

Federal agency for medicines and health products

The implementation of the EU CT Regulation : Overview of the different projects in progress

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1: Overview of the Regulation

Scope:

- Only interventional studies of medicinal products
- **No distinction between « commercial » and « non commercial sponsors »**
- Risk based approach : introduces the concept of **'low-intervention trials'**.
- NIMPs (now auxiliary medicinal products) are included .

Major advantages:

- Streamlined submission and review process for trial applications via the EU portal and database
- Enhanced communication and cooperation between Member States
- Simplified safety reporting
- Increased transparency

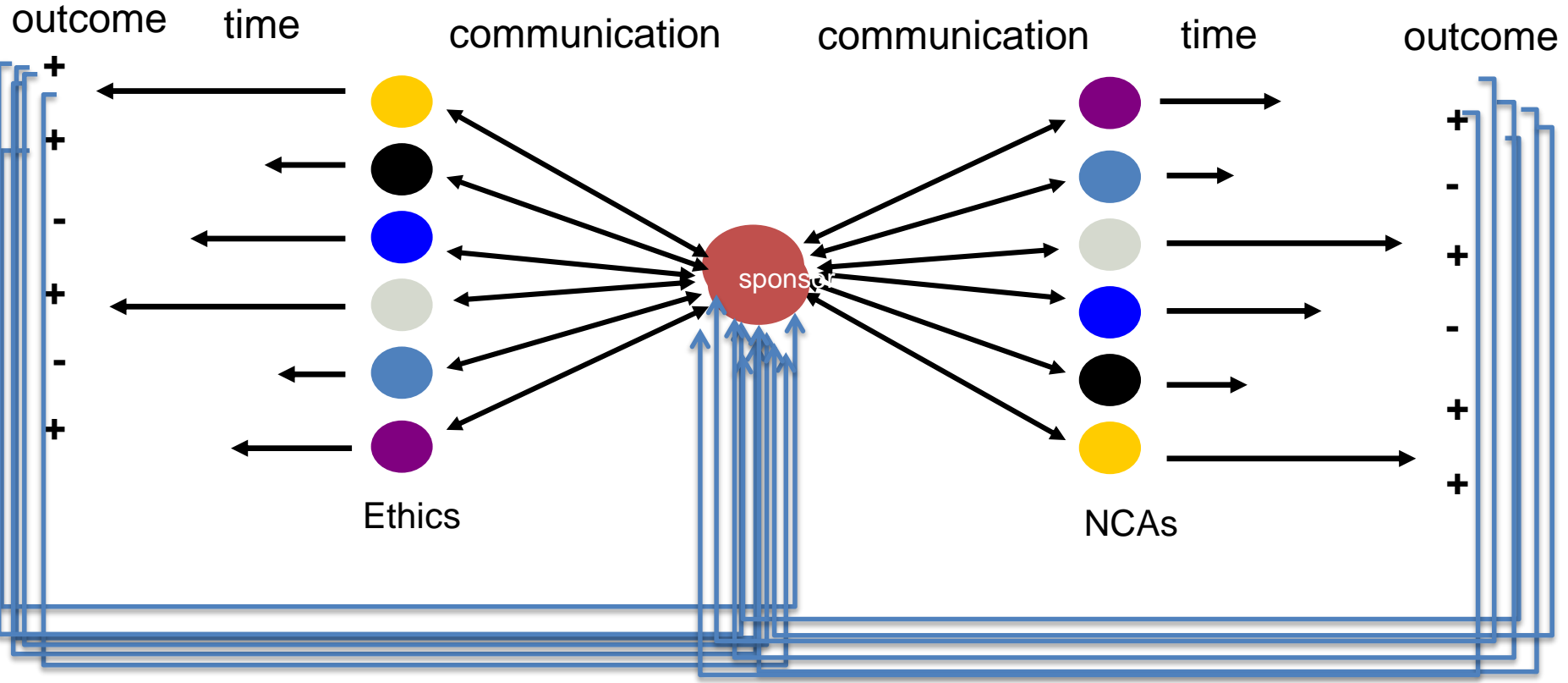


1: Overview of the Regulation : New simplified procedure :

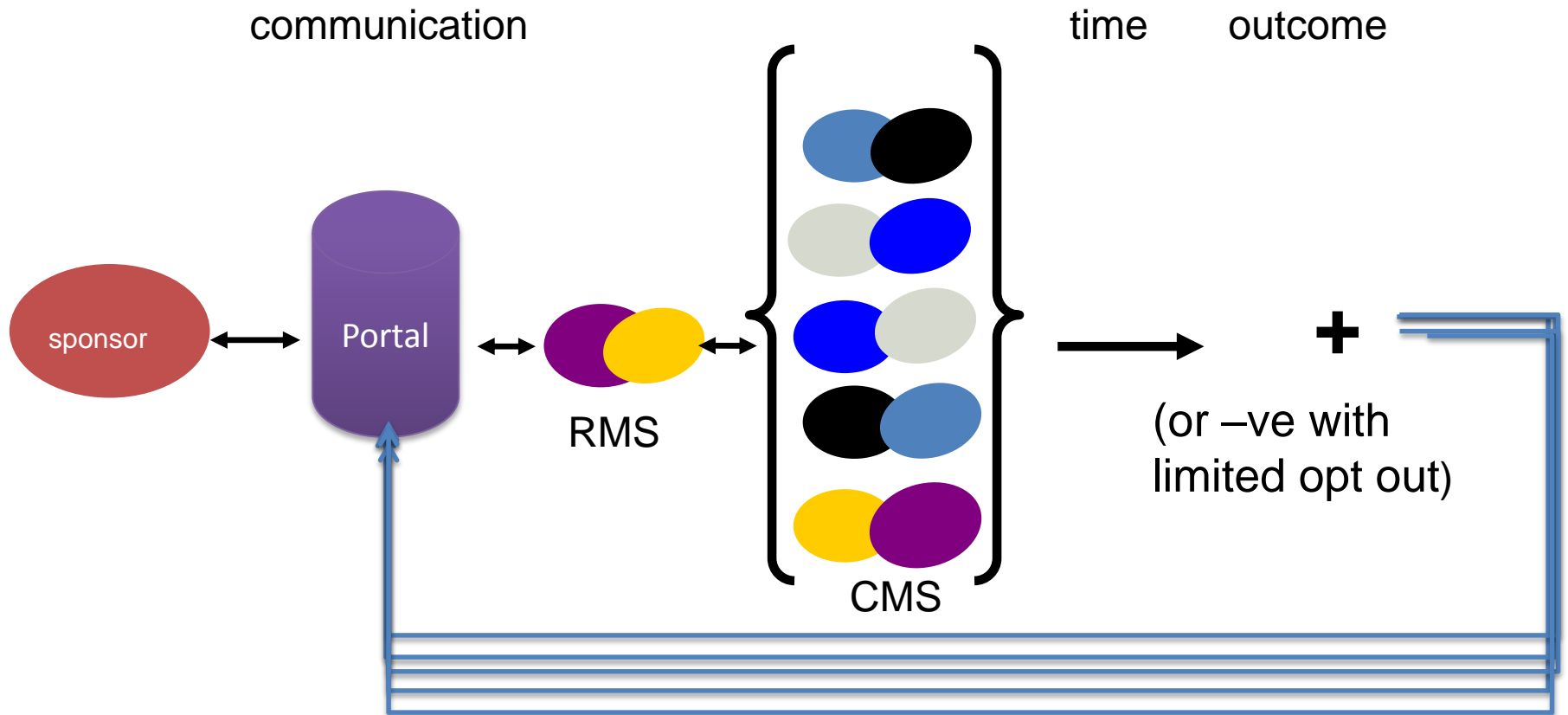
- **Single EU Portal & Database**
- **Single dossier and single submission**
- **Sponsor can propose Reporting MS**
- **Coordinated assessment for multi-state clinical trials**
 - Part I – joint assessment by all concerned MS (NCA+EC), led by RMS
 - Part II – National assessment only (R&D offices and Ethics Committee)
- **Clear timelines (extended compared with Directive),
concept of tacit approval**



EU Multi-national clinical trials: current situation



EU Multi-national clinical trials: under new Regulation



1: Overview of the Regulation : Transparency :

The Regulation requires that information contained in the clinical trial database shall be publicly available unless one or more of the following exceptions apply:

- protection of personal data
- protection of commercially confidential information, in particular taking into account the marketing authorisation status of the medicinal product, unless there is an overriding public interest
- protection of confidential communication between Member States in the preparation of their assessment
- protection of the supervision of clinical trials by Member States



1: Overview of the Regulation : Transparency :

- Disclosure rules published in October 2015: EMA/42176/2014
- Includes descriptions of what and when documents may be made public depending on stage of development, type of trial (therapeutic vs non-therapeutic) and type of document.
- Publication rules based on three categories of trials
 - Category 1: Phase 1, bioequivalence / bioavailability / biosimilar trials
 - Category 2: Phase II and III (ie not Cat 1 or 3)
 - Category 3: Phase IV and low-intervention trials

Provides balance between encouraging innovation and providing extensive public information on clinical trials conducted in EU.



The publication of some information from the EU Portal and Database will be deferred. The length of this deferral is dependent on the trial's categorisation which is explained in the table below:

CATEGORY 1	CATEGORY 2	CATEGORY 3
Pharmaceutical development clinical trials	Therapeutic exploratory and confirmatory clinical trials	Therapeutic use clinical trials
<ul style="list-style-type: none"> • Phase I trials • Phase "0" trials • Bioequivalence and bioavailability trials • Similarity trials for biosimilar products • Other trials to determine equivalence 	<ul style="list-style-type: none"> • Phase II trials • Phase III trials 	<ul style="list-style-type: none"> • Phase IV • Low-intervention clinical trials

Exceptions to the transparency are the paediatric trials (all phases) which still need to be submitted within 6 months to NCAs and should be published as per Regulation (EC) No 1901/2006: this has not been amended by the CT regulation.

Section of trial document		CATEGORY 1	CATEGORY 2	CATEGORY 3
Main Characteristics of the trial		For a subset of information and up to the time the CT Results Summary is posted (Justification)	No deferral	No deferral
Trial related documents	Subject Information sheet			No deferral
	Protocol			
Product related Documents	IB	Up to the time of MA using this trial or up to 7 years after the end of the trial, whichever is earlier	Up to the time of MA using this trial or up to 5 years after the end of the trial, whichever is earlier	
	IMPD, S&E			
Assessors documents / data	Request for information	MS decides but takes into account the exceptions of the legislation and the deferral time proposed by the sponsor		No deferral
	Assessment Report (I&II)			
	Conditions			

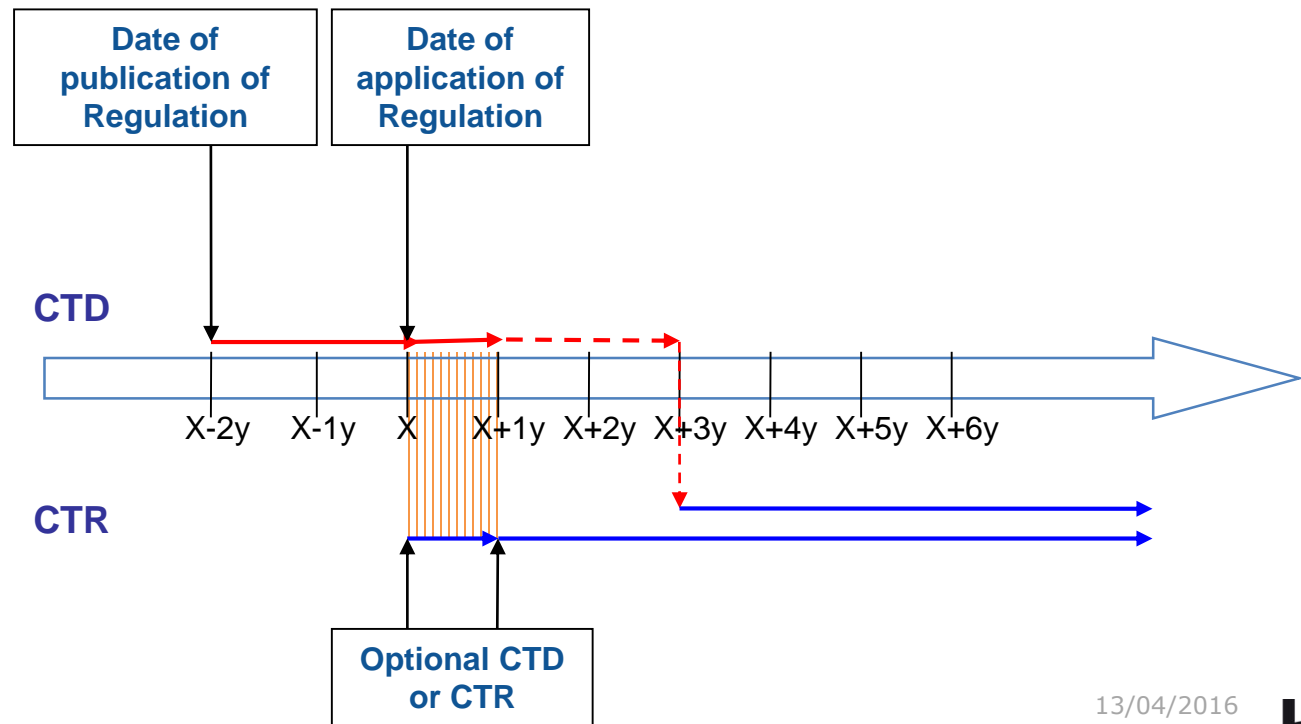
Section of trial document		CATEGORY 1	CATEGORY 2	CATEGORY 3
Substantial Modification		Deferral possible only for changes or additions to data/documents not yet made public because of the legal deadline is not reached or a deferral was requested. Publication will take place when the legal deadline is reached or deferral deadline expires.		
Notifications	Unexpected events, urgent safety measures	Up to the time when summary results are posted - except for early terminations for reasons involving subject safety or if Corrective measures (Justification)	No deferral	No deferral
Clinical Trials Summary Results	Scientific Summary	Up to 18 months after the due date for the publication of the summary of results (usually 12 months after the end of the trial unless article 37(4) applies) (Justification)	No deferral	No deferral
	Lay person		No deferral	No deferral
Clinical Study Report		No deferral	No deferral	No deferral

Section of trial document		CATEGORY 1	CATEGORY 2	CATEGORY 3
Supervisory measures	Serious Breaches	If the sponsor requested a deferral up to the time of publication of summary results the same will apply here.	No deferral	No deferral
	Inspections Reports (EU)			
	Inspections Reports (by third country CA)			
Supervisory measures	Union Controls	No deferral		
	Corrective Measures			

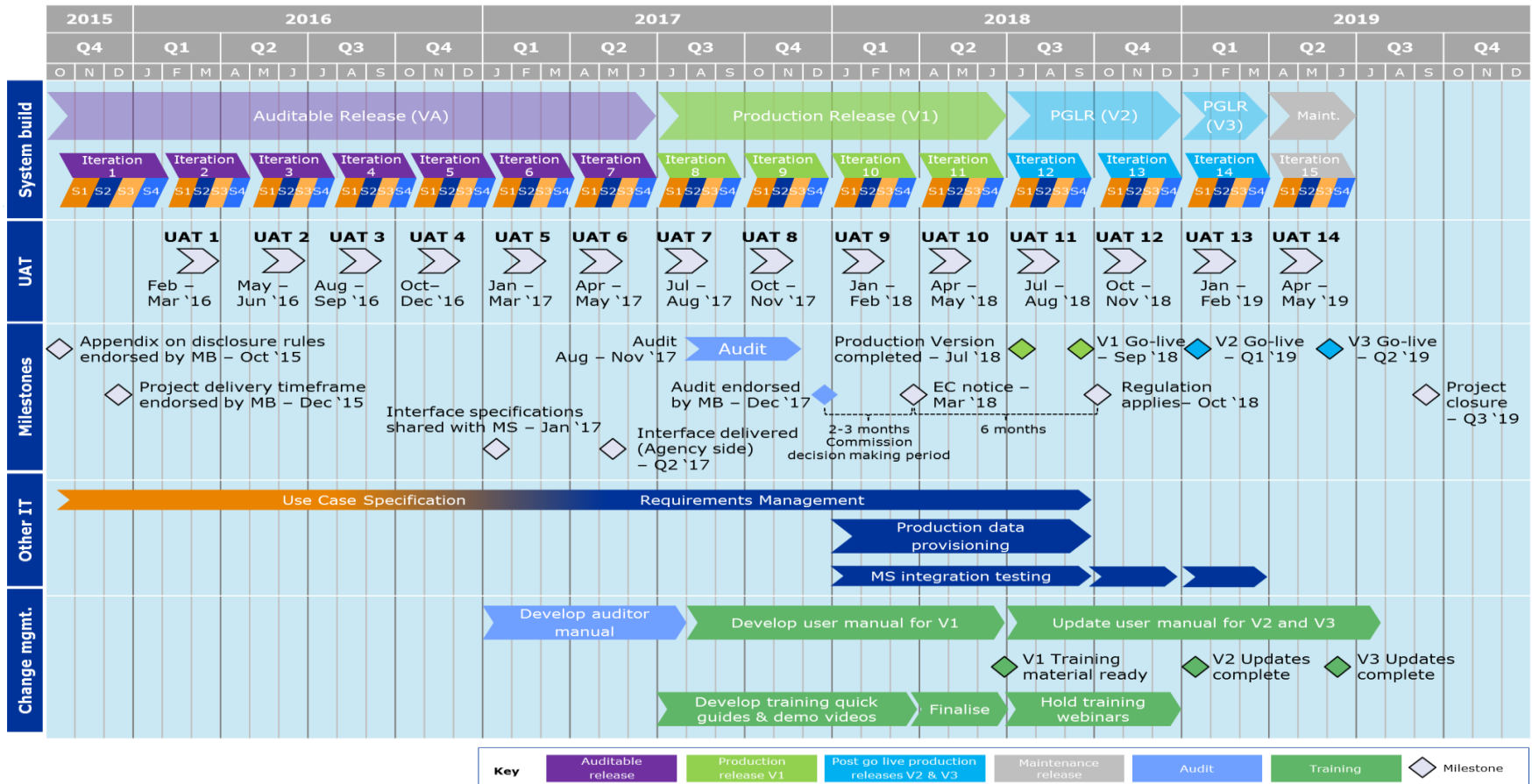
1: Overview of the Regulation : Implementation :

Article 99 shall apply “no earlier than 28th May 2016” (6 months after successful audit of IT system). **Now expected Autumn 2018**

Transitional aspects: cfr EC guidance document out for consultation (comments till 1st of November 2016)



1: Overview of the Regulation : Implementation : Critical step remains the development of the EU Portal and D-base



2 : Implementation at national level :

Disclaimers

- Major highlights
- Currently discussed with different concerned partners
- Final validation by the strategic cell of our Minister



2 : Implementation at national level : legislative framework (1)

- **New law related to interventional clinical trials with medicinal products (EU CTR Regulation)**
- **Law 7 May 2004 : to be revisited mid long term ?**
- **Royal decrees**
 - **Organisation of the workprocesses**
 - **Fees**
 - **...**



2: Implementation at national level : legislative framework (2)

- **FAMHP : Role of national contact point**
- **Independent « College » is hosted at the Federal Service of Public Health**
- **College coöperates in a 1:1 relationship with famhp**
- **Role and Responsibilities of this « College » are mainly :**
 - **Coordination and organisation of the work related to the « ethical evaluation »**
 - **Quality Assurance function**



2: Implementation at national level : legislative framework (3)

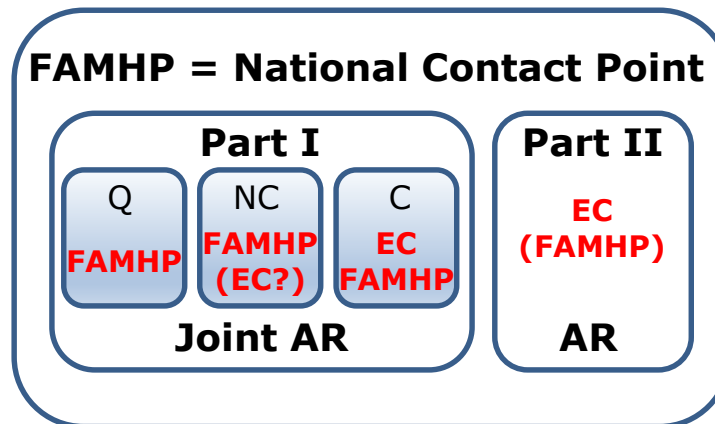
- **Members of the College will be assigned by the Minister**
- **Decentralised system : evaluation by recognised ethics committee**
- **Famhp responsible for recognition and inspection of those ethics committees (criteria to be defined by RD)**
- **Appeal can be introduced @ Commission for medicinal products (famhp activities) and @ College (ethics committees)**



2: Implementation at national level : workprocess flow (1)

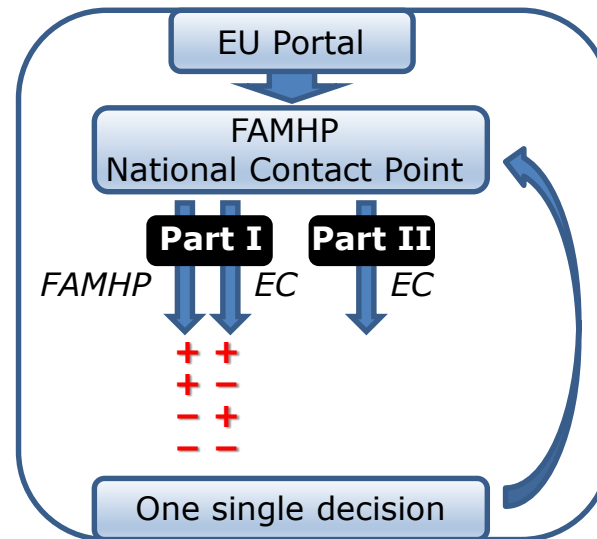
1. FAMHP = National Contact Point

AR Part I:	Quality:	FAMHP
	Non-Clinical:	FAMHP (EC?)
	Clinical:	EC and FAMHP
AR Part II:		EC (FAMHP)



2: Implementation at national level : workprocess flow (2)

2. Evolution towards “College” in a one-to-one relationship with FAMHP



3. Independent ethical evaluation

4. Representation of lay-men / patients

5. Added value of co-assessment (touch with medical reality)

6. Short timelines for phase 1 trials will be maintained

7. Pilot joint assessment FAMHP-EC foreseen early 2017



2: Implementation at national level :

- **Preparing the pilots :**
 - **Start Q1 2017**
 - **Representative sample of different types of trials**
 - **Open for all sponsors**
 - **Communication to different stakeholders foreseen in the upcoming months**

- **Facilitating patient recruitment :**
 - **Initiative of the Strategic cell**
 - **Working groups installed**
 - **Optimisation of collaboration between centres**
 - **IT systems needed**
 - **Particularities for Phase 1 trials and Vaccine trials**



3 : Scientific/regulatory advice @ EU and national level

- New and challenging task
- Link with **national innovation office** (national scientific-regulatory advice) and SAWP at EMA
- First in men Guidance document revisited (CTFG-CHMP)
- Increasing demands on :
 - Matrix trials
 - Master protocols and appendices
 - Biosimilars
 -



4 : EC Regulations

- **Implementing regulation on GCP :**
 - **Second public consultation (end of October)**
 - **Adoption December 2016**
- **Delegated regulation on GMP for IMP :**
 - **Second public consultation to be launched November 2016**
 - **Q1 2017 Council-EU parliament**
 - **Publication April 2017**



5 : EC Guidelines (1)

- Guidelines on GMP for IMP (finalised by EC end 2016 and published in April 2017)
- Transition period : practical organisation (comments awaited for 1 st November)
- **Risk proportionate approaches in clinical trials**
- Summary of clinical trial results for Laypersons
- Definition of IMP and AMP
- Ethical consideration for clinical trials on medicinal products with Minors (Ready for publication end 2016/beginning 2017)
- Rest of Eudralex Volume 10 will be issued as EMA guidelines.



5 : EC Guidelines (2)

Guideline on risk proportionate approaches in clinical trials within the scope of the Regulation :

ec.europa.eu/health/files/clinicaltrials

- Low interventional trials
- Risk assessment areas :
 - Safety reporting
 - IMP management
 - Traceability and accountability
 - Trial management
 - Monitoring
 - Trial documentation
 - Content of the Trial Master File
- Need for further finetuning after adoption ?



Thank you for your attention



Contact informations

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