Future Regulatory Challenges for *In Vitro* Diagnostics

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European Regulation of IVDs

- **Covered by Directive 98/79/EU**
- **Transposed into individual member states national law**

Purpose:

Harmonise regulations across Europe

Free movement

Safety

Patients, Users, all others

Performance

As claimed in the labelling

What products are covered?

- *In Vitro* diagnostic medical devices
  - reagents
  - calibrators, control materials
  - devices for self testing
  - instruments
  - specimen receptacles
- Accessories
- Devices for performance evaluation
- Regulation is risk based

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What's NOT covered?

- General laboratory equipment – a common error!
- Any device….not providing information on a pathological or physiological condition, therapy, congenital abnormality, or donor/donation compatibility
  - On samples provided from the human body
- Examples include..
  - In Vivo
  - Non-Medical, including…
    - Forensic
    - Medico-Legal
    - Veterinary
    - Lifestyle

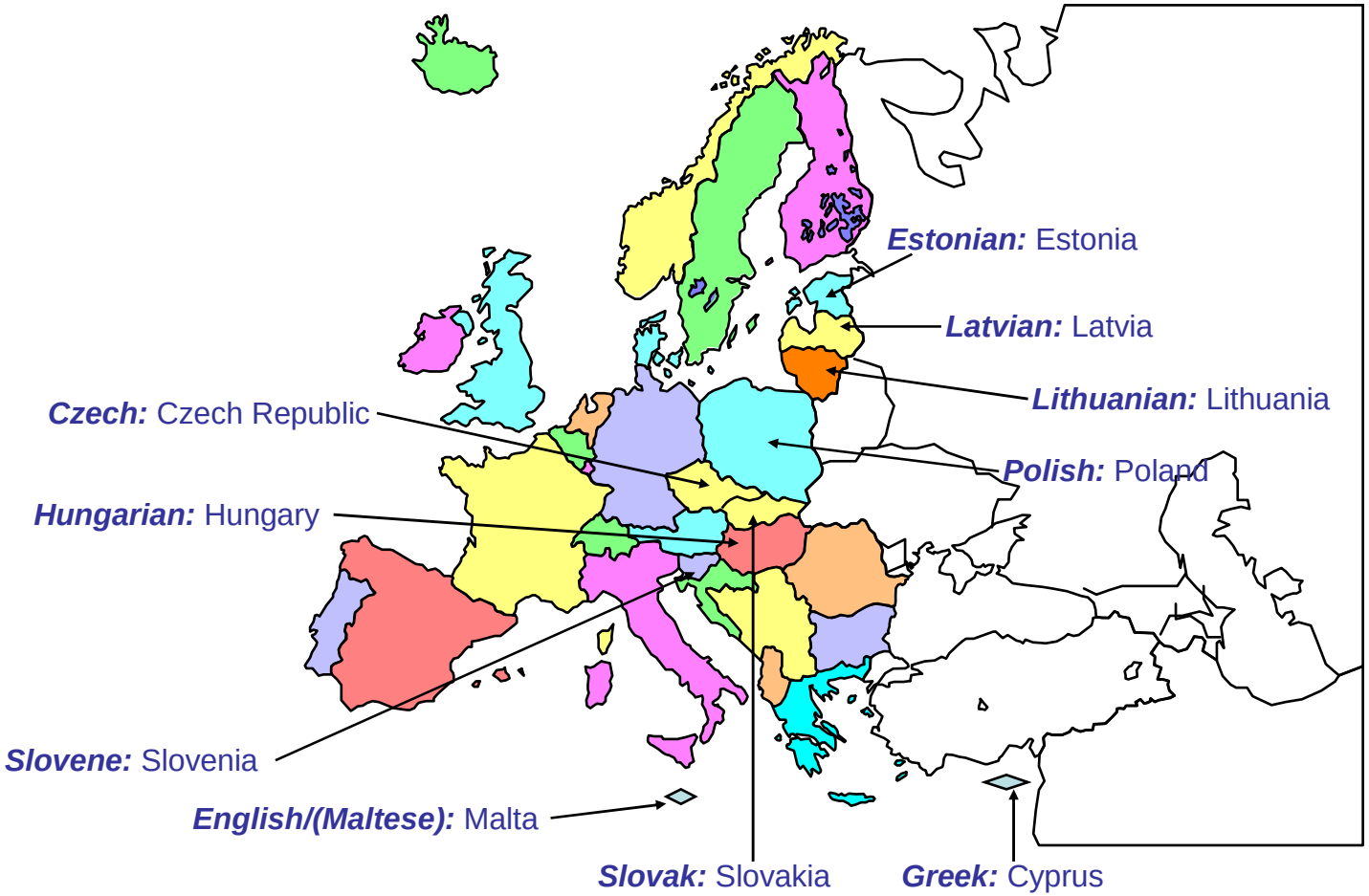
Who is responsible?

1. Manufacturer - Places device on market under his own name
   - Responsible for design, manufacture, packaging and labelling *regardless of whether he performs these operations himself*
   - Takes responsibility for compliance with all IVD Directive requirements
   - Authorised Representative for manufacturers outside the EU
2. Competent Authorities
   - Regulatory authorities of member states e.g. MHRA (UK)
   - Registration and performance monitoring
3. Notified Bodies
   - independent third party, designated by member states CAs
   - contracted by manufacturers
   - pre-market approval of products

4 User - Correct storage and use of product

Challenge: LANGUAGE REQUIREMENTS

31 countries
25 languages
EEA plus Switzerland
EFTA - EU plus Iceland, Norway, Liechtenstein, and Switzerland



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Software

- Any software which is necessary for the proper application of the IVD MD as intended by its manufacturer is covered by the Directive.
- The scope of the Directive ends when the manufacturer's intended purpose of the device has been achieved, i.e. when the measuring signal is available to the user in the form intended by the manufacturer. Any software that processes the analytical result beyond that point is outside the scope of the Directive
- BUT – safe in combination…..??

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Structure

- 35 Recitals - each beginning **Whereas,** these lay out the purposes of the directive

- 24 Articles – these set out the requirements of the directive

- 10 Annexes – these contain the detail for the Articles

Essential Requirements

- General Requirements
  - safety
  - performance
  - acceptable risk
    - Persons and environment
    - ISO 14971
  - stability
    - life of product
    - storage and transport
- Design and Manufacturing Requirements
  - specific properties e.g. chemical & physical
  - labelling and instructions for use

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HARMONISED STANDARDS

- Complementary to Essential Requirements
- Voluntary
- Presumption of conformity
- Check Europa website for list http://ec.europa.eu/enterprise/newapproach/standardization/harmstds/reflist/invimedd.html

COMMON TECHNICAL SPECIFICATIONS

- Mandatory
- Currently for Annex II List A
- Each lot requires NB approval
- Analytical and diagnostic specificity and sensitivity

Quality System

Minimum requirements

- Organisational structure and responsibilities
- Manufacturing processes and systematic control of production
- Means to monitor the performance of the quality system

Must incorporate all IVDD requirements

ISO 13485:2003 generally accepted as the Gold Standard

Technical File

- All documents required to show compliance with Directive
- Reviewed by Notified Body for ‘higher risk’ devices
- Could be requested by Competent Authority
- Evidence of compliance
- Risk Management

Registration

Manufacturer

- Name and address
- Information on devices
  - Identification
  - Code
  - Performance evaluation (Annex II and Self-test)
  - Significant change
  - Discontinuation
  - “New” test

Competent Authority

- May request label and instructions for use (Annex II and Self-test)

Fees: http://www.opsi.gov.uk/si/si2009/pdf/uksi_20090383_en.pdf

Post-marketing surveillance

- Systematic and global procedure
- Appropriate to risk of product
- Review internal and external information
- Report risk to health incidents to Competent Authority

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Vigilance

- Competent Authority's responsibility
  - Monitor the market
  - Evaluate centrally
  - Inform the Commission
  - Inform other member states
- Manufacturer's responsibility
  - Report incidents immediately, not later than …
  - Public health issue 2 days
  - Incidents 10 days
  - Near incidents within 30 days
  - Outside area, asap
  - Don't forget your NB if appropriate
- MEDDEV Guidelines published June 07
- MHRA guidance on website


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Considerations for Manufacturers

- Non accredited laboratory services
  - No HCP involvement guaranteed
  - Analytical and clinical validation?
  - Off lable use?
  - No specific regulation or regulator
- Unanticipated supply chain
  - E.g. internet
    - Language / units
    - Can self testers buy professional use product?

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Other considerations for Manufacturers

- Service Support and User Training
  - Avoid “local fixes”
  - Avoiding anecdotal “improvements”
  - Align training to IFUs
  - How do you react to unapproved use of your product?
  - Is information from Customer Support used in post market surveillance?
  - Spotlight now on point of care devices
  - Excellent source of surveillance info

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Other considerations for Manufacturers

- Safe in Combination
  - Essential Requirement B3 and B8.7
    - “the whole combination…..must be safe and must not impair the …performance..”
    - “if…used in combination or connected to other medical devices…sufficient details of characteristics” for safe and proper use.
  - Do you offer YOUR solutions with third party products
    - e.g.UPS / Accessories / Reagents / Robot / Water / Incubator
  - Foreseeable misuse?
  - MHRA
    - Guidelines for Users on website

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Other considerations for Manufacturers

- Sales and Marketing
  - Aligning claims to labelling
    - avoiding exaggerated claims
    - Alignment of literature
      - e.g.User Guides, Promotional Material
    - Distributors
      - Check Vigilance and PMS
  - “It does exactly what is says on the tin !”
    - ..and nothing more can be claimed!!
    - Evidence is in the technical file

Review of the directive

Why?

- Directives are typically reviewed after 5 yrs
- “Defective directive”
- Introduction of new tests
- Technology changes

Review of the directive

What may change?

- Inclusion of stand-alone software
- State of the Art
- Adoption of a risk-based classification
- Regulation of genetic testing and direct to consumer kits
- Extension of scope to cover diagnostic services
- In-house manufacture
- Performance evaluation, Clinical utility & validity

THANK YOU!

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