Will the new EU Medical Device Regulation Mean *More* Trials at *More* Cost but *More* Reward?

Greer Deal, Director
Global Regulatory Services (GRS)

Thursday 17th October 2013
M11 MedTech Forum Event, Harlow

1. Where were we?

2. Where are we now?

3. Where will we be?

1. Where were we?

Rules relating to safety & performance of MedDevs were harmonised in Europe in the 1990s

The New Approach

- A concept to facilitate the free movement of goods in Europe whilst ensuring a high level of protection for consumers
- The elimination of barriers to trade through technical harmonisation

How?

By harmonising ERs only and applying the “general reference to standards” formula and the principle of mutual recognition

The New Approach

A core legal framework consisting of 3 directives:

- Directive 90/385/EEC (active implantable medical devices)
- Directive 93/42/EEC (medical devices)
- Directive 98/79/EC (in vitro diagnostic medical devices)

Supplemented by several modifying and implementing directives, including the last technical revision brought about by

Directive 2007/47/EC

Directive 2007/47/EC

- Resolve issues arising from technical progress, multiple interpretations and misunderstandings
- Attempted to force industry to take clinical evaluation more seriously
- Prior to the 2007 revision there were concerns re sufficiency and adequacy of clinical data for all classes of device

2. Where are we now?

Directive 2007/47/EC

The definition of a Medical Device amended to clarify that software placed on the market on its own could be a Medical Device if it satisfied the definition

ie a Medical Device is:

An instrument, apparatus or appliance (including ***software***) intended by the manufacturer to be used with humans for

- Diagnosis, prevention, monitoring, treatment or alleviation of a disease, or compensation for an injury or handicap
- Investigating, replacement or modification of the anatomy or a physiological process
- Controlling conception
- But which does **not achieve its principle intended action by physiological, immunological or metabolic means**, but be assisted in its function by such means.

Software can be incorporated in medical devices or exist as stand alone software.

- Active Implantable medical devices
- Software that directly controls an apparatus such as radiotherapy treatment
- As an accessory to a medical device
- **Software used on mobile devices- “apps”**

A new ER was introduced by 2007/47/EC :

- *For devices which incorporate software or are medical software in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification.*

Software as medical devices:

- **Software** that carries out further calculations or interpretations of captured patient data for a **therapeutic purpose**, e.g. radiation treatment planning, medication dosage calculations

- **Software** that carries out further calculations, enhancements or interpretations of captured data for a **diagnostic purpose**, e.g. tele-health and remote diagnostics, mass screening and risk assessment tools, helpline/telephone services algorithms

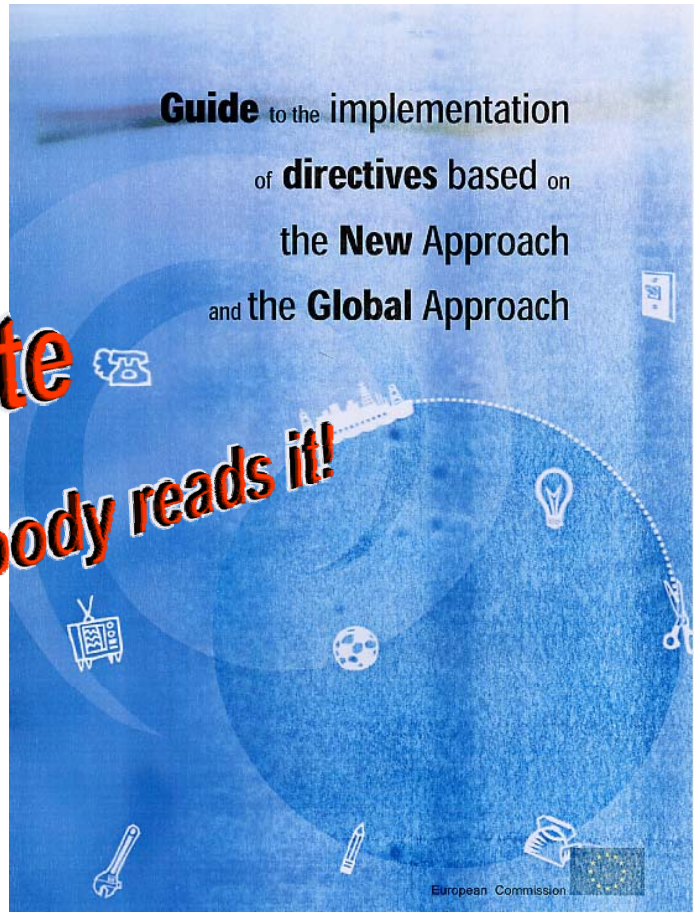
Software which **don't** qualify as medical devices:

- Software only intended for archiving/ retrieving patient records/images **without intending to change or interpret them**
- Electronic prescription software that only replaces conventional paper-based prescriptions and sends them out to a pharmacy
- Patient administration software that only deals with appointments, admissions, referrals and billing/invoicing

EU “BLUE GUIDE” or “BLUE BOOK”

GRS®
global regulatory services

Guide to the implementation of directives based on the New Approach & the Global Approach



Out of Date

...but then virtually nobody reads it!

Read this to fully understand the Directives!

General Perception:

Clinical evidence for medical technology **does not necessarily have to be presented** for compliance…

… but it **does and must be scientifically undertaken using a risk based approach!**

All devices, regardless of Class require “clinical evaluation”, i.e. a clinical literature review and / or a clinical investigation

Demonstration of conformity with the Essential Requirements must include a clinical evaluation in accordance with Annex X (Annex I, 6a)

There **must be** a clinical investigation/trial for Class III or implantable devices unless there is justification to rely on existing clinical data

"**clinical data**": the safety and/or performance information that is generated from the use of a device (from bench testing to clinical trials in human subjects). Clinical data are sourced from:

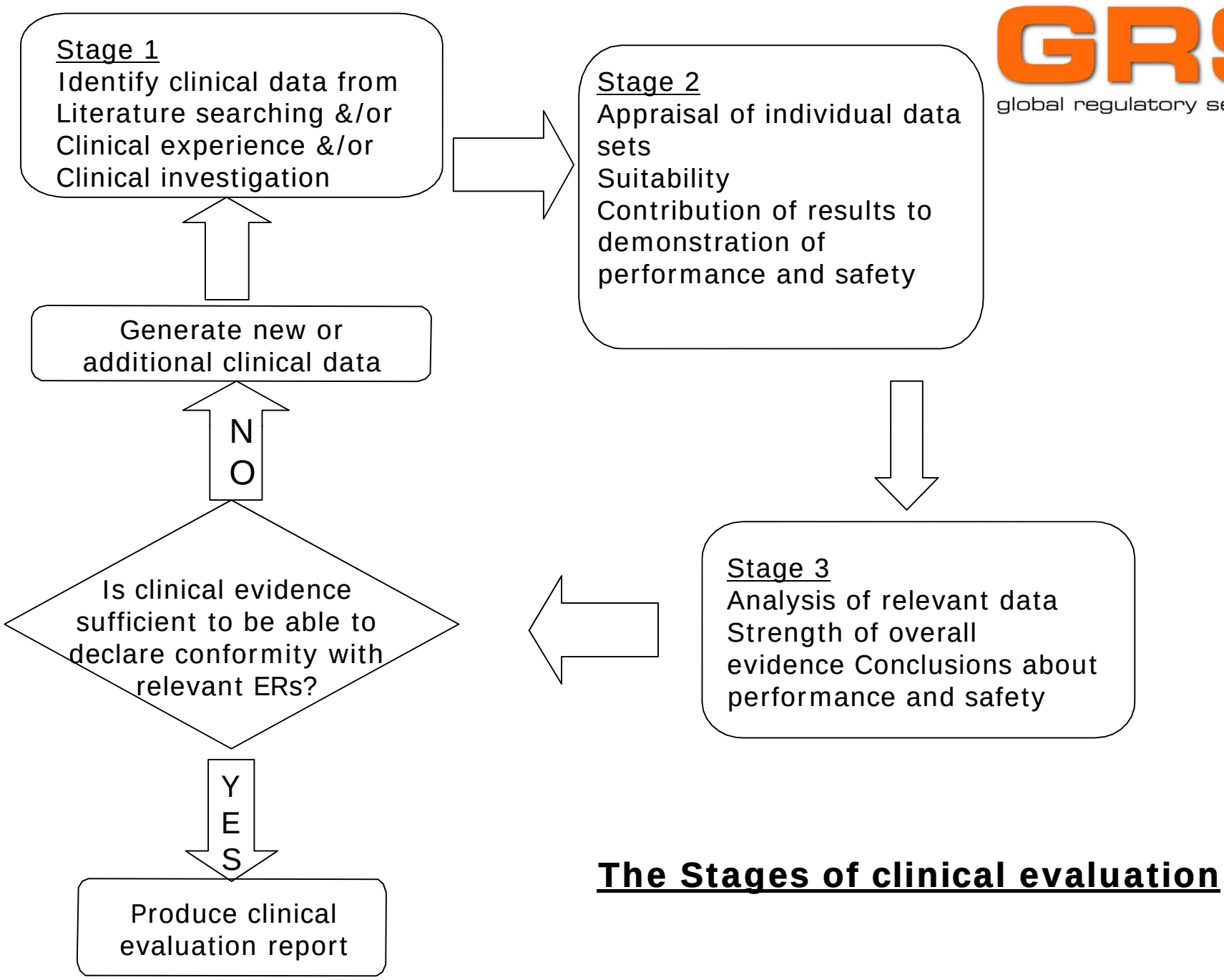
- clinical investigation(s) of the device concerned; or
- clinical investigation(s) or other studies reported in the scientific literature, of a similar device for which equivalence to the device in question can be demonstrated; or
- published and/or unpublished reports on other clinical experience of either the device in question or a similar device for which equivalence to the device in question can be demonstrated

"**clinical evaluation**": the evaluation of clinical data

Harmonised standard for clinical investigation is:

EN ISO 14155:2011

Clinical investigation of medical devices for human subjects – Good Clinical Practice (ISO 14155:2011)



The Stages of clinical evaluation

The Reality:

Class I CE Marking standards are variable

'Compliance' for the simplest devices is 3 months to >1 year (including clinical evaluation)

Some companies are 'risk takers' by getting to market first without being fully compliant

Avoidance of "Clinical Evidence", literature route used inappropriately, too few clinical trials

3. Where will we be?

- Medical Device **Regulations**
- The Commission to vote on proposal on 22 October 2013 during a plenary session
- **Tougher new regulatory framework** requiring some devices to go through a pre-market assessment process by the EMA
- Two Regulations to replace the existing three directives
- Reinforced rules for clinical investigations
- Adoption of Regulations expected in 2015, full implementation by 2018

Proposed Regulation:
Clinical Evidence for Medical Devices

- **Improves and clarifies** the **requirements** for the generation of clinical evidence and clinical investigations/trials

- Manufacturers may no longer solely rely on data from clinical investigations. They must also **include a clinical evaluation of literature** to demonstrate the safety and performance of their devices. The regulation introduces the term **'clinical evaluation report'** when referring to the outcome of a manufacturer's clinical evaluation

- Introduction of the term **'sponsor'** who takes responsibility for beginning and managing a clinical investigation/trial

Proposed Regulation: Clinical Evidence for Medical Devices *cont…*

- All medical devices made available, except custom devices or intended for clinical investigation, **must include a clinical evaluation** to demonstrate conformity with the Essential Requirements
- A clinical evaluation is **thorough, objective and proportionate** to the risk and intended use of the device. The annex sets out the circumstances where manufacturers may use clinical data which is sourced from studies on a similar device (termed ‘equivalence’).
- Intention to **reduce times and bureaucratic burden** and to add certainty to the justification when new or additional clinical investigations are not necessary
- A new system for **centralisation of notifications** is introduced as well as a **severe adverse event reporting system** to ensure patient and consumer safety.

Proposed Regulation: Clinical Evidence for Medical Devices *cont…*

- Emphasis on **protection of subjects** undergoing clinical investigations and measures related to establishing requirements for extended post marketing clinical follow-up
- **Post-market clinical follow-up** will most probably have its own section
- The manufacturer to **proactively collect and evaluate clinical data from the use of a device** in order to check its safety and performance and detect any emerging risks. NB The manufacturer's post-market clinical follow-up evaluation report forms part of the manufacturer's overall clinical evaluation.

Proposed Regulation: Clinical Evidence for IVDs

- The Proposed **Regulation** is likely to be implemented across the EU during **2015 or 2016**
- Clinical Evidence and Clinical Investigations/Trials are **new** concepts in IVD legislation
- **Data** is required on the **ability of the test** to provide information on a specific clinical condition
- If clinical performance data is not used to demonstrate clinical evidence, this must be **justified**
- A '**clinical evidence report**' to be included in the manufacturers' technical documentation.

Proposed Regulation: Clinical Evidence for IVDs cont …

- Manufacturers must **keep** available the relevant technical documentation on performance evaluation for **five years after the end of the evaluation**. Clinical performance data should be updated throughout the lifecycle of the device.

- It is **likely** that manufacturers will need to have a **post-market clinical follow-up plan** consisting of documented methods and procedures to pro-actively collect clinical evidence data from actual use of the device. This data is then expected to be used in the development of risk management, design and clinical performance documentation.

Will the new EU Medical Device Regulation Mean *More* Trials at *More* Cost but *More* Reward?

More Trials? Yes

More Cost? Yes

But ...

Clinical evidence is already an EU legal requirement

New regulation

- does **not increase amount** of clinical evidence
- it **increases the importance** of clinical evidence

i.e. can you substantiate your product claims when subject to truly independent peer review?

NB Clinical Evidence and Clinical Investigations / Trials are **new concepts** in IVD legislation

More Reward? Yes

- ✓ better assessment clinical data
- ✓ better assessment need for clinical trials
- ✓ better focused, uniform trials
- ✓ safer trials

- ➢ patient safety
- ➢ user safety
- ➢ better purchasing decisions
- ➢ better value
- ➢ less litigation
- ➢ no loss sales, reputation
- ➢ customer satisfaction
- ➢ continued market viability


♫ Lah lah ♫
♫ lah ♫
I can't hear you!

Acknowledgements

GRS®
global regulatory services

bsi.

MDC Medical Device Consultancy

MHRA
Regulating Medicines and Medical Devices

Global Regulatory Services

www.globalregulatoryservices.com

Driving innovation to market success™

Mrs Greer Deal

greer@globalregulatoryservices.com