Clinical Trial College

The mission of an independent entity between the FAMHP and the ethics committees

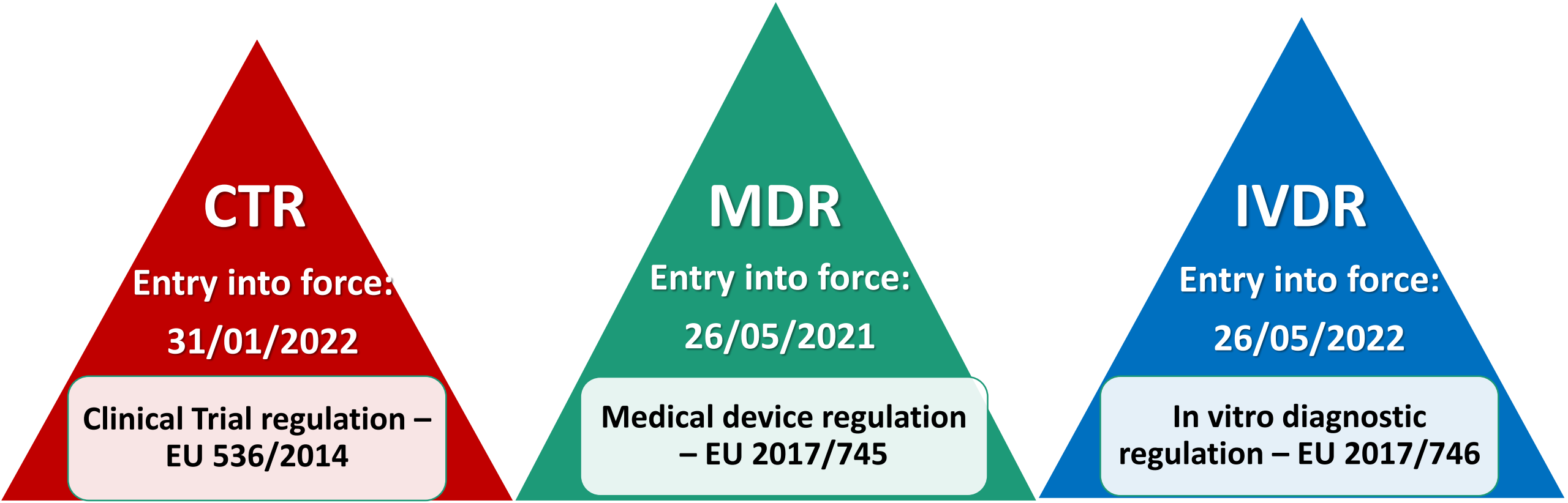
ZNA symposium 03/06/2023

Congrescentrum Ter Elst, Edegem

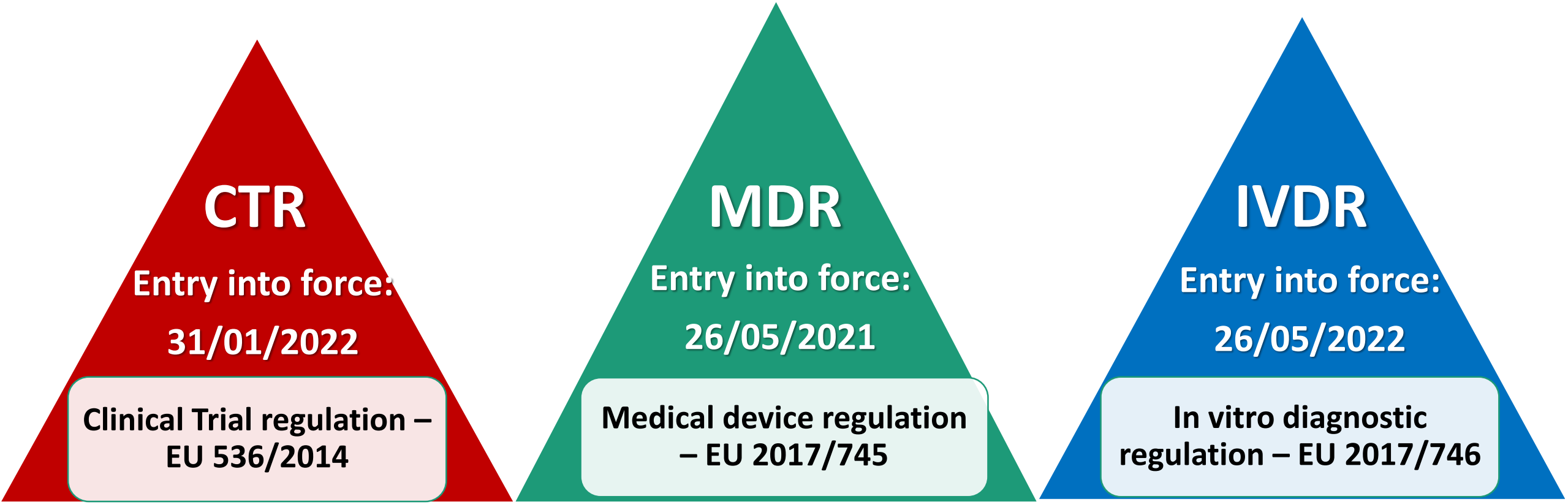
federal public service
HEALTH, FOOD CHAIN SAFETY
AND ENVIRONMENT

Prof. em. L. Van Bortel, Chairman
K. Anciaux, Coordinator

New European regulations



New European regulations



Belgian law:

7/05/2017

Belgian law:

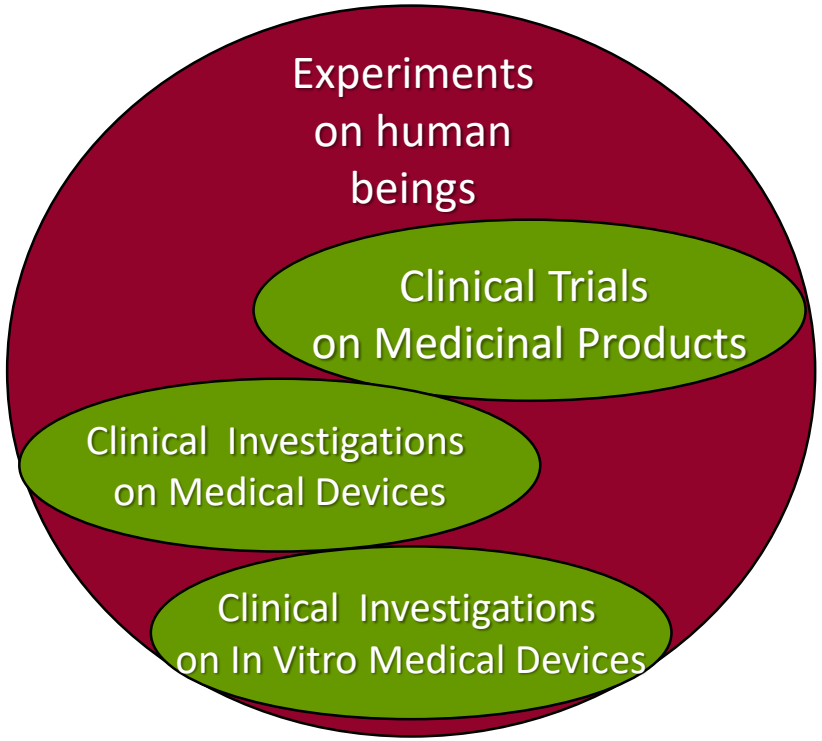
22/12/2020

Belgian law:

15/06/2022

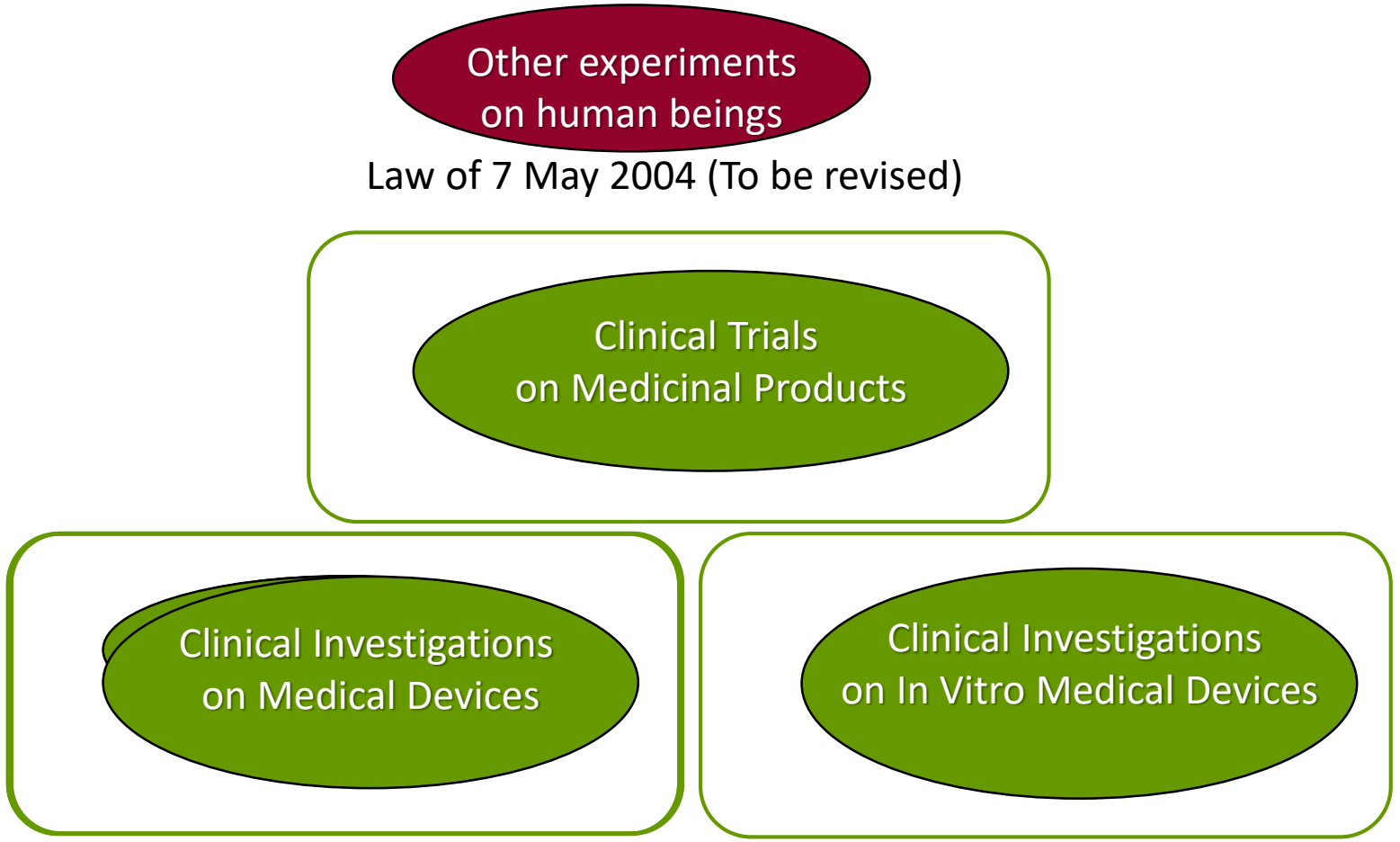
New Belgian Laws partially replacing Law of 7 May 2004

- **Previous situation**



Law of 7 May 2004

- **Current situation**



Highlights of the European Regulations

CTR

CTIS=Clinical trial Information system

European portal and database developed by EMA

Coordinated review

a) 1 single application via **CTIS** for all member states (MS) concerned

b) One of these MS is designated as **reporting** MS (RMS) and provides a single opinion to the sponsor (incl coordinated review by other MS concerned)

c) within the timelines as set out in this Regulation

MDR/IVDR

EUDAMED European database on medical devices

Developed by European Commission

Eudamed is not yet available for the coordinated review

Coordinated review (future)

a) 1 single application via **Eudamed** for all member states (MS) concerned

b) One of these MS is designated as **coordinating** MS and provides a single opinion to the sponsor (incl coordinated review by other MS concerned)

c) within the timelines as set out in this Regulation

Implementation of CTR, MDR & IVDR in Belgium highlights

- National contact point (NCP): FAMHP **(Law of 7 May 2017, Art. 4; CTR, Art 83)**
- The FAMHP and the Evaluating EC are jointly in charge of the evaluation
- Reorganisation of the ethics assessment/ECs
  - 1 independent EC involved per assessment

    Persons assessing the application independent of :
    - The sponsor
    - The clinical trial location
    - The investigators involved
    - natural or legal persons financing the clinical investigation

    and are free of any other undue influence

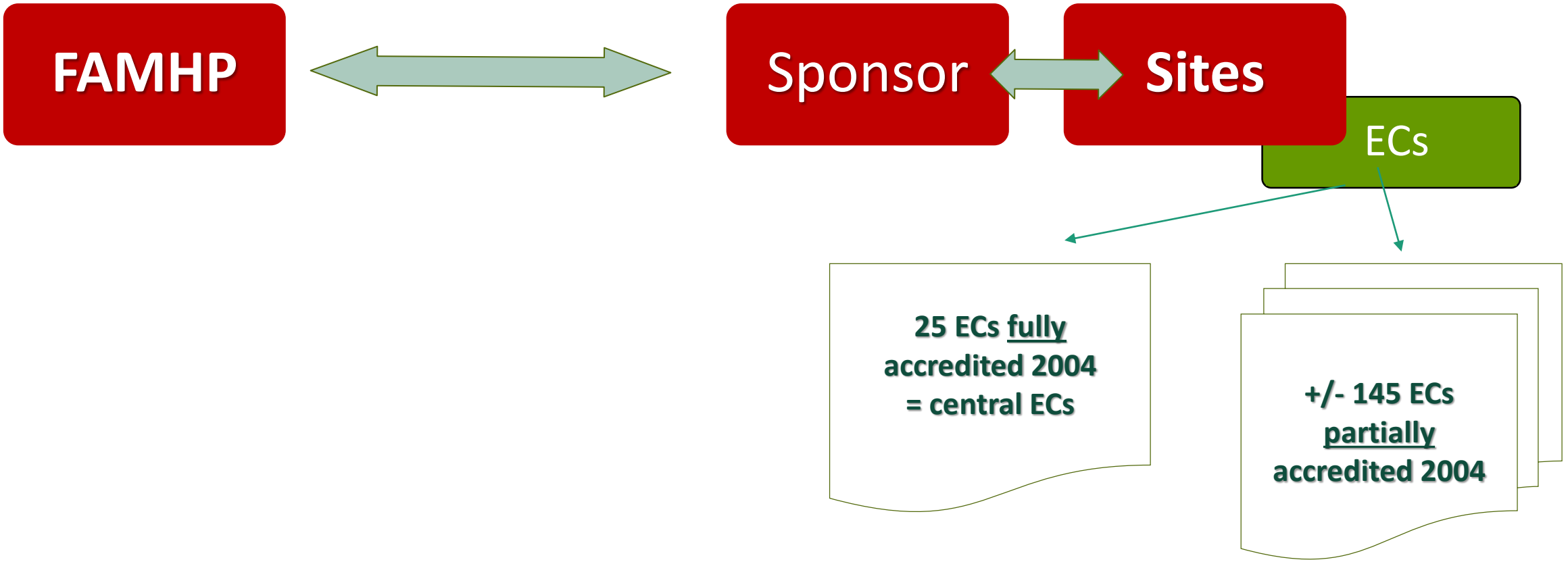
    Involvement of laypersons is mandatory (in particular patients or patients' organisations)

    Need for sufficiently large expertise and experience amongst the members of the EC

    Harmonised procedures amongst ECs
  - Creation of a "College"

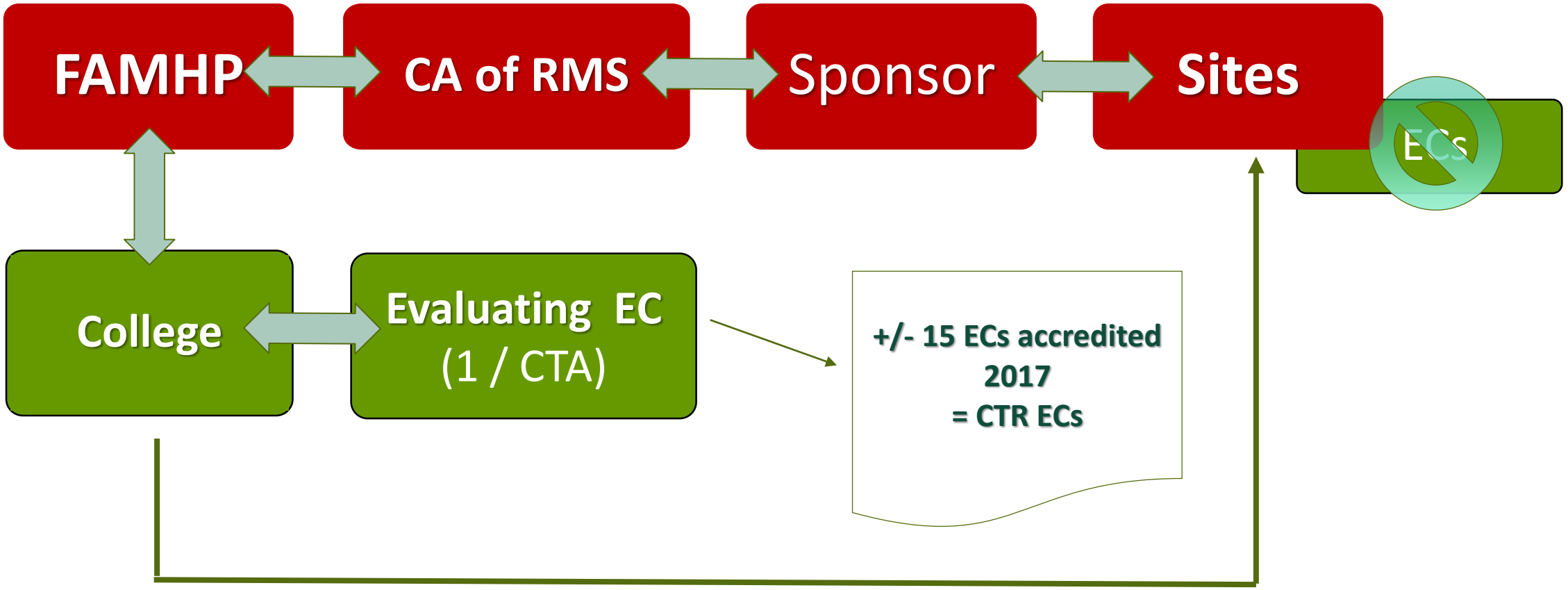
Organization of ethical review in Belgium under CTD

- **CTD & Belgian Law 2004**



Organization of ethical review in Belgium under CTR/MDR/IVDR

- **CTR & Belgian law 2017, MDR & Belgian law 2020, IVDR & Belgian law 2022**



Creation of the College: Ministerial Decree

SERVICE PUBLIC FEDERAL SANTE PUBLIQUE, SECURITE DE LA CHAINE ALIMENTAIRE ET ENVIRONNEMENT

[C − 2021/41548]

18 MAI 2021. — Arrêté ministériel portant nomination des membres, du président et du vice-président du Collège visé dans la loi du 7 mai 2017 relative aux essais cliniques de médicaments à usage humain

Le Ministre de la Santé publique,

FEDERALE OVERHEIDSDIENST VOLKSGEZONDHEID, VEILIGHEID VAN DE VOEDSELKETEN EN LEEFMILIEU

[C − 2021/41548]

18 MEI 2021. — Ministerieel besluit houdende benoeming van de leden, van de voorzitter en ondervoorzitter van het College zoals bedoeld in de wet van 7 mei 2017 betreffende klinische proeven met geneesmiddelen voor menselijk gebruik

De Minister van Volksgezondheid,

- Independent College created within the Federal Public Service of Health, Food Chain Safety and Environment.

More information:
www.ct-college.be

- The legislation defines the mission, organisation, composition of the College and its collaboration with FAMHP and evaluating ECs.

Composition of the College (Board)

Effective member	*Substitute member*
MDs with experience in Phase I trials	
Lucas Van Bortel, Chairman (NL)	Rene Westhovens (NL)
Didier Verhoeven (NL)	Philip Debruyne (NL)
Experts in quality control systems	
Hilde Nevens, Vice-Chairman (NL)	Joline Goossens (NL)
Lawyers	
Bruno Fonteyn (FR)	Hélène Garnier (FR)
Evelien Delbeke (NL)	Moustapha Assahraoui (NL)

Mission of the College

1° Single point of contact between FAMHP and ECs
2° Assignment of EC in charge of evaluation of clinical study applications
- ✓ Objective criteria defined by legislation
- ✓ Cannot be the EC of the study site(s)

3° Ensure a consistent application of the law by the ECs.
Recommendations to the ECs can be made.
4° Formulate advices on the application of the regulations and legislation
5° Coordinate, harmonise, support, evaluate and follow-up the quality control activities carried out by the ECs.
Recommendations to the ECs can be made.
6° Support ECs in the evaluation of applications,
7° Submit annual activity report to Minister and Parliament

Law of 7 May 2017, Art. 9. §3

Organisation of the College

Rules of internal order: Royal Decree

SERVICE PUBLIC FEDERAL SANTE PUBLIQUE, SECURITE DE LA CHAINE ALIMENTAIRE ET ENVIRONNEMENT

[C − 2021/34185]

26 NOVEMBRE 2021. — Arrêté royal portant approbation du règlement d'ordre intérieur du collège tel que visé dans la loi du 7 mai 2017 relative aux essais cliniques de médicaments à usage humain

PHILIPPE, Roi des Belges,

FEDERALE OVERHEIDSDIENST VOLKSGEZONDHEID, VEILIGHEID VAN DE VOEDSELKETEN EN LEEFMILIEU

[C − 2021/34185]

26 NOVEMBER 2021. — Koninklijk besluit houdende goedkeuring van het huishoudelijk reglement van het College zoals bedoeld in de wet van 7 mei 2017 betreffende klinische proeven met geneesmiddelen voor menselijk gebruik

FILIP, Koning der Belgen,

Mission of the College

Tasks delegated to admin staff FPS Health

1° **Single point of contact between FAMHP and ECs**

2° **Assignment of EC in charge of evaluation of clinical study applications**

- ✓ Objective criteria defined by legislation
- ✓ Cannot be the EC of the study site(s)

3° **Ensure a consistent application of the law by the ECs.**
Not delegated: *Recommendations to the ECs can be made*

4° Not delegated: Formulate advices on the application of the regulations and legislation

5° **Coordinate, harmonise, support, evaluate and follow-up of the quality control activities carried out by the ECs**.
Not delegated: *Recommendations to the ECs can be made*

6° **Support ECs in the evaluation of applications**,

7° Prepare annual activity report for the Minister and Parliament.

Law of 7 May 2017, Art. 9. §3

Organisation of the College
Admin staff FPS Health

Project lead CTR	Sébastien Vanhiesbecq (FR)
Project lead MDR/IVDR	Michelle Fonteyne (NL)
Project lead Quality	Katelijne Anciaux (NL)
Project lead IT	Julien Frgacic (FR)

File managers

Marlène Keck-Antoine (FR)	Lisa Reyckers (NL)
Jean Pirard (FR)	Annelies Marin (NL)
Bram Ottenbourgs (NL)	Julie Seronvalle (FR)

Organisation of the College

Admin staff FPS Health

Admin staff organizes :

- Infosessions for ECs: 3/year
- Working group meetings with ECs and FAMHP: 1/month
- Meetings College-FAMHP about dossier related issues
- Q&A sessions for ECs: 1/week
- College Board meetings

Organisation of the College

College Board meetings and achievements

- **Meetings**: monthly

  in case of urgencies ad hoc meeting or via written consultation
- Admin staff reports on **delegated tasks**
- Discuss **questions** from ECs, sponsors or admin staff
- Prepare **advices** : e.g.
  - advice to ECs on safety assessment, https://overlegorganen.gezondheid.belgie.be/nl/documenten/advies-voor-belgische-ecs-aangaande-het-beoordelen-van-veiligheidsrapporten-ctr-dossiers
  - advice to Minister on ombudsfunction,

Organisation of the College

College Board meetings and achievements

- Discuss, adapt and/or endorse **templates and procedures** : e.g.
  - site suitability statement template and CV Investigator template: https://www.fagg.be/nl/menselijk_gebruik/geneesmiddelen/geneesmiddelen/onderzoek_ontwikkeling/klinische_proeven/europese
  - endorsement e-ICF guidance, https://overlegorganen.gezondheid.belgie.be/nl/documenten/guidance-sponsors-use-electronic-informed-consent-interventional-clinical-trials-belgium
  - procedure for assignment of the evaluating EC, see next slides
  - Tool for Quality Control by ECs, see next slides

College Board – assignment of the EC

Criteria

1) The EC must be currently **recognized** under the law of 07/05/2017
2) The EC doesn't have any quality issue
3) In case of Phase 1 CTA : the EC is **recognized for phase I** trials
4) In case of **appeal** : the EC that already assessed the dossier is excluded
5) The EC is **independent of all the sites** involved in the study and of the **sponsor**
6) The EC **expertise** domain(s) matche(s) the therapeutic domain(s) of the study
7) Language of ICFs
8) there any **connection between the study application with a former one**: e.g. in case of a
   - Resubmission
   - Extension study

College Board - Tool for Quality Control by ECs

1° Single point of contact between FAMHP and ECs

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3° Ensure a consistent application of the law by the ECs.
Recommendations to the ECs can be made.

4° Formulate opinions on the application of the regulations and legislation

5° Coordinate, harmonise, support, evaluate and follow-up of the quality control activities carried out by the ECs
Recommendations to the ECs can be made.

6° Support ECs in the evaluation of applications

7° Submit annual activity report to Minister and Parliament

Law of 7 May 2017, Art. 9. §3; Mission of the College

College Board - Tool for Quality Control by ECs

- 3 areas to check and report on
  1. Legal requirements on composition, responsibilities and training of the members of the EC
  2. Document management (e.g. minutes, archiving)
  3. Operational functioning of the EC (samples to be checked)
- Supplementary questions
- Recommendations

College Board - Tool for Quality Control by ECs

- Yearly reporting
  - 1st reports required January 2024 for the year 2023
  - Self-assessment
  - Independent internal audit every 3 years
- Evaluation of Tool
  - Try out for 2022
  - After 1st year of use
  - Scoring system to be developed

College Board - Tool for Quality Control by ECs

- Benchmarking
  - Between ECs based on report integrating all data (anonymised)
  - Identification of quality improvement needs
  - Identification of other needs (e.g. resources, ...)

roles and responsibilities of quality control

FAGG-AFMPS

Evaluatie erkenningsaanvraag/Evaluation de la demande d'agrément

Toekennen v/d Erkenning/Accorder l'Agrément

Inspectie/Inspection

ECs/CEs

Opzetten van kwaliteitssysteem/Developper système de qualité

Opzetten systeem van kwaliteitscontrole/Mettre en oeuvre un système de contrôle qualité

College

Toezicht/opvolgen kwaliteitscontrole door de ECs

Surveiller/suivre le contrôle de la qualité effectué par les CEs

College Board - mission

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Law of 7 May 2017, Art. 9. §3; Mission of the College

College Board – Ensure timelines are followed

	Examples of timelines for EC in CTR					
	Multinational			Mononational (BE= RMS)		
	BE=RMS		BE= MSC	Phase II-IV		Phase I
	IN	SM	IN/SM	IN	SM	IN/SM
1st round	23 days	16 days	9 days	36 days	30 days	10 days
2nd round	12 days	12 days	10 days	12 days	12 days	7 days

IN= Initial application

SM= substantial modification application

RMS: Reporting member state

MSC: Member state concerned

College Board – Ensure timelines are followed

- Follow-up of timelines via KPIs
- When no advice of the EC is received timely :
  - Application is approved tacitely
  - EC will not receive a fee : Royal Decree of 21/05/2023, still to be published

Art. 4. Les montants sont versés au Comité d'éthique à condition que ce dernier remette son évaluation et son avis dans les délais communiqués par le Collège.

Art. 4. De bedragen worden gestort aan het Ethisch comité op voorwaarde dat het zijn evaluatie en zijn advies binnen de door het College meegedeelde termijnen bezorgt.

CT College and Belgian Association of Research Ethics committees (BAREC)

The College considers ECs and BAREC in particular, as an important stakeholder to fulfill its missions

Joint meetings are organized between the Boards of College and BAREC