EU COMBINE project overview

ACT EU MSP annual meeting 22 October 2024

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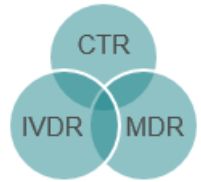
Olga Tkachenko, Unit D3 Medical devices

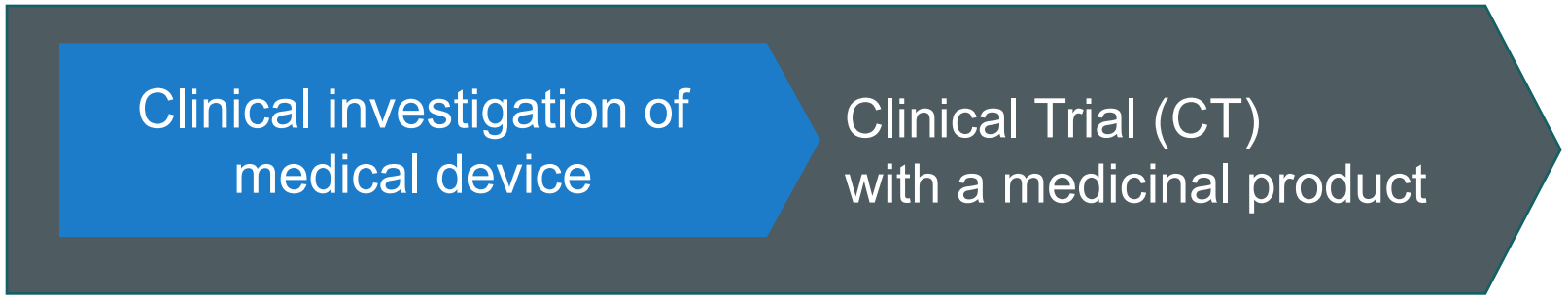
DG SANTE, European Commission

Implementing 3 regulations together…

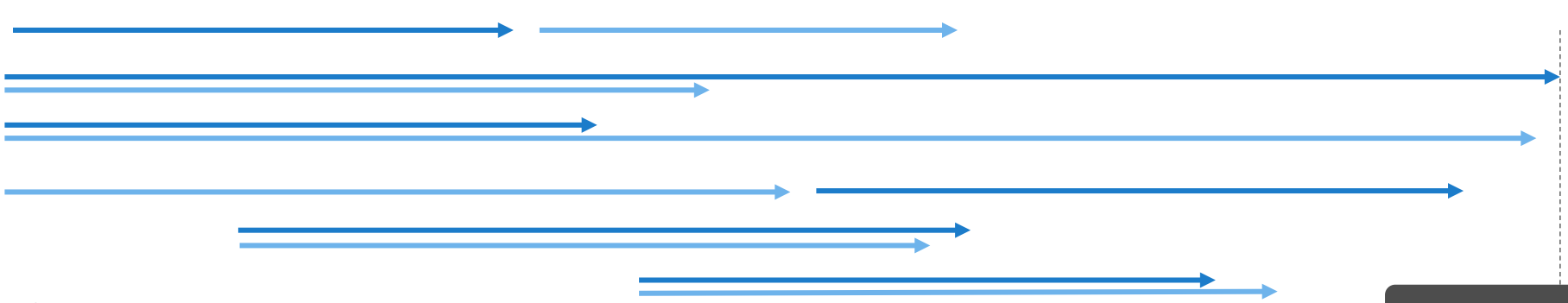


- CTR applicable since 21 January 2022: Coordinated in CTIS, remains complex
- MDR applicable since 21 May 2021:
- IVDR applicable since 21 May 2022:

Not yet coordinated. Eudamed for national CA 2027.
For MS CA coordinated process 2029 (not ethics)



CT: CTIS – one entry with coordinated CA and ethics assessments



Clinical investigation of MD/ Performance study of IVD: National procedures by competent authorities (CAs) and ethics committees – currently no coordination

delay of CT initiation

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Scope of ‘COMBINE’ Project

Combined study (informal definition): clinical trial of a medicinal product together with a performance study of an IVD or a clinical investigation of a medical device.

- The MDR, IVDR and CTR contain requirements for the respective individual authorization for clinical investigation, performance studies or clinical trials processes.
- Scope of project (long-term): clarify and work towards aligning the interface between clinical trials of investigational medicinal products, performance studies of in vitro diagnostics and clinical investigations of medical devices.
- Scope of analysis phase: understand challenges and obstacles on the way to alignment of the three frameworks (MDR, IVDR, CTR) that overlap in combined studies and propose ways forward.

1	**Analysis of the challenges** at the interface between MDR, IVDR, CTR
2	**Possible development of ways forward a**iming to align the interface

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Member State groups to involve

Expert group of national competent authorities

Clinical trials of medicines

- Clinical Trials Advisory Group
- Clinical Trials Coordination Group

Medical devices

- Medical Device Coordination Group
- 2 of its 13 subgroups: IVD and CIE (Clinical Investigation and Evaluation)

Ethics

- MedEthics EU (voluntary coordination between national ethics committee representatives)

Set-up of COMBINE so far

15 MS,
55+ experts
4 functional areas

- **Project group** involving competent authorities from CT, MD and IVD field, medical research ethics committee representatives and the EMA
- **Stakeholder reference group** spanning CT, MD and IVD sectors, patients and clinical professionals.
- **Steering board** of competent authorities and European Commission
- Outcomes to be endorsed by the relevant authority groups (Medical Device Coordination Group, relevant Clinical Trials groups)

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Stakeholder reference group

ACRO (Association of Clinical Research Organizations)
AMDM (Association of Medical Diagnostics Manufacturers)
Biomedical Alliance in Europe
COCIR
Conect4Children Stichting
EAN (European Academy of Neurology)
EATRIS (European Infrastructure for Translational Medicine)
ECRIN (European Clinical Research Infrastructure Network)
EUCOPE
EuropaBio
EAAR (European Association of Authorised Representatives)
EFPIA (European Federation of Pharmaceutical Industries and Associations)
EHA (European Hematology Association)
EORTC (European Organisation for Research and Treatment of Cancer)
EPF (European Patients' Forum)
ESMO (European Society for Medical Oncology)
MedTech Europe
MPP Association
NBCG-Med (Notified Body Coordination Group)
TEAM-NB (European Association for Medical Devices of Notified Bodies)
VE (Vaccines Europe)

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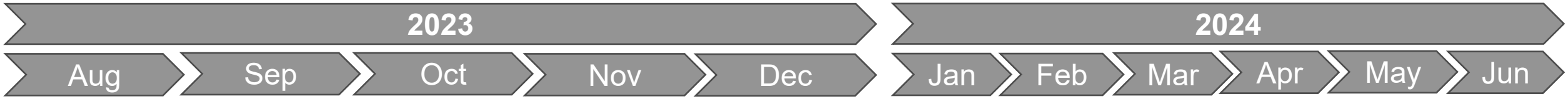
High-level timeline for phase 1



PHASE 1

1. Issue list
2. Mapping of IVDR/MDR/CTR EU landscape
3. Mapping of relevant activities
4. Proposals for solutions

Deliverable: document describing 3 analysis elements & proposed solutions

Preparation for phase 2

Planning for possible development of solutions

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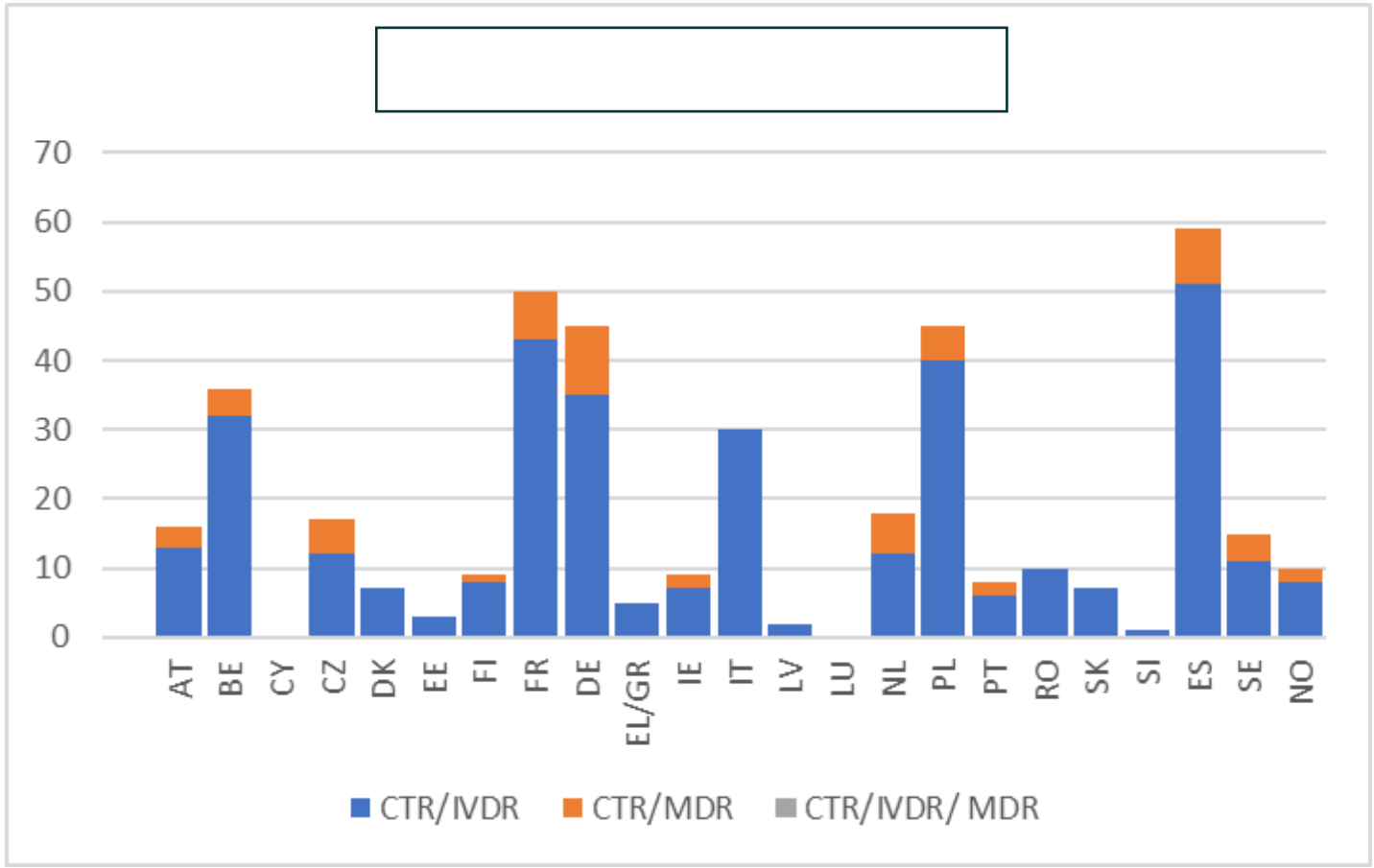
Total Combined study applications per year

≠ number of combined studies – many studies are multi-country

Total: 402



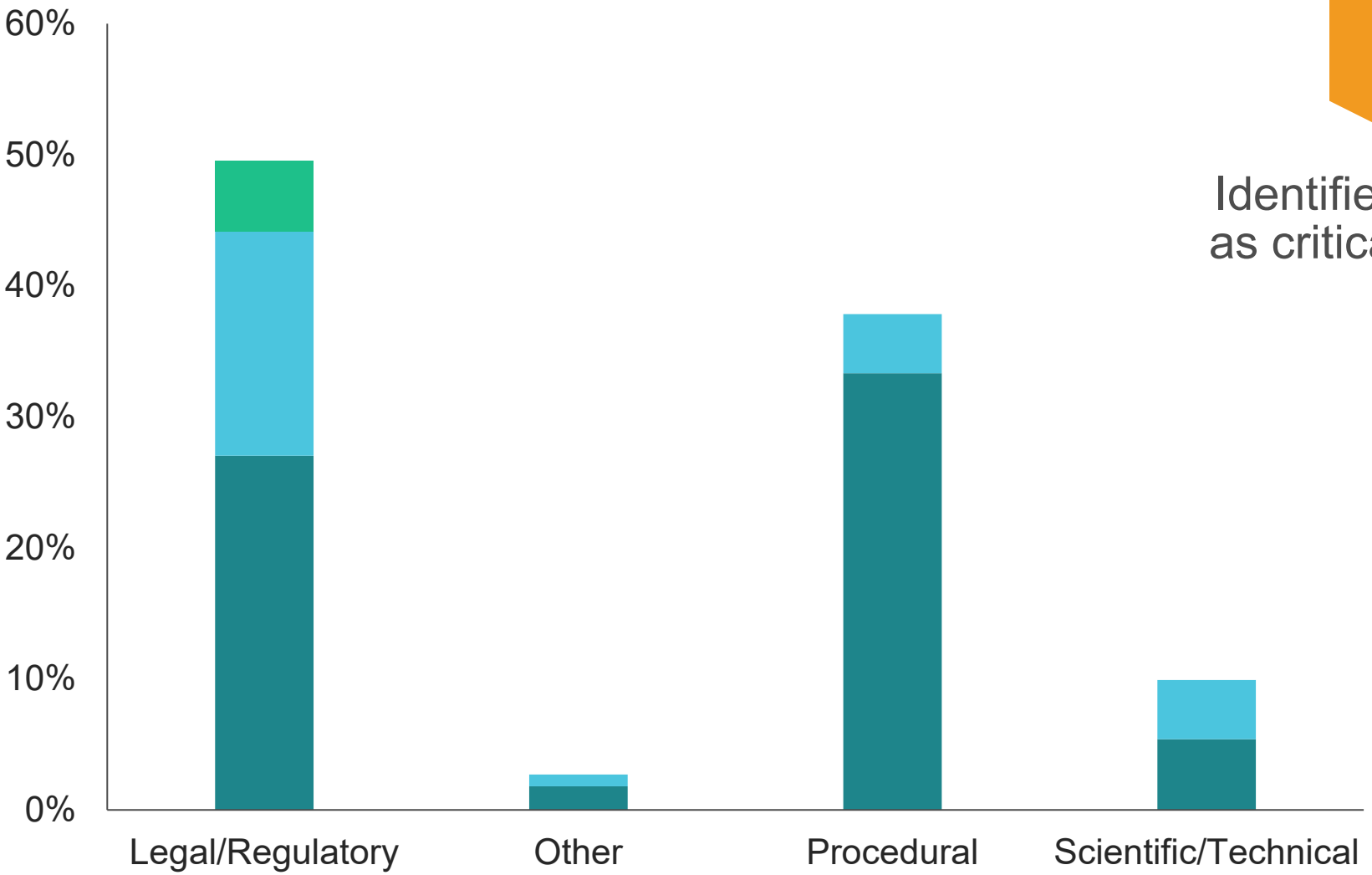
Most are multinational:

CTR/IVDR: 96%

CTR/MDR: 88%

About ¾ of all performance study applications for an IVD are combined with a CT of a medicine

Nature of issues



78
Issues collected

Identified as critical
50%

MDR
IVDR
Interface

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SUMMARY OF PROPOSED WORK ITEMS TO ADDRESS ISSUES FOR COMBINED STUDIES.

Group	#	Item
Coordinated Assessment	1.1	CI/PS CA Coordinated Assessment
	1.2	Aligning Ethics Assessment Procedures (MS level)
	1.3	Coordination between CTR & CI/PS CA Assessment (Single Application)
	1.4	IT Infrastructure
Alignment	2.1	Align MS positions
	2.2	Develop Understanding
	2.3	Improve Sponsor awareness
Guidance & Clarity	3.1	IVDR/MDR Topics
	3.2	Common Topics
	3.3	CTR Topics
Communication & Dialogue	4.1	Scientific/Technical Advice
	4.2	Open dialogue/ exchange of best practice
	4.3	Training Initiatives
	4.4	Encourage creation of cross functional national teams at a member state level (CT/CI/PS)

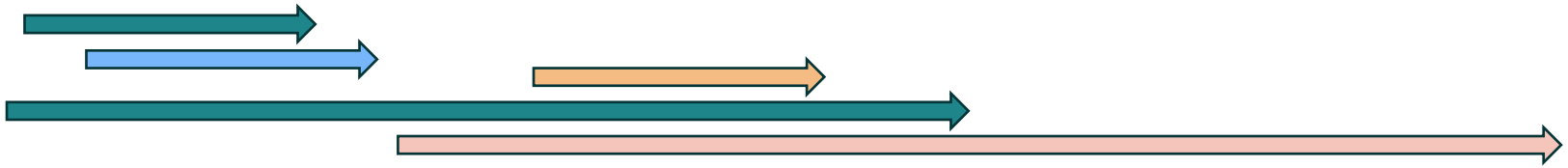
These were ideas for actions that could address most of identified issues – more than 50 individual actions proposed.

To be addressed **after** the analysis phase:
- prioritisation
- concrete plans for implementation

Approach for phase 2: from project to programme

- Working across fields with established groups
- For **sector-specific issues** relevant to the interface, projects in each respective group
- Projects **on the interface** can be initiated and done jointly
- Overview of all ongoing work + stock-stock-taking together as we go
- Stepwise progress to ensure feasibility

Inclusive, pragmatic, staggered



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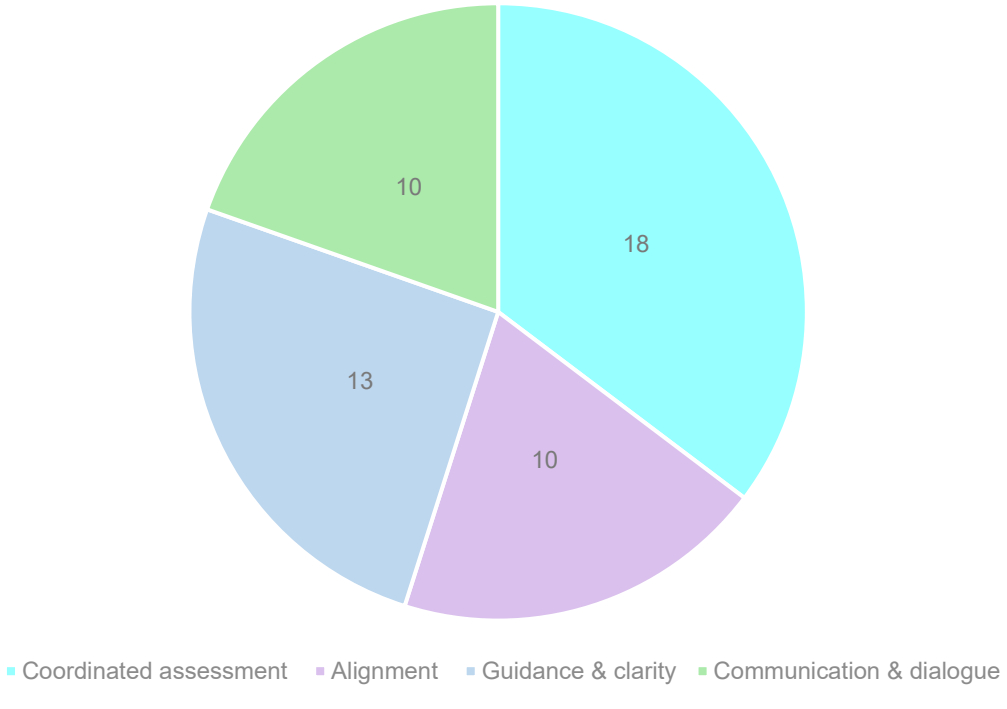
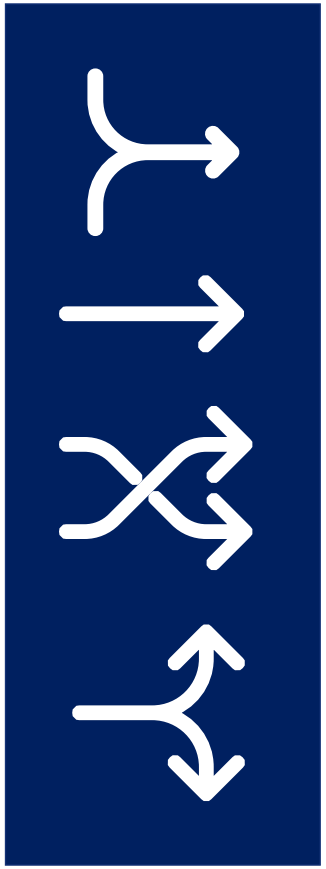
From proposed solutions to programme plan

Proposed solutions
COMBINE analysis report





Phase 2 actions
Programme plan:

51 proposed work items

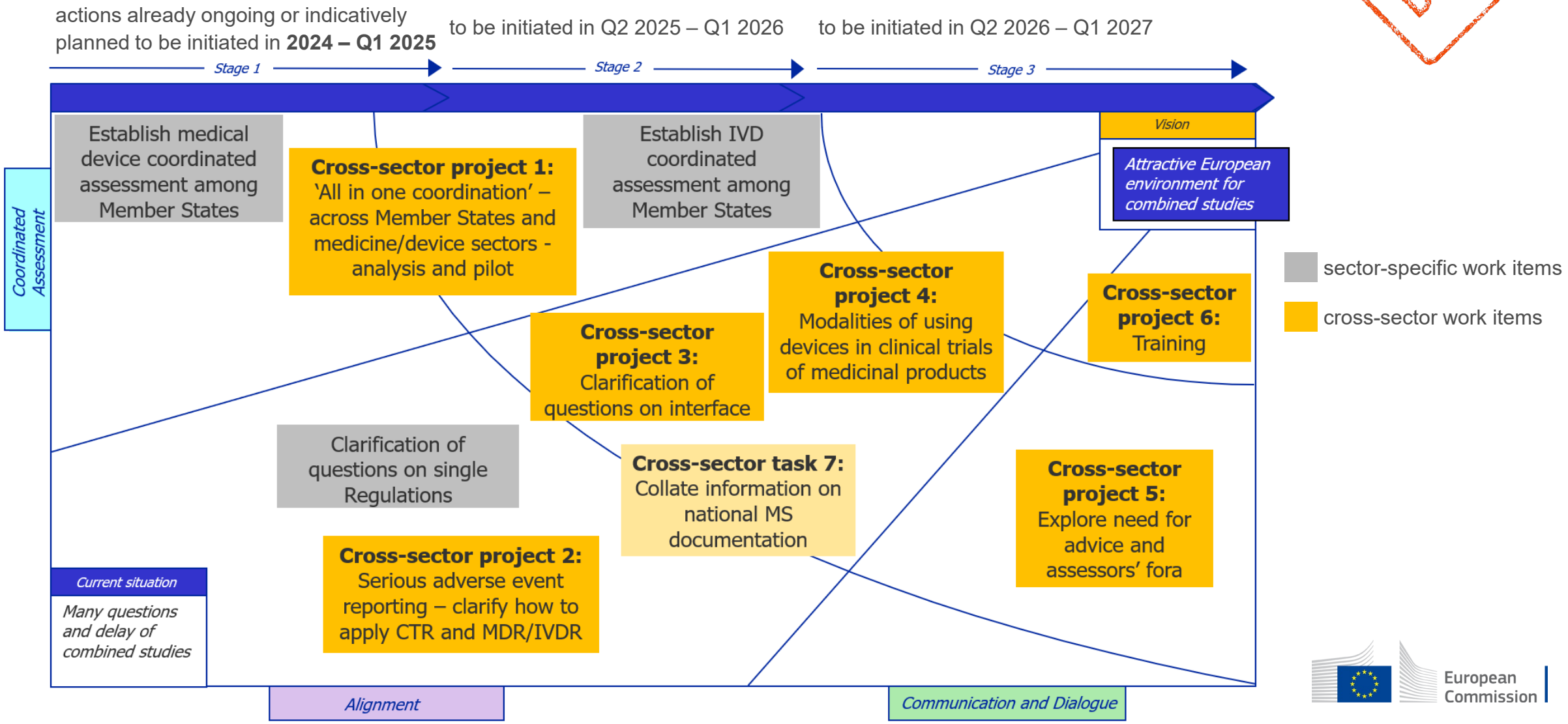
78 issues mapped

6 cross-sector 'COMBINE' projects and **1** task

Several sector-specific task forces/projects to be mapped and interlinked

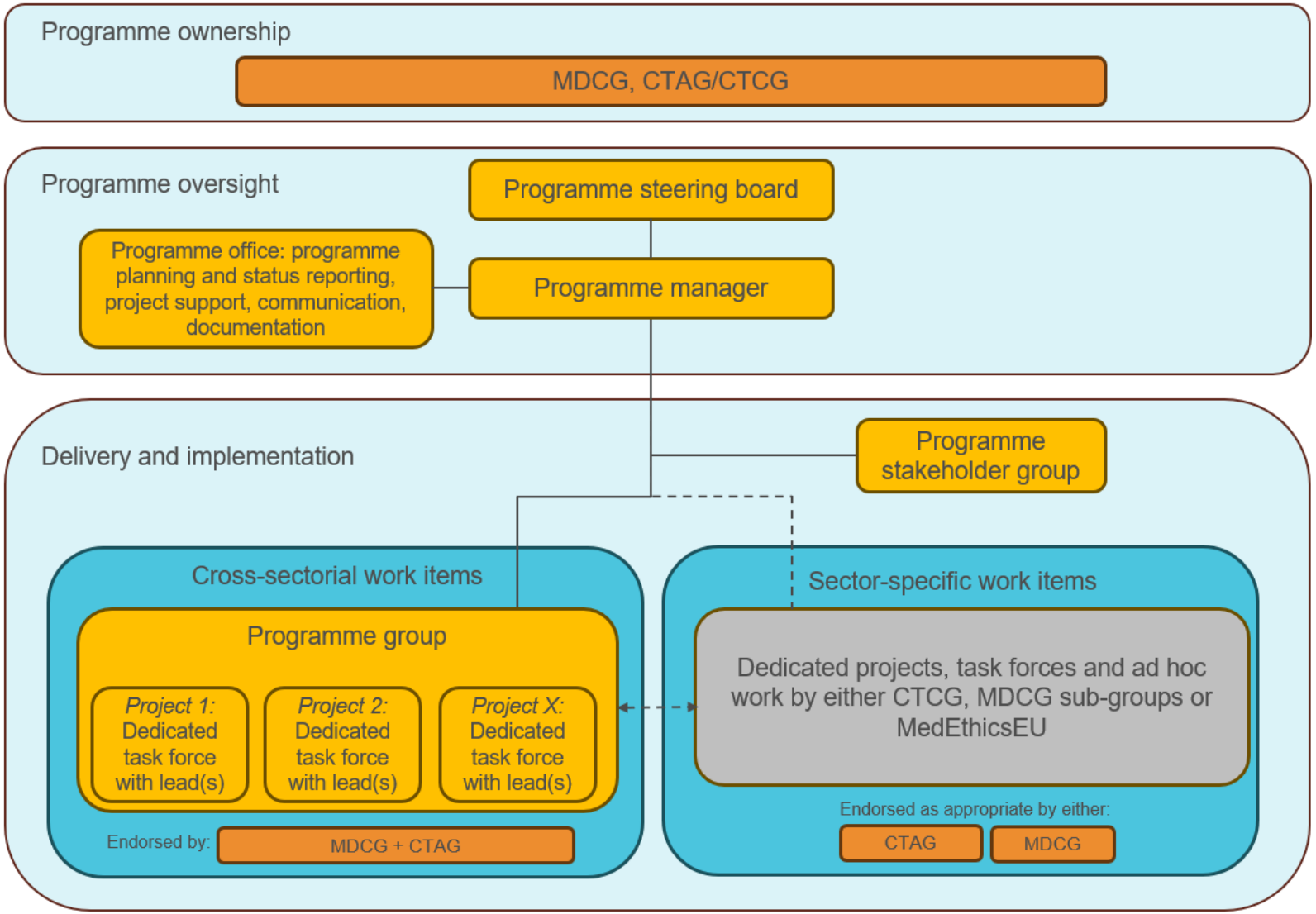
78 issues to be addressed

Summary of proposed programme activities



Proposed programme governance

DRAFT



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High-level timeline for phase 2 – from project to programme

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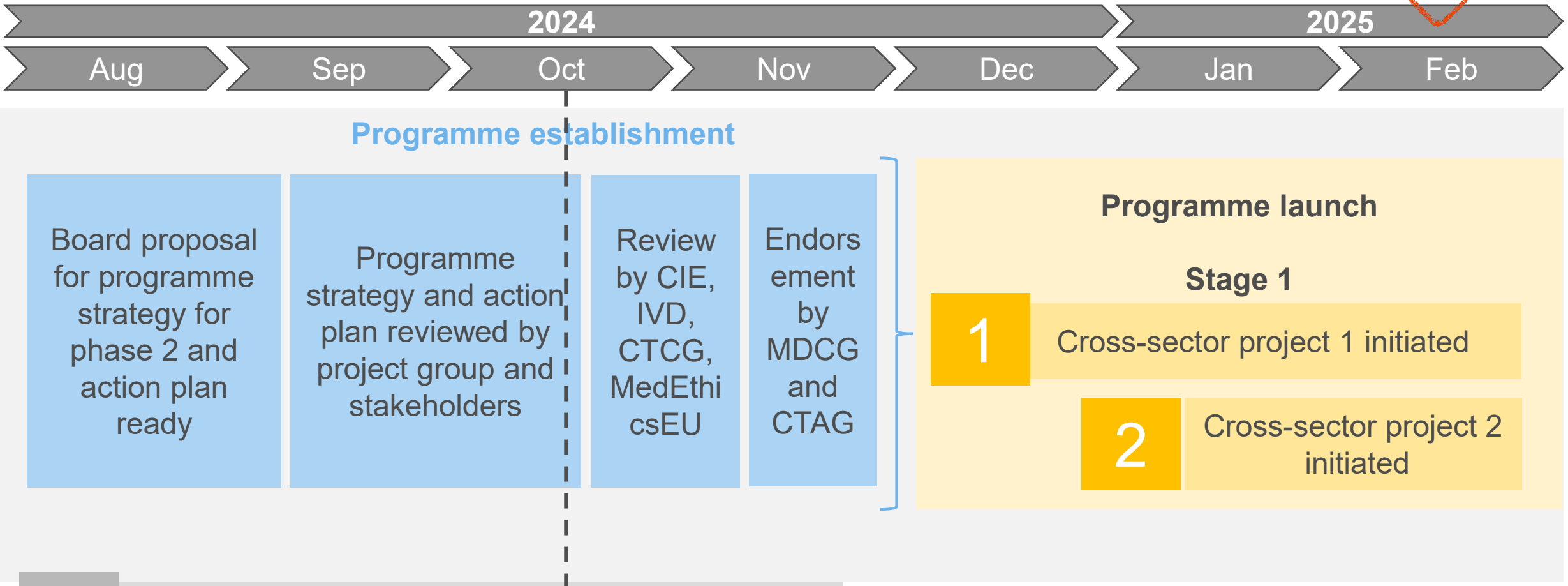

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- Information on COMBINE webpage :

Combined studies - European Commission (europa.eu)

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Thank you

Any questions?