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An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Clinical investigations of medical devices

Regulatory viewpoint

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HRB-TMRN Meeting, UCC, 13 May 2016

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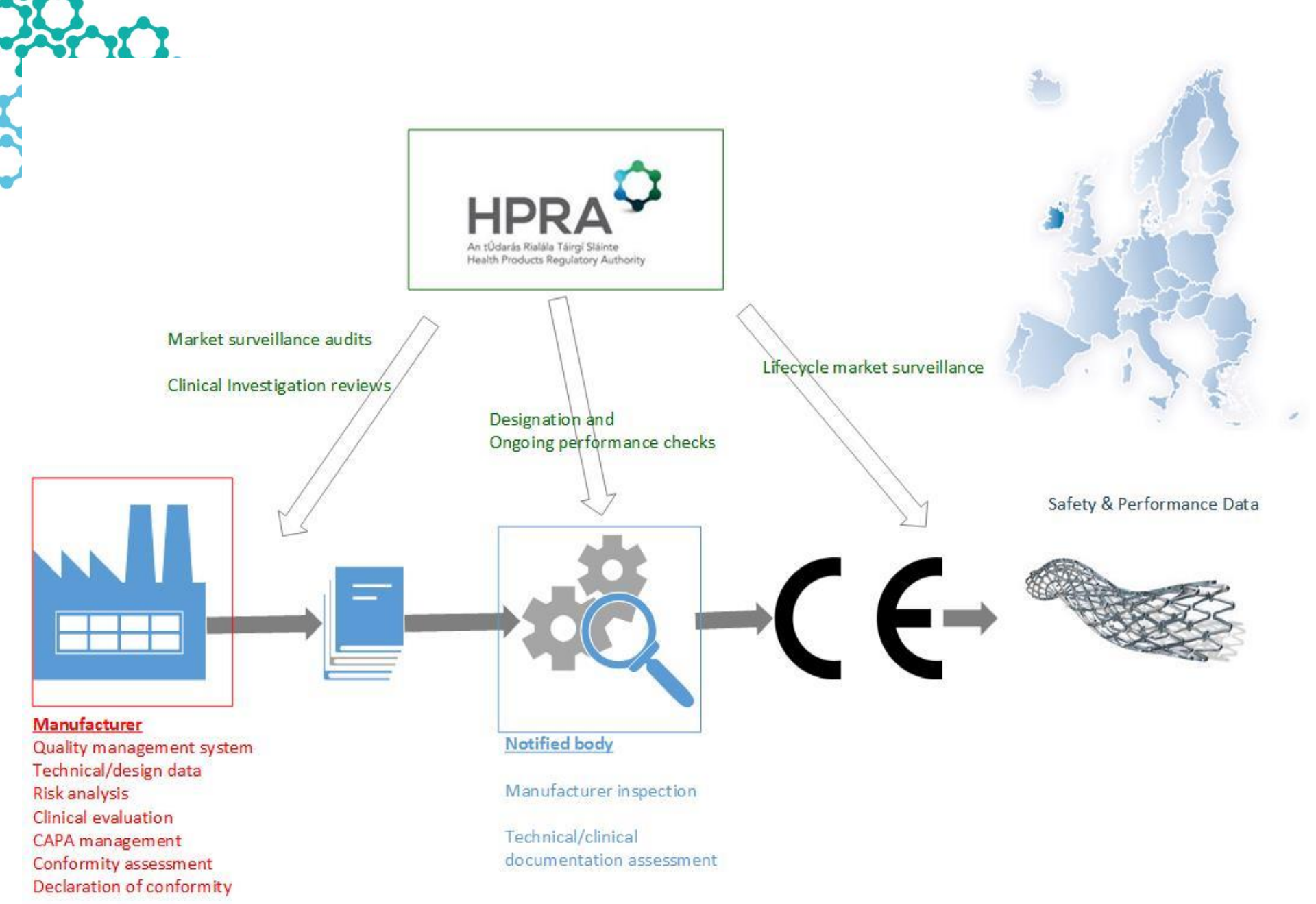
Health Products Regulatory Authority

To protect and enhance public and animal health through the regulation of medicine, medical devices and healthcare products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Market surveillance audits
Clinical Investigation reviews
Designation and
Ongoing performance checks
Lifecycle market surveillance
Safety & Performance Data
Manufacturer
Quality management system
Technical/design data
Risk analysis
Clinical evaluation
CAPA management
Conformity assessment
Declaration of conformity
Notified body
Manufacturer inspection
Technical/clinical
documentation assessment

Innovation of medical devices

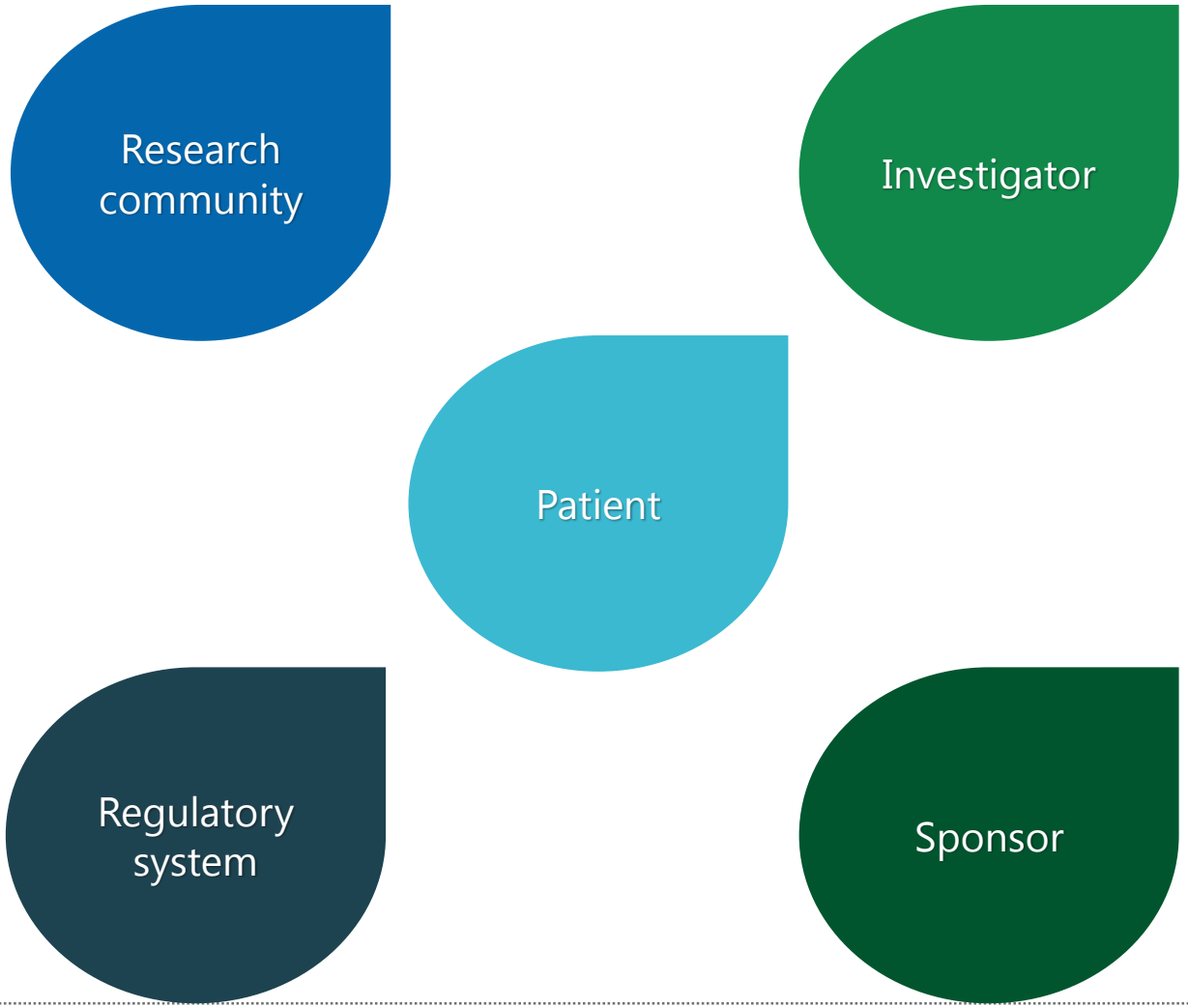
- Safe and scientific innovation
- Early awareness & education
- Early engagement with regulatory process
- Consistent, predictable & scientific regulatory system
- Timely access for safe & performing technologies

What is a clinical investigation?

- *'clinical investigation' means any systematic investigation in one or more human subjects, undertaken to assess the safety or performance of a device*[1]

[1] 2012/0266 (COD) 12040/1/15 REV 1. ENISO14155:2011

What's the role of HPRA for CIs



What needs HPRA review?

Needed	Not needed
• Commercial sponsors	• Academic/ clinical origin
• Regulatory purposes for EU	• Post-market studies
• Academic/clinical origin	?

What are the requirements?

- Article 15, Annex I, Annex VIII and Annex X of Directive 93/42/EEC

- ENISO 14155:2011 – Clinical investigation of medical devices for human subjects – Good clinical practice

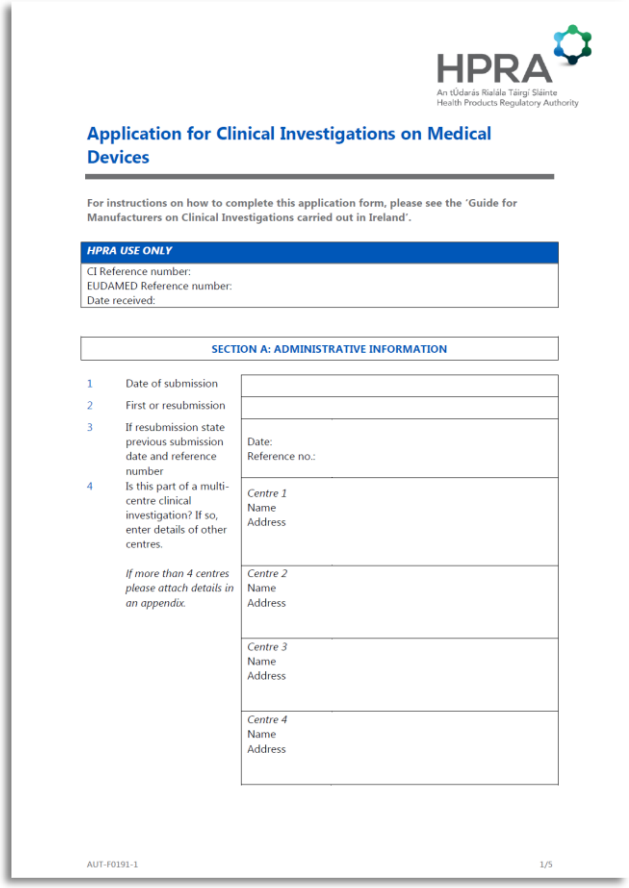
- MEDDEV Guidance

MEDDEV 2.7/2	Competent Authorities
MEDDEV 2.7/3	Serious adverse event reporting
MEDDEV 2.7/4	Manufacturers & notified bodies

http://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework/index_en.htm

Regulatory submission[2]

- Device identification data
- Clinical investigation plan
- Clinical investigator's brochure
- Confirmation of insurance of subjects
- Informed consent documentation
- Statements – conformance with ER, blood derivatives, animal tissues
- EC opinion and details covered in review
- Investigators and investigation sites
- Place, date and duration of CI
- And…… Results of risk analysis and solutions to ER



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Application for Clinical Investigations on Medical Devices

For instructions on how to complete this application form, please see the 'Guide for Manufacturers on Clinical Investigations carried out in Ireland'.

HPRA USE ONLY
CI Reference number: EUDAMED Reference number: Date received:

SECTION A: ADMINISTRATIVE INFORMATION		
1	Date of submission	
2	First or resubmission	
3	If resubmission state previous submission date and reference number	Date: Reference no.:
4	Is this part of a multi-centre clinical investigation? If so, enter details of other centres.	*Centre 1* Name Address
	If more than 4 centres please attach details in an appendix.	*Centre 2* Name Address
		Centre 3 Name Address
		Centre 4 Name Address

AUT-F0191-1 1/5

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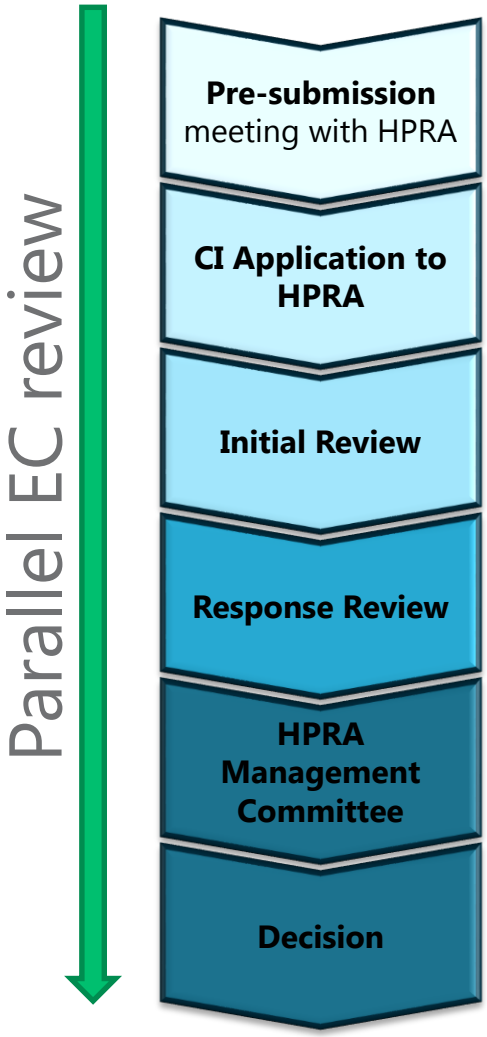
[2] Directive 93/42/EEC, Annex VIII 2.2 and 3.2

[3] AUT-F0191-1

HPRA Review Process

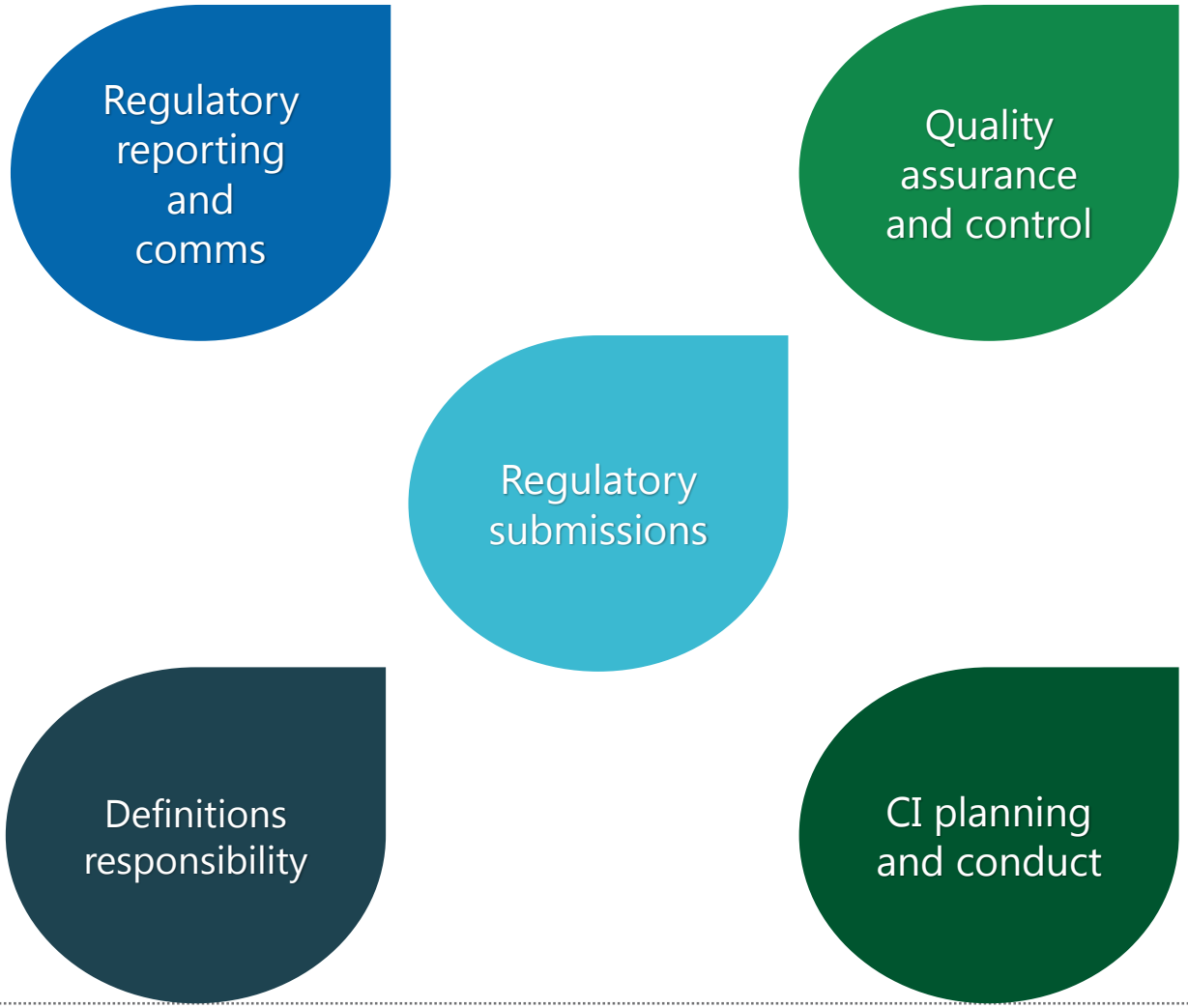


- Pre-submission engagement encouraged
- Submission to Decision is a 60 day process
- Day 1 – clock starts/EU notification – unique CIV ID
- Day 30 response from HPRA with questions / queries

  'Stop-clock' procedure if required
- Day 60 – decision from HPRA – notification to sponsor

  - EU notification

What are the sponsor's responsibilities?



What are the investigator's responsibilities?

Serious adverse event reporting

'All serious adverse events must be fully recorded and immediately notified to all competent authorities of the Member States in which the clinical investigation is being performed.'[4]

MEDDEV 2.7/3 SAE Report Table v2																			
EUDAMED - ID:																			
Title of Clinical Investigation:																			
CIP Number:																			
Contact person (Name, Address, E-Mail, Telephone Number)											**Device type:**								
MS+NCA Reference Numbers for all participating Countries:											**Reference Member State:**								
No. of Patients enrolled to date total:		**No. of Patients enrolled to date** (date of report) **per country:**									**No. of Invest. Devices used to date total:**			**No. of Invest. Devices used to date per country:**					
Date of Report:	dd/mm/yyyy																		
Status: A, M, U	**Date Sponsor received Report of SAE (dd/mm/yyyy)**	**Country code**	**Study Center**	**Patient ID Code**	**SAE ID Code**	**Date of Procedure/ First Use (dd/mm/yyyy)**	**Date of Event Onset (dd/mm/yyyy)**	**SAE OR Dev. Def.**	**Description of event**	**action/ treatment/patient outcome**	**Relationship to Procedure: not related OR unlikely OR possible OR probable OR causal relationship**	**Relationship to Investigational Device: not related OR unlikely OR possible OR probable OR causal relationship**	**Unanticipated SADE: Yes OR No**	**Treatment Arm: Investigational Device/ Control Group/ blinded/ n.a.**	**Event Status: Resolved/ Resolved with Sequelae/ Ongoing/Death**	**Date of Event Resolution (dd/mm/yyyy)**			

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[4]Annex X, 2.3.5 Directive 93/42/EEC (as amended)

[5]MEDDEV 2.7/3 SAE Report Table v2

Final report

- Written report[6]
- Overview of device, investigation design & methodology, deviations, analysis, stats and critical appraisal
- Including data from all sites and subjects
- Review of report by coordinating/principal investigators – agreed by signature

[6]EN ISO14155:2011, 7.3. Annex D.

Common pitfalls

- Incomplete applications
- No design freeze – iterative development
- Poor awareness of regulatory requirements
- Essential Requirements not addressed
- Clinical evaluation/clinical develop plan
- Risk analysis
- Clear endpoints

Changing legislation[7]

- Detailed requirements for application, conduct and assessment of clinical investigations
- Fewer exemptions – more clinical investigations
- All clinical investigations require notification – commercial, academic/clinical, post-market
- Increased provisions for protection of patients and vulnerable populations

[7] 2012/0266 (COD) 12040/1/15 REV 1 Chapter VI Articles 49 – 60 aa and Annex XIV

Changing legislation

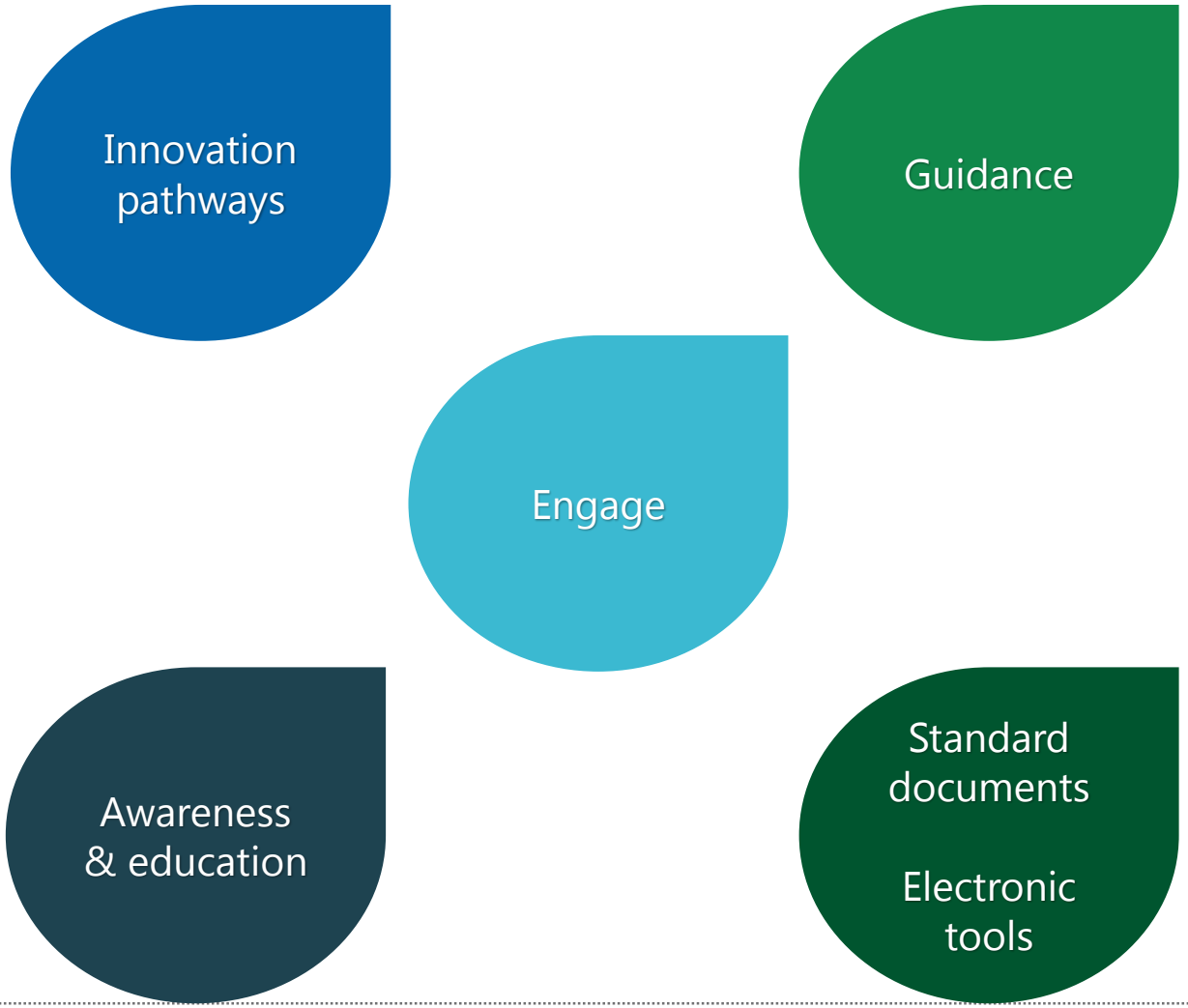
- Increased provision for monitoring – obligations on sponsors, investigations, authorities (site inspections)
- Coordinated assessments
- Increased transparency on clinical investigations – increased notifications
- Increased alignment with CTR

Changing legislation

Academic/clinical 'non-regulatory' investigations

- Ethics committee and scientific review (possibly NCA application)
- Sponsor for each investigation
- Protection of subjects
- Informed consent
- Conformance with applicable performance and safety requirements
- Qualification of investigations
- Increased national provisions

What can the HPRA do to help?



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Thank you.
Q&A

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