried out otherwise.*
- Even in those exceptional circumstances:
  - the data must be anonymised or pseudonymised under the *highest technical standards*
  - *all necessary measures shall be taken to prevent re-identification of the data subjects*
  - *such processing shall be subject to prior authorisation of the competent supervisory authority*
- Deletes the references to *patient registries* in Article 81(2), making it harder to argue that registries (let alone health technology assessments) are research
- Deletes the qualifier *so long as these purposes can be fulfilled* in Article 83(1)(b) which otherwise allows the use of identifiable information if this is required to conduct the research

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Albrecht version of Article 83

*1. … personal data not falling within the categories of data covered by Articles 8 and 9 may be processed for historical, statistical or **scientific research purposes** only if:*
*(a) these purposes **cannot be otherwise fulfilled** by processing data which does not permit or not any longer permit the identification of the data subject;*
*(b) data enabling the attribution of information to an identified or identifiable data subject is **kept separately** from the other information.*

*1a. Subject to the exception in paragraph 1b, data falling within the categories of data covered by Articles 8 and 9 may be processed for historical, statistical or scientific research only with the **consent** of the data subjects.*

*1b. Member States law may provide for exceptions to the requirement of consent for research, as referred to in paragraph 1a, with regard to research that serves an **exceptionally high public interests**, if that **research cannot possibly be carried out otherwise**. The data in question shall be **anonymised**, or if that is not possible for the research purposes, pseudonymised under the **highest technical standards**, and all necessary measures shall be taken to prevent re-identification of the data subjects. Such processing shall be subject to prior authorisation of the competent supervisory authority, in accordance with Article 34(1).*

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Consent & Derogations

- Consent alone will be a "brave" justification for data processing
- Articles 81 and 83 become crucial
- If Albrecht's amendments are accepted, it will be difficult to justify many registry studies, retrospective studies or health technology assessments under the *research* derogation
  - Article 83 will only be available for the processing of sensitive personal data (broadly defined) if:
    - There is an exceptionally high pubic interest
    - The research cannot be conducted data cannot take place in any other way
    - The data is anonymised or pseudonymised to the highest technical standards
- Even if Albrecht's amendments are not accepted, significant work will be needed to justify many studies (particularly any study re label extensions, comparisons with competitors, health economics or retrospective studies)

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Data Portability: Albrecht ideal

- Data Subject right to access data includes a right to data portability
  - … the right, to obtain **free of charge** the **data concerning them** also in **commonly used, interoperable, and where possible open source electronic format**
    - The data subject shall have the right to obtain from the controller communication of the personal data undergoing processing. Where the data subject makes the request in electronic form, the information shall be provided in an **electronic and structured format which is commonly used and allows for further use by the data subject**, unless otherwise requested by the data subject
  - If data subjects want to exercise their right to access their personal data, it should be provided to them in an **electronic format which they can use**. This further use includes the **right to move it to other platforms and services** if the data subject wants this. The right to data portability, therefore, is a mere specification of the right to data access.
- How to comply?

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Compliance Suggestions (1)

- Minimise the amount of data (especially patient data) gathered in Europe
  - Consider where to start new studies
- Start exporting data outside Europe (provided data subject consented)
- Ensure unequivocal consent to export data and that the safe harbour etc justifications are robust
- Invest in procedures for obtaining consent (or re-consenting)
  - Adopt new procedures re consent to data processing separate from other consents
  - Consider closely the specificity and explicitness of the consent for every project
  - Adopt (and revisit) clear forms for consent and associated processes
  - Address the prospect of serendipitous discoveries

Compliance suggestions (2)

- Start anonymising (or key-coding) new and historical data
  - Obtain consent to anonymise or pseudonymise existing data
  - Invest in tools to key-code data as higher standards will be required
- Significant work will be needed to justify many studies (particularly any study re label extensions, comparisons with competitors, health economics or retrospective studies)
  - Implement rigourous assessments and justifications for both study and the processing (not just which derogation applies)
- Adopt mechanisms for assessing the state of the art and information in public domain
  - Consider delegation to ethics committee

Genetic Obsession

- The drafts of the IVD Regulation and the Data Protection Regulation reflect paranoia about genetic data and genetic tests
- As a result, many assays of genetic material or markers may trigger:
  - data protection laws
  - IVD laws (even if there no medical purpose or diagnosis for an individual)
- Many analyses conducted in the course of a clinical trial, clinical investigation, PMCFU or health technology assessment may inadvertently trigger IVD laws

Obsession with genetics 1: IVD Reg

- All ***genetic tests*** as Class C devices (Rule 3)
- A device must comply with the Regulation even if it is never in the EU if:
  - it is used to test genetic material (irrespective of purpose?)
    - Query a predisposition to a medical condition or disease or an assay with no medical purpose or an assay regarding relative risk
  - the results of the diagnosis are communicated to a European citizen and
  - the test is offered as a *commercial activity*
- Why is this the case, if the test is not itself a medical device or an IVD?
  - Consider an assay that includes a test which does not identify the individual or provide any diagnosis, but rather the genetic status of tumour receptors
- In addition, Data Protection issues come in to play
  - Once a medical device, PMS and vigilance obligations apply
  - Must reconcile Data Protection Principles with Med Dev requirements

Obsession with genetics 2: IVD Reg

- Rapporteur adds definition of ***genetic test***: a test that is carried out for **health purposes**, involving analysis of human biological samples and aimed specifically at identifying the **inherited genetic characteristics of a person**
  - Query an assay which does not diagnose a specific condition?
  - Query an assay not intended to used for a "medical purpose"?
- A genetic test must also:
  - be conducted by a Doctor
  - only be used if:
    - the rights, safety and well-being of the test subjects are protected;
    - the resulting data generated are expected to be reliable and robust; and
    - the doctor gives the test subject:
      - appropriate information on the nature, the significance and the implications of the genetic test;
      - comprehensible counselling re medical, ethical, social, psychological and legal aspects; and
      - the test subject gives free and informed consent

Obsession with genetic testing 2: DPR

- ***genetic data***: all *personal* [identifiable] data, relating to the inherited genetic characteristics of an individual as they result from an analysis of a biological sample from that individual, in particular by chromosomal, DNA or RNA analysis (or equivalent)
  - There is no requirement that the genetic data itself might enable the identification of the data subject
- Dynamic test as regards likelihood of identification of individual requires ongoing assessment of "state of the art" and information in public domain
- On balance, *genetic data* may well come to be considered as a separate category of data

Medical Devices Regulation Proposal

Politics, politics

- Revision already started in 2008 with consultations but dossier became political with several medical devices scandals in EU market (MoM hips, PIP breast implants)
- Dalli Action plan running in the background
- ENVI rapporteur obviously overshooting to reach compromise

To PMA or not to PMA

- EU Commission decided against US FDA style PMA because of costs and limited added value
- Rapporteur ENVI committee EU Parliament wants PMA as political project
- Current trend points towards 'technical compromise' between Commission and Parliament
- Member states are the dark horse – most are against PMA

Introduction of new concepts

- ENVI rapporteur:
  - Efficacy
  - Randomised controlled trials as default

Clinical performance / efficacy?

- Medicinal products trials: "ascertaining its (their) safety and/or efficacy"
- Medical devices [currently]: "demonstrate the safety and performance of their devices"
- MDR proposal: inconsistent language
  - Explanatory note 3.6: "performance of the clinical evaluation needed to demonstrate the safety and performance of their devices"
  - (34) 'clinical investigation' means any systematic investigation in one or more human subjects, undertaken to assess the safety or performance of a device;
- But:
  - Article 26 requires "summary of safety and clinical performance"

Clinical performance / efficacy?

Amendment ENVI rapporteur:

- "to verify the clinical safety and efficacy of the device, including the intended benefits to the patient, when used for the intended purpose, in the target population and in accordance with the instructions of use;"

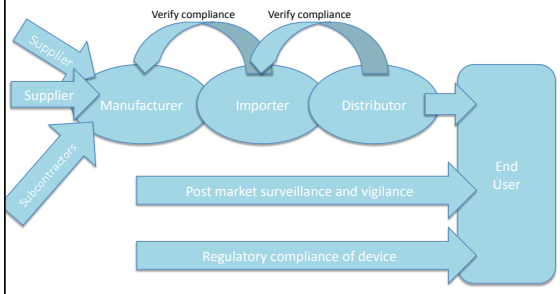
and

- "Performance should notably be understood broadly so as to encompass efficacy and benefit to the patient, which shall be checked in cases where clinical investigations apply."

Clinical Evaluation & Clinical Investigation

- New:
  - For pre-market evaluations, a mere literature route for new applications will be highly unlikely to be accepted;
    - Substantial equivalence will not be considered sufficient justification for not doing a clinical investigations.
  - Introduction of the "sponsor";
  - All clinical investigations (both pre-market and post-market) are to be registered and will be published on the central EU database which will be publically accessible;
  - Clinical studies conducted in multiple member states, will require only one approval; however, local legislations might still apply;
  - Post marketing clinical follow-up studies shall be planned, unless duly justified.

Supply chain controls



Qualified person / parallel trade

- Manufacturer's organisation must have access to a 'qualified person' responsible for regulatory compliance.
  - Similar requirements exist in EU legislation on medicinal products and in the national laws transposing the Directive on medical devices in some Member States.

- A distributor, importer or other natural or legal person shall assume the obligations incumbent on manufacturers if he does any of the following:
  a) makes available on the market a device under his name, registered trade name or registered trade mark;
  b) changes the intended purpose of a device already placed on the market or put into service;
  c) modifies a device already placed on the market or put into service in such a way that compliance with the applicable requirements may be affected.

Parallel trade

- Modification of a devices already placed on the market does not include:
  - translation of IFU
  - repackaging for parallel trade purposes

HOWEVER (part implementation of pharma repacking case law ECJ)

- Repackaging must not affect the condition of the device
- Repacker must indicate the activity carried out together with his name, registered trade name or registered trade mark and the address at which he can be contacted and his location can be established on the device or, where that is not possible, on its packaging or in a document accompanying the device
- Quality management system for translation and preservation of original condition of the device and that the packaging of the repackaged device is not defective, of poor quality or untidy
  - QS must be certified by notified body
  - QS must include vigilance feedback to manufacturer
  - prior notice and mockups must be supplied to authorities and manufacturer if requested

Traceability, registration, summary of safety and performance, Eudamed

- Aim Commission: address one of the main shortcomings of the current system: lack of transparency:
  - a requirement that manufacturers fit their devices with a Unique Device Identification (UDI) which allows traceability.
    - UDI system will be implemented gradually and proportionate to the risk class of the devices;
  - a requirement that manufacturers/authorised representatives and importers shall register themselves and the devices they place on the EU market in a central European database;
  - an obligation for manufacturers of high-risk devices to make publicly available a summary of safety and performance with key elements of the supporting clinical data;

Reprocessing

- Commission proposal:
  - reprocessing is treated and regulated like manufacturing
- ENVI rapporteur:
  - fiction that all devices can be reprocessed unless proven otherwise
- Rest of ENVI and amendments:
  - strict controls on reprocessing, but disagreement about how and what exactly (e.g. negative list)

Notified Bodies

- Proposal contemplates
  - a shake-out of about 75% of current notified bodies (20-25 remaining) with recertification under stricter requirements and tighter supervision by notifying member states
  - Mandatory unannounced audits of manufacturer and critical subcontractors
- ENVI amendments:
  - Less freedom for notified bodies to outsource work

Notified Bodies

Transitioning to notified body accreditation 2.0:

- Designations under AIMD, MDD, IVD become void at the date of application of the regulation
- EC Certificates issued before MDR enters into force remain valid until expiration date
- EC Certificates issued after MDR enters into force become void 2 years after the date of application of the MDR
- Certificates against MDR can only be issued by notified bodies designated under MDR before the date of application of MDR

Aim: make notified bodies more of an extension of competent authorities' market surveillance paid by industry

Notified Bodies

In the mean time

- Notified Bodies Code 3.0
  - Contains specifics on unannounced audits and many other interesting subjects
- Commission recommendation on unannounced audits in pipeline
  - Currently planned for September 2013
  - Will trigger applicability of unannounced audit section of Notified Bodies Code 3.0

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Vigilance and market surveillance

- Have their own chapter in the MRD now (chapter VII)
- Reflect the strong political desire to remedy the problems behind the PIP and metal-on-metal hips cases
- Vigilance incorporates vigilance MEDDEV 2.12/1
- Reporting via EUDAMED of
  - Serious incident
  - Corrective action
- Member States must take measures to encourage healthcare professionals, users and patients to report to their competent authorities suspected serious incidents

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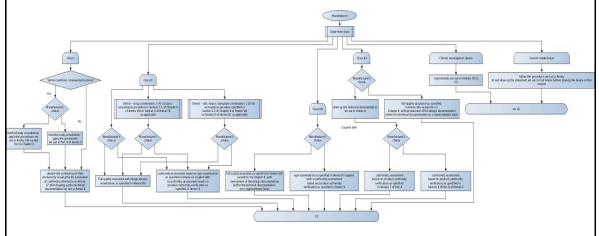
Conformity assessment routes overview (no big changes)



Money money money

- The Commission, the Member States and the designated EU reference laboratories will charge fees for various activities
- implementing acts to set the level and structure of fees

Commission
- EUDAMED registration fees
- Fees for scientific advice provided at the request of a manufacturer or notified body

Member States
- Fees for the designation and monitoring of notified bodies
- May levy fees for the activities based on MDR, provided that the level of the fees is set in a transparent manner and on the basis of cost recovery principles

EU Reference Laboratories
- Fees for scientific opinions provided to notified bodies and manufacturers

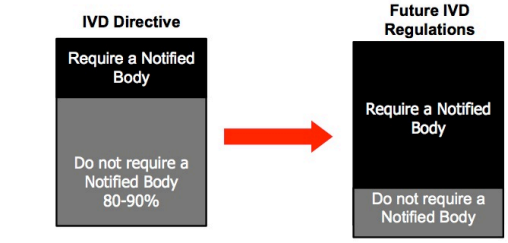
IVD Regulation Proposal

IVD Regulation Proposal

- Runs in tandem with Medical Devices Regulation proposal
- Shares procedural framework with Medical Device Regulation Proposal
- Big 'political' themes:
  - Companion diagnostics
  - Genetic testing
  - Home brew devices

Quantum leap in regulatory burden

Quantum Leap



Source: BSi

Conformity assessment

- Biggest changes because of implementation of GHTF classes A-D
- The existing modules established under the 'New Approach' do not change – see annexes VIII to X, however
  - EC verification module was deleted
  - The concept of batch testing has been clarified

CLASS	RISK LEVEL	GHTF EXAMPLES
A *Similar to general IVDs*	Low Individual Risk and Low Public Health Risk	Instruments, reagents e.g. prepared selective culture media specimen receptacles
B *No IVDD equivalent*	Moderate Individual Risk and/or Low Public Health Risk	Self tests *All IVDs not in A, C or D e.g. Vitamin B12, Point of Care, Urine test strips.*
C *Similar to Annex II list B*	High Individual Risk and/or Moderate Public Health Risk	Blood glucose self testing, HLA typing, PSA, screening, Rubella *STD, Cancer markers, cardiac markers, genetic tests*
D *Similar to Annex II list A*	High Individual Risk and High public Health Risk	HIV Blood donor screening, HIV Blood diagnostic

Source: BSi

Conformity assessment

- See GHTF SG1-N46:2008 "Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices" for model
- Class A devices : sole responsibility of the manufacturer, except if intended for near-patient testing, have a measuring function or are sold sterile
- Classes B, C and D : notified body involvement
  - Class D: explicit prior approval of the design or of the type of the device and of the quality management system before they may be placed on the market
  - Class B and C devices : the notified body checks the quality management system
    - Class C: in addition of QMS notified body check the technical documentation of representative samples.
- After initial certification, notified bodies shall regularly conduct surveillance assessments in the post-market phase.

Common Technical Specifications

- Where no harmonised standards exist or where relevant harmonised standards are not sufficient, the Commission shall be empowered to adopt common technical specifications (CTS) in respect of
  - the general safety and performance requirements set out in Annex I,
  - the technical documentation set out in Annex II or the clinical evidence and
  - post-market follow-up set out in Annex XII.
- Compliance with CTS is presumption of compliance with Annexes
- Like with standards, diverge allowed but must be justified

Clinical

- Clinical data requirements depend on risk class of IVD
- Annex XIII : rules for the conduct of interventional clinical performance studies and other clinical performance studies where the conduct of the study, including specimen collection, involves invasive procedures or other risks for the subjects of the studies
  - applies only to clinical performance studies carried out for regulatory purposes
- The concept of 'sponsor' introduced and aligned with proposal for Clinical Trial Regulation

Vigilance and market surveillance

- Vigilance
  - Introduction of EU portal for reporting of serious incidents and corrective actions taken by manufacturers.
    - Information will be automatically made available to the national authorities concerned
    - Coordinating authority that takes direction in coordinating the analysis of the case in multinational matters
- Market surveillance
  - Emphasis on work-sharing and coordination
  - Use of pan-EU electronic system on market surveillance
  - Procedures for compliant and non-compliant devices presenting a risk to health and safety at national level
  - Procedure for national preventive measures with respect to potential risk related to a device or a specific category or group of devices

Companion Dx

- New regime
- New definition "a device specifically intended to select patients with a previously diagnosed condition or predisposition as eligible for a targeted therapy"
- Class C risk classification, although this is up for debate in amendments
- Design or type examination
  - whereby the notified body shall consult one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC or the European Medicines Agency (EMA) in accordance with the procedures set out in Section 6.2 of Annex VIII and in Section 3.6 of Annex IX.
- Also consultation in case of changes affecting the suitability of the device in relation to the medicinal product concerned are made

Transitional regime

- Complex
- Sunshine clause – you can comply prospectively
- Certificates issued by notified bodies under old IVD directive
  - prior to the entry into force of this Regulation shall remain valid until the end of the period indicated on the certificate
    - except for certificates issued in accordance with Annex VI of Directive 98/79/EC which shall become void at the latest two years after the date of application of this Regulation.
  - after the entry into force of this Regulation shall become void at the latest two years after the date of application of this Regulation.
- ALL notified bodies will be decertified and have to be recertified under new requirements during transition period

Unannounced factory inspections

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- Minimum once per 3 years, more frequent for high risk devices, timing to be unpredictable
- Checks will look at:
  - Manufacturing in line with documentation?
  - At least one critical process out of:
    - Design control, purchasing, incoming materials, assembling, sterilisation, packaging product QC
- Design Examination/Type Examination sample several products at end of line or warehouse
  - Test in house or in external labs
  - Sampling and test criteria determined in advance
  - If impossible take samples from market, where needed supported by CA
  - Compare with existing technical documentation, test protocols and results

Transparency

Clinical Trial Data

- Latest Draft of the Clinical Trials Regulation tabled in January 2013
- Controversial mandatory moves to complete transparency
  - Heated debate between Industry Bodies and Ben Goldacre (author of Bad Pharma and co-founder AllTrials)
- On 30 April, European Medicines Agency publishes final advice from clinical-trial advisory groups
  - protecting patient confidentiality;
  - clinical-trial-data formats;
  - rules of engagement;
  - good analysis practice;
  - legal aspects
- Apart from some technical issues, little consensus arising from advisory groups. See the following from the advisory group on legal aspects:
  - *The Group has not managed to find an agreement about commercially confidential information.*

Impact

- Impact on Pharmaceutical and Biopharmaceutical Sector
  - Already seeing increased investment in competitive intelligence
  - Relatively little active engagement from researchers, clinicians or reimbursers
- Uncertainty is concerning for sector
  - Prospect that this will exacerbate the current decline in clinical trials conducted in Europe

Court Cases

- 25 April 2013, European Court granted interim injunctions preventing the EMA from disclosing detailed pre-clinical and clinical data contained in the dossiers supporting the applications for EU MAs for Humira (AbbVie) and Esbriet (InterMune)
- The companies argued that disclosure of the information would damage legitimate commercial interests for various reasons including that disclosure would:
  - facilitate competitor applications or developments
  - undermine the ability to obtain patent rights based in part on such data
  - prevent it from obtaining regulatory data protection in countries where prior public disclosure precludes such rights
- Final court cases unlikely to be heard until 2014
- Initially, the EMA stated that it would consider each application for access of a case-by-case basis
- In May 2013, the EMA wrote to applicants who have sought have access to such data saying that they will not disclose information

Publicity of data / transparency

- Recital 20: In order to increase transparency in the area of clinical trials, clinical trial data submitted in support of a clinical trial application should be based on **clinical trials recorded** in a publicly accessible database. **Clinical trial data** based on clinical trials conducted before the date of application of the present Regulation should be registered in a **public register** which is a primary or partnered registry of the international clinical trials registry platform of the WHO.
- Recital 20a: Clinical trial data should **not be considered commercially confidential** once a marketing authorisation has been obtained.
- Article 34 (3): Within one year from the end of a clinical trial, the sponsor shall submit to the EU database the **clinical study report**, including a lay summary of the clinical trial.
  - Clinical study report: a report containing the **full protocol** and any subsequent modifications and dates thereof, a statistical analysis plan, **summarised efficacy and safety data** on all outcomes, and individual anonymised patient data in the form of tabulations or listings

Publicity of data / transparency

- Publication of **clinical study report** in public database
  - full protocol (plus modifications)
  - statistical analysis plan
  - summarised efficacy and safety data on all outcomes
  - individual anonymised patient data in the form of tabulations or listings
- Clinical data deemed not commercially confidential after market access
  - How will that work: automatically deemed in the public domain?
  - Impact on existing NDAs?
  - What about Article 39 TRIPS?

Impact on Medical Devices

- Will the new regime for medical devices be influenced by that of medicines?
  - Simultaneous revision of MDD and of Clinical Trials Directive
  - Med Dev Regulation borrows inconsistently from ICH 1996
  - Call for "pharma-style" PMA has also led to favouring of controlled randomized trials as gold standard
- Alignment with well-established Pharma practice at Union level may conflict with international approach to medical devices
  - Proposed MDD Recital (21) The definitions in … medical devices, for example regarding … clinical investigations and vigilance, should be aligned with well established practice at Union and international level...
  - (47) The rules on clinical investigations should be in line with major international guidance in this field, such as the international standard ISO 14155:2011 on GCP for clinical investigations of medical devices for human subjects and the most recent (2008) version of the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects
- Art. 6: Harmonised standards relating to among others clinical investigation still provide presumption of conformity

Clinical performance / efficacy?

- DRB report amendments says randomized controlled trials to prove clinical efficacy and safety - the use of any other design or study has to be justified
  - Performance should notably be understood broadly so as to encompass efficacy and benefit to the patient, which shall be checked in cases where clinical investigations apply. This is crucial to ensure that devices are technically achieving the aim for which they were designed and produced, but also bring benefit to the patient and are efficient when used in real-life.
  - Annex XIV – Part I – paragraph 2 – point 2.1. Clinical investigations shall be performed on the basis of an appropriate plan of investigation reflecting the latest scientific and technical knowledge and defined in such a way as to confirm or refute the technical performance of the device, the clinical safety and *efficacy* of the device when used for the intended purpose in the target population and in accordance with the instructions of use, and the manufacturer's claims for the device as well as the safety, performance and benefit/risk related aspects referred to in Article 50(1);

Proposals re Med Dev data

- Proposed addition to Article 53(2a) of MDR re clinical trials database for medical devices
  - Upon a reasoned request, **all information on a specific medical device available in the electronic system shall be made accessible** to the party requesting it, save where the confidentiality of all or parts of the information is justified on any of the following grounds:
    (a) protection of personal data …;
    (b) protection of commercially sensitive information; and
    (c) effective supervision of the conduct of the clinical investigation by the Member State(s) concerned.
  - See also proposed Recital (37): Adequate levels of access for the public and healthcare professionals to those parts of Eudamed's electronic systems which provide key information on medical devices that may pose a risk to public health and safety is essential. Where such access is limited, it should be possible, upon a reasoned request, to disclose existing information for medical devices, unless the limitation of access is justified on grounds of confidentiality.

Thank You

- The information in this presentation is provided for information purposes only. The information is not exhaustive. While every endeavour is made to ensure that the information is correct at the time of publication, the legal position may change as a result of matters including new legislative developments, new case law, local implementation variations or other developments. The information does not take into account the specifics of any person's position and may be wholly inappropriate for your particular circumstances. The information is not intended to be legal advice, cannot be relied on as legal advice and should not be a substitute for legal advice.
- Unless otherwise stated, the information is limited to the position in England and Wales.

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Links

- Joint Statement from biomedical research community re data protection: http://www.wellcome.ac.uk/stellent/groups/corporatesite/@policy_communications/documents/web_document/wtvm054713.pdf
- Advice to EMA from clinical-trial advisory groups: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/04/news_detail_001778.jsp&mid=WC0b01ac058004d5c1
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