The CTR implementation at national level information session 4

14th of September 2017

Program

1. CTR implementation legal: state of affairs:
   - EU Portal and Data base: impact on entry into force of CTR
   - National (RD operational & fees)
2. Recognition of ECs
3. Patient representation
4. Feedback working group and pilot projects
   - State of affairs
   - Practical “tips&tricks”
5. Planning

! Please sign the attendance list

1. EU Portal and Database:
impact on entry into force of CTR

- 16/06/2017: press release of EMA management Board
- Entry into force CTR postponed to 2019
- EMA's priority = high quality and functional system
- New delivery timeframe is expected in October 2017
- In Belgium work on implementation (pilot projects, working groups, …) will **continue** as planned in order to be entirely ready when needed.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/06/news_detail_002764.jsp&mid=WC0b01ac058004d5c1

Press release

16/06/2017

EMA Management Board: highlights of June 2017 meeting

Focus on Brexit preparations and the development of the EU clinical trial portal and database

Brexit preparations

Entry into application of EU Clinical Trial Regulation postponed to 2019

The Board discussed the progress made regarding the development of the EU clinical trial portal and database. Due to technical difficulties with the development of the IT systems, the portal's go-live date has to be postponed. EMA is working closely with its IT service provider to ensure that corrective measures are implemented and will closely monitor progress. The Board was informed about the mitigation measures taken and the revised plan from the developer. The Agency will provide an update at the next meeting of the Management Board in October 2017 where a new delivery time frame will be discussed once progress with development has been confirmed. Due to these delays, the EU Clinical Trial Regulation will now come into application in 2019 instead of October 2018, as previously scheduled.

EMA's priority is to ensure that a high quality and functional system is delivered to the EU regulatory network and its stakeholders.

1. Implementation on the national level:

Royal Decree

D. Kleinermans (Ministry of Social Affairs and Public Health)

- “operational” Royal decree: state of affairs

- Fees: financing of the evaluation procedure

Federal Agency for Medicines and Health Products

2. Recognition of ECs

P. Vankeerberghen

famhp

.be

Introduction

Cave: slides based on current status RD (work in progress)

Overview

- Expected timing for dossier submission
- Procedure: what and when
- Criteria

Expected timing

2 slots per year foreseen for submitting applications to famph:

- dossier submitted before May 1st – possible recognition on Oct 1st of the same year
- dossier submitted before Nov 1st – possible recognition op April 1st of the following year

First possible submission: before May 1st 2018

→ Regulation expected to enter into force in 2019, second possibility to submit before Nov 1st 2018 if dossier not ready for submission before May 1st 2018

Procedure

- Who submits application for recognition: the hospital or legal person exploiting the EC by means of the form of which the model will be fixed by the Minister
- Dossier needs to be complete (including the mandatory annexes)
- Dossier can be submitted entirely electronically (advanced electronic signature necessary e.g. EID) or by registered post
- Within 30d after receipt notification by FAMHP on completeness
- If incomplete, 15d for EC to complete, 10d for FAGG to notify whether admissible
- Possibility for famhp to ask supplementary questions, to request an evaluation by the College on the EC, to request any inspection that is deemed useful

Recognition criteria (1):

- Mandatory annexes of the application:
  - Description of the quality system and a copy of every procedure (more details further)
  - Description of the registration and management system for conflicts of interest
  - Names, gender, capacity of the members of the EC as well as their declaration of interest
  - Certificate of an insurance civil liability for the members of the EC

- Commitment to using the EU assessment report templates

- Documentation on:
  - Ensuring valid decisions by the EC (more than half of the effective members present (written advice counts on the dossier for quorum), exception foreseen by means of a written procedure)
  - Having a president with sufficient experience in a fully recognised EC within the scope of 7/5/2017 or 7/5/2004
  - Both healthcare practitioners, including at least 2 physicians, as well as non-healthcare practitioners present
  - Patient representative or his substitute present

Recognition criteria (2):

- When deciding on a phase 1 trial, additional presence required of: (i) an experienced clinical pharmacologist, (ii) a member experienced in evaluating phase 1 trials, (iii) a representative of healthy volunteers (who has already participated in clinical trials, who is not a healthcare practitioner and who will not participate in the clinical trial to be evaluated)

- The EC needs to prove the following documents will be preserved at least 25 years after the end of the clinical trial: written procedures, invitations for the meetings to the members, decisions and all related documents, minutes and attendence lists of the members, communication with the College, archive register

Recognition criteria (3):

Documentation on the quality system containing at least the following procedures:

- Composition of the EC complete with qualifications of its members as well as documentation on how they were nominated
- Obligations and responsibilities of its members as well as documentation of trainings, documentation on tasks and responsibilities of the administrative staff
- Planning, notification to the members and organisation of the EC meetings
- The evaluation process of initial applications, substantial modifications and additions of Belgium to a clinical trial
- Formulating the advices, documented motivation
- Making appeal to external experts, external patient representatives and any other external person
- The decision making procedure and the written procedure
- Document management and archiving
- Communication between the EC and other stakeholders
- Confidentiality rules
- Redacting and updating procedures

Recognition criteria (4):

- Statement by the EC agreeing to participate to the meetings organised by the College and to the work processes initiated by the College
- Statement by the hospital(s) or the legal person agreeing to provide the necessary resources (financial, logistic, administrative) to the EC enabling the execution of its task within the scope of the law of 7.5.2017 and this RD
- Statement by the EC agreeing to evaluate the clinical trials appointed to them by the College (legitimate circumstances beyond one's control will be foreseen)

Your medicines and health products, our concern

famhp

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3. Patient representation (1)

L. Marynen (FPS Health)

CTR 536/2014: "Member States should ensure the involvement of laypersons, in particular patients or patients' organisations"

Law 7 May 2017: One of the minimal required EC members:

- 10° un représentant des patients.
- 10° een vertegenwoordiger van de patiënten.

Draft Royal decree:

- "Il ne peut pas être un professionnel des soins de santé"
  "mag geen gezondheidszorgbeoefenaar zijn"
- federations of patients' organisations

3. Patient representation (2)

L. Marynen (FPS Health)

Challenges:

- Practical implementation of the Law (finding a patient representative):
  - In consultation with federations of patients' organisations
  - Profile "ideal" patient representative?
- Feasibility in terms of "workload"
  - Work sharing?
- "Education"

4. Feedback working group pilot projects

P. Vankeerberghen (FAMHP), L. Marynen (College, FPS Health)

- Working group
  - 3 meetings since 15/6/17 (last information session): 29/6/17; 27/7/17; 7/09/17
  - EC representatives: UZ Gent, Erasme, UZ Leuven, J. Bordet, AZ Delta, OLVZ Aalst
  - New members

- Subjects discussed:
  - All practical issues met during first pilot projects => see “practical tips and tricks”
  - Feedback EU, questions received from ECs, …
  - ICF document (comments, **revision template**)

4. Feedback pilot projects

Trials in the pilot

First wave – till beginning Sept 2017: 4 (almost) finished

Domain: three oncology, two neurology

One non commercial trial

Evaluating ECs: Erasme, UZ Leuven, UZ Gent, OLVZ Aalst, UZ Brussel

Second wave – Sept – Dec 2017: foreseen

Domain: three oncology, one neurology, one immunology, one gastroenterology

Two non-commercials trial– of which one is pragmatic

Evaluating ECs: AZ Delta, UCL, CHU Liège, other ECs to be assigned

Call for third wave is ongoing

4. Feedback pilot projects

First Findings

- The first 4 dossiers were approved (3 with commitments)
- Timelines are respected, with effort, 2nd round is difficult
- Staffing is not evident
- Shortlist candidate trials requires continuous adaptation, which is normal
- The full correspondence between sponsors (sites), agency (NCP) college and evaluating EC is intense – portal should facilitate.
- Intense learning curve and change for sponsors, famhp, college and ECs.
- More pilot projects are needed in 2018 in order to gain experience (As only 1 EC is involved per pilot)

Lessons learned are valuable: experience must be obtained from all participants, including EC's and sponsors. Evaluating EC now evaluates a site (and a trial) unknown to them.

4. Pilot projects:
learning by doing

- Timesheeting document (excel template) was developped

- Post evaluation survey (survey monkey) to rate your experience and give feedback. 3 versions (EC-college-famhp)

- Next information session: first overview + Feedback from you?
  - *How do you prepare as an EC for the CTR? (within or outside the pilot project). How will you organise the work, best practices, …*

4. Pilot projects:

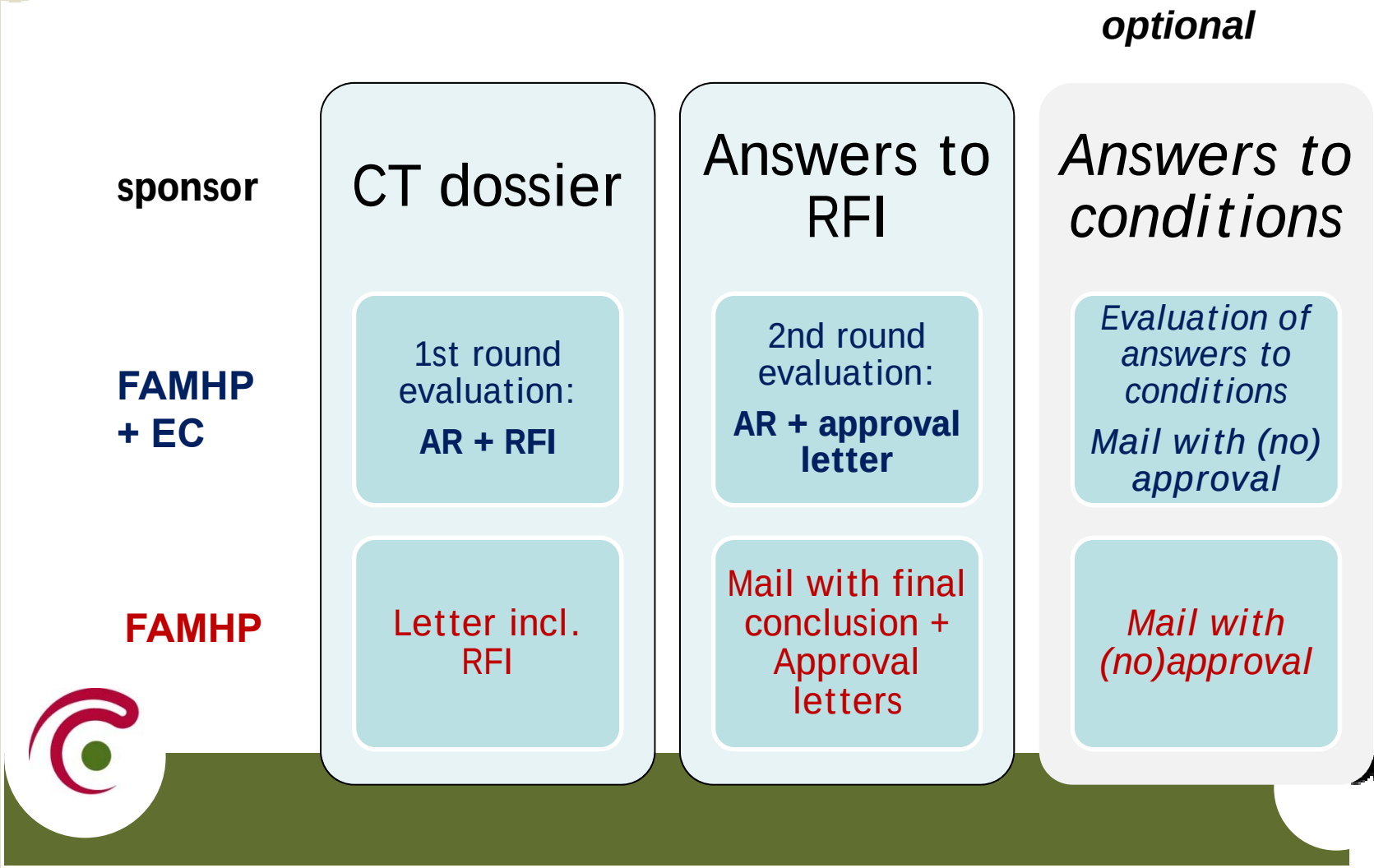
Practical tips and tricks

K. Anciaux (FPS Health)

Highlights new workprocessflow

- Outcomes of discussions with Working Group

4. Pilot projects:
Refreshment



4. Pilot projects:

Practical tips and tricks: Assessment report

When to complete which section ? Table in new version of workprocessflow:

Timing		FAMHP	EC
Part I			
1st round AR	Section 1-4	x	
1st round AR	Section 5	x	x
1st round AR	Section 6		optional
1st round AR	Section 7	x	
1st round AR	Section 8	x	x
1st round AR	Section 9	x	
	Section 10 (NA)		
1st round AR	Section 11	x	
2nd round AR	Section 12	x	x
2nd round AR	Section 13	x	x
Substantial modification	Section 14	x	x[4]
Part II			
1st round AR	Section 1-14		x
2nd round AR	Section 15-16		x
Approval letter			
2nd round AR		x	x

4. Pilot projects:
Practical tips and tricks: Assessment report

Completion of part I – section 5?

- Assessed by both FAMHP and EC
- Comments of both parties taken into account
- Grey/blank to indicate end responsibility for completing
  - Grey: FAMHP=lead
  - Blank: EC=lead
- Goal = administrative work sharing and facilitating consolidation

4. Pilot projects:

Practical tips and tricks: Assessment report

Workspace

Assessors findings/observations

Will not appear in final AR (=not published in EU portal)

Part I-5:

Only to be completed by lead

Assessors comments

Comments from both FAMHP & EC are taken into account

Part I-5:

Obligatory for lead

If none-lead: put "**FAMHP**" or "**EC**" before comment

If question: put "**Q**" at end of question & add to RFI-list (5.6.1)

4. Pilot projects:
Practical tips and tricks: RFI & ICF

RFIs

- Questions to be sent to the sponsor should be as clear as possible and not subject to interpretation
- Only one round of questions

Assessment of ICF in one language

Other languages are responsibility of sponsor

- Footnote added to template approval letter
- Information to be added to sponsor guidance

4. Pilot projects:
Practical tips and tricks: ICF comments and questions

Language of comments on ICF:

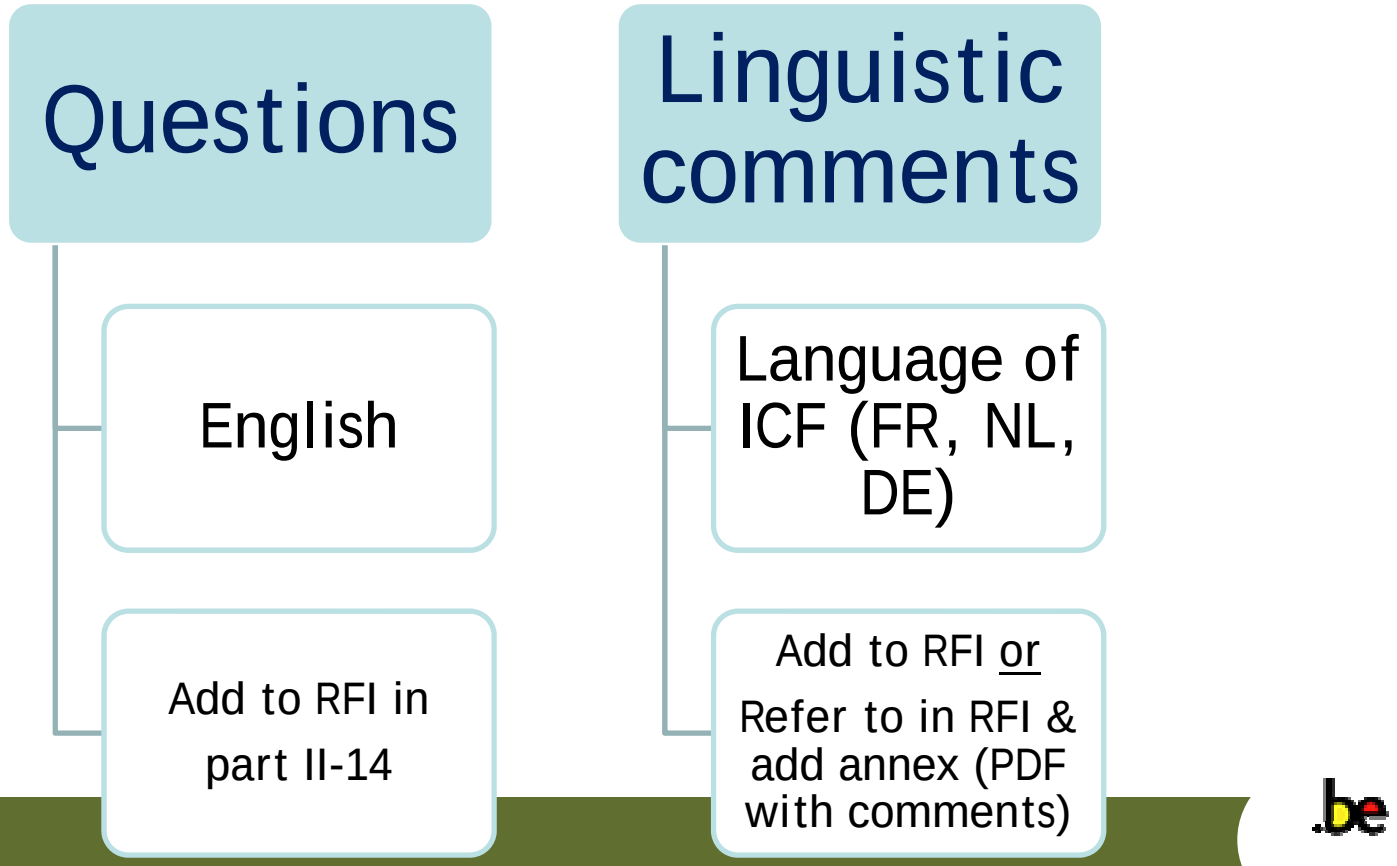
- *Questions* mentioned in AR (Part II –14) should be given in English
- *Linguistic comments* on non-English documents (e.g. ICFs) can be given in the language of the document (FR, NL, DE)
  - **Add linguistic comments as "comments" to the PDF document and refer to in the AR (Part II – 14, RFI),** f.i. add an additional number in the RFI list with the following text : "please also consider the remarks/comments provided in the appended ICF when providing your answers to the RFIs". -> Add PDF as annex to AR.

or

  - **Add linguistic comments to the list in the AR (Part II – 14, RFI)**

4. Pilot projects:

Practical tips and tricks: ICF comments and questions



4. Pilot projects:

Practical tips and tricks: Authorisation subject to conditions

Authorisation subject to conditions

- When and how?
- Procedure (see new version of workprocessflow)

4. Pilot projects:

Practical tips and tricks: Authorisation subject to conditions

An authorisation subject to conditions means that the clinical trial

- may not begin at the moment the conditional approval E-mail is sent to the sponsor.
- can only begin provided that the sponsor can fulfill the conditions within a limited delay (approx. 10 days).

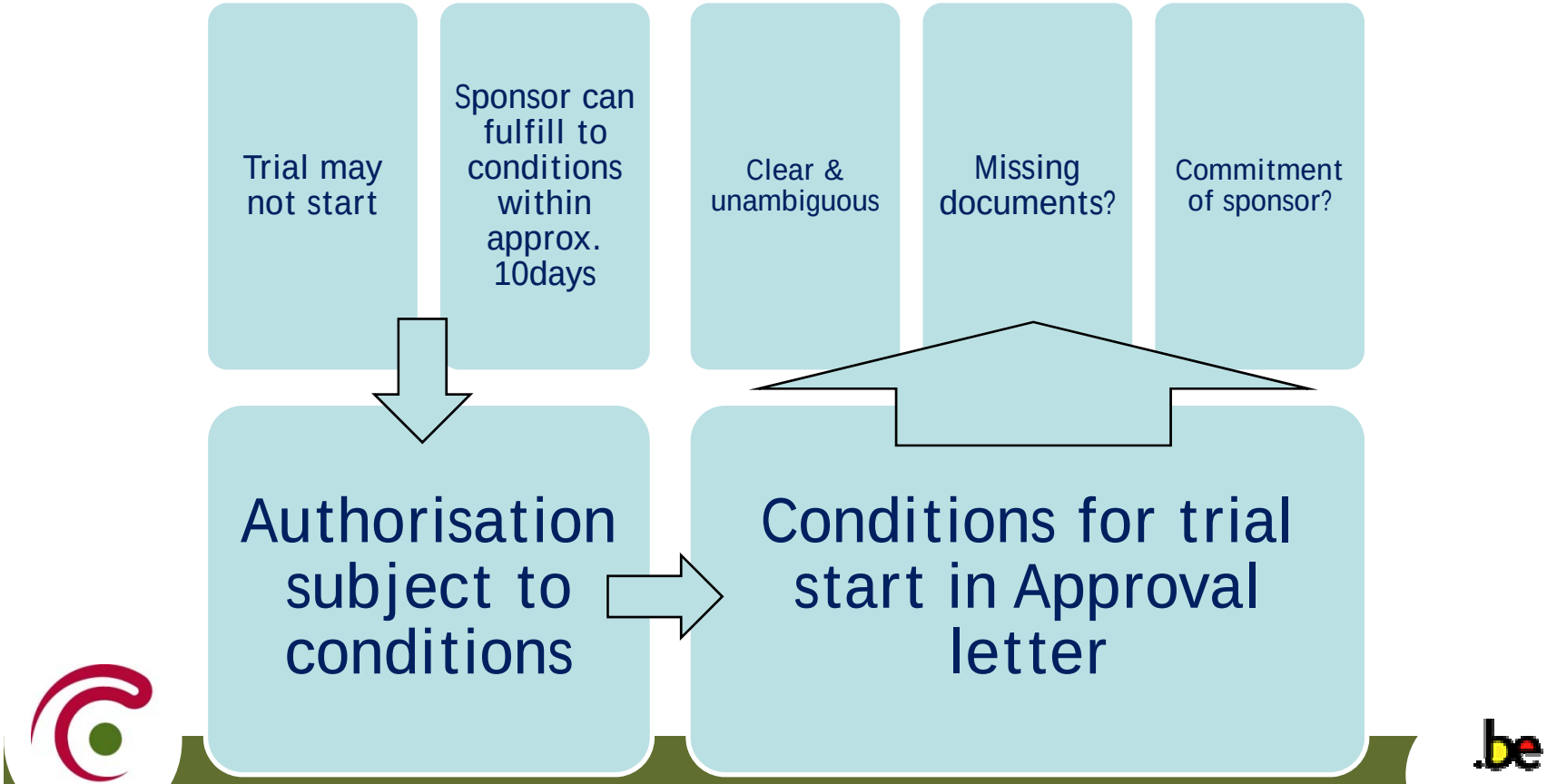
The formulation of the conditions in the Annex of the conditional approval letter should be clear and unambiguous on :

- which information/documents should be provided by the sponsor or
- which commitment should be fulfilled by the sponsor

before authorisation of the start of the trial.

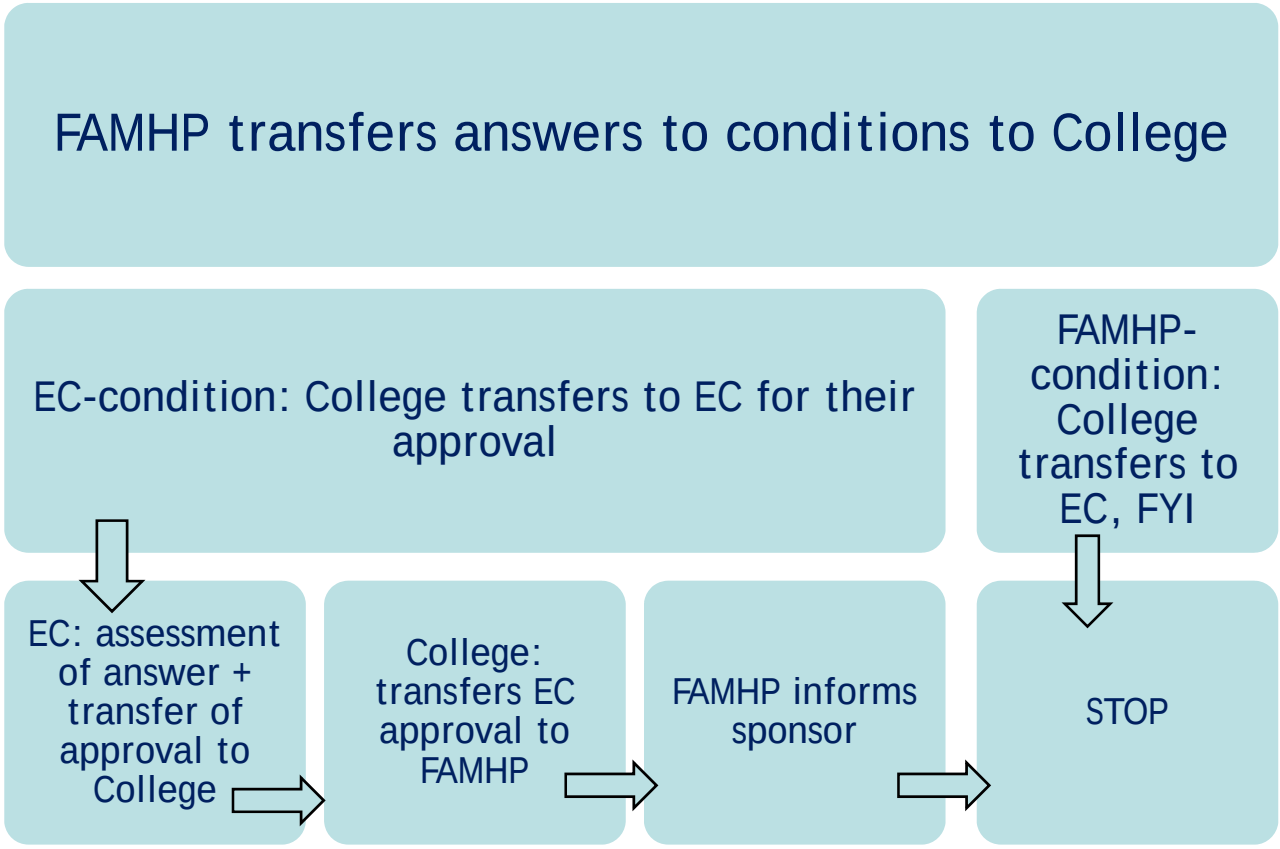
4. Pilot projects:

Practical tips and tricks: Authorisation subject to conditions



4. Pilot projects:

Practical tips and tricks: Authorisation subject to conditions



4. Pilot projects:
Practical tips and tricks

Send mails always to ct.college@health.belgium.be:

- ct.college mailbox checked regularly; if we are in meeting we do not follow our personal mailboxes
- When we use eudralink we have no other choice than that the mail is send via our personal e-mail address, we (try to) put ct.college e-mail address always in cc: so if you reply to all: it will be send to ct.college-mailbox

Always include the EudraCT n° in the heading of your mail, and in the name of the files:

- there is no reference to the study number in the content of the Assessment report: so if the document is saved in the wrong folder: it cannot be retrieved that the report belongs to another study

Send confidential documents, always through eudralink (zip):

- e.g. the assessment report, refusal letter, …

4. Pilot projects:
Practical tips and tricks

We will transfer you shortly a link to a google drive where you will always find the actual versions of the documents you need:

- 1 EC-College-NCP Internal CTR Pilot workprocessflow
- 2 Assessment report templates (part I & II)
- 3 Timesheeting template
- 4 Approval letter templates
- 5 A document containing the URL to FAMHP site with information for sponsors on pilot projects: (guidance, structure of application dossier, …)

❖ No installation of software, nor set up of an account is needed

❖ **TO DO by EC coordinator: add the link to your favorites!**

5. Planning:

- Next meeting: Thursday **December 7th 2017** – Eurostation 19.30h

- Comments on Barec ICF template? (interventional trial on adults)
  - Send to: **ct.college@health.belgium.be**
  - Deadline: **10/10/2017**
  - 1 language is sufficient
  - Consolidated at EC level

5. Planning:

Upcoming events:

- **Symposium FAMHP on clinical trials (patient centricity)**

  26 September 2017 @ Pullman Hotel, Brussels

  https://www.fagg-afmps.be/en/news/symposium_on_clinical_trials_26_september_2017

- **2nd KCE trials Symposium**

  Real-world evidence: randomised trials in daily practice

  28 November 2017 @ Pacheco centre, Brussels

  http://www.kce.fgov.be/en/event/real-world-evidence-randomised-trials-in-daily-practice-2nd-kce-trials-symposium

- **Infosession with stakeholders**

  Feed-back pilots “lessons learned and next steps”

  1 December 2017 @ Eurostation, Brussels

Thank you for your attention