Introduction to European HTA work and how HTAs and regulators will cooperate under the HTA Regulation

2022 annual meeting of the members and Coordinating Group of Enpr-EMA

4 October 2022

Presented by Niklas Hedberg (EUnetHTA 21) and Michael Berntgen (EMA)

Outline

1. HTA cooperation in Europe – experiences and future expectations
2. Background of the collaboration between regulators and HTAs on European level
3. Looking ahead: collaboration under the new HTA Regulation
4. Ongoing implementation activities under the joint EMA / EUnetHTA21 work plan

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European collaboration between regulators and health technology assessment bodies

Joint work plan (2021-2023) between EMA and European HTA bodies facilitated through EUnetHTA21

Introduction

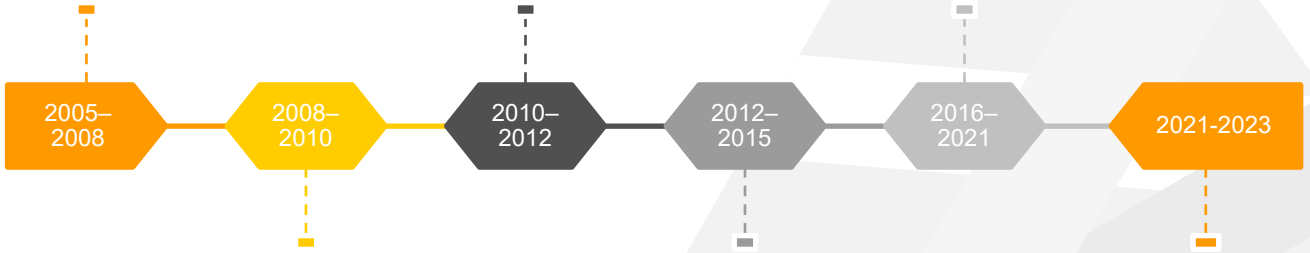
EMA and the previous European Network for Health Technology Assessment (EUnetHTA), which was established through consecutive Joint Actions of which the last one concluded in May 2021, started their collaboration in 2010 based on recommendations from the High-level Pharmaceutical Forum[1], with the aim to harness synergies between regulatory evaluation and health technology assessment (HTA) along the lifecycle of a medicine. A first EMA-EUnetHTA work plan was established for the years 2012-2015 and a report on the outcomes of this joint work published in April 2016. Subsequently, a second joint work plan for the years 2017-2021 was agreed and a report published in June 2021.

Following up on the achievements through such cooperation and the mutual trust and understanding developed through this joint technical work, EMA and EUnetHTA at their last bilateral during Joint Action 3 (minutes) agreed to establish a list of priority areas for future collaboration between regulators and HTA at European level to continue future collaborative work. The overall goal of such collaboration is to improve efficiency and quality of processes, whilst respecting the respective remits of different decision makers, and ensure mutual understanding and dialogue on evidence needs, to facilitate access to medicines for patients in the European Union.

Subsequent to the award of the "Service contract for the provision of joint Health Technology Assessment (HTA) work supporting the continuation of EU cooperation on HTA" to the EUnetHTA21 consortium, the European Commission has invited EMA and EUnetHTA21 to establish a joint work plan for delivering on the previously identified priorities. Deliverables on HTA side will either be actioned by EUnetHTA21 if related to their service contract delivery, or alternatively through individual HTA bodies from the consortium or beyond, who are from a European (EU/EEA) Member State and express interest to participate. In the latter situation, individual HTA bodies represent their own position and not the views of EUnetHTA21. In addition, all deliverables part of EUnetHTA21 will be subject to a public consultation, to which EMA is invited to participate.

EMA and the EUnetHTA21 secretariat will keep an oversight of all activities.

The **history** of EUnetHTA



A commission call is answered by 35 organisations in Europe and the EUnetHTA project begins.

EUnetHTA Joint Action 1 is launched. Their goal was to put into practice an effective and sustainable HTA collaboration in Europe that brought added value.

EUnetHTA Joint Action 3 is launched. This phase aims to define and implement a sustainable model for the scientific and technical cooperation on Health Technology Assessment (HTA) in Europe.

The **next part of the EUnetHTA project is launched** and is funded via the contribution of it's participants. They prepare a proposal for the first Joint Action

EUnetHTA Joint Action 2 is launched. The project aims to strengthen the practical application of tools and approaches to cross-border

HTA Service Contract is awarded to the EUnetHTA 21 Consortium

The Consortium is responsible for building on the work of the previous JAs

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27 Member States – 27 Pharma Systems

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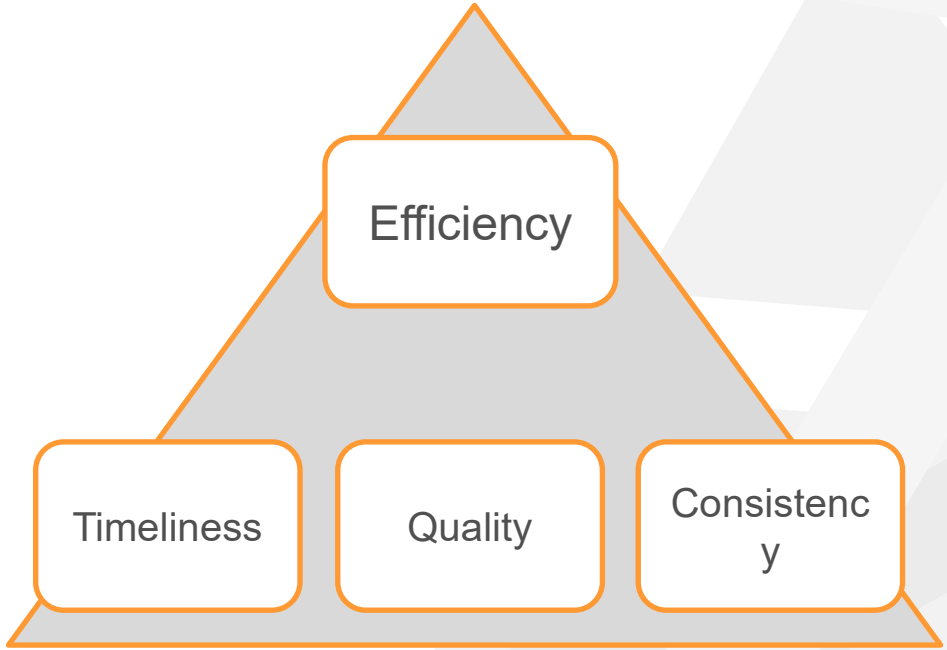
- Single licensing system
- Single EU legislation
- Well defined and agreed assessment criteria

- 27 different HTA and Pricing&Reimbursement systems
- National legislations
- Different methodologies and assessment criteria

Key benefits of collaboration on HTA



The common ground: evidence as basis for decision making

Starting point: decision makers have different objectives

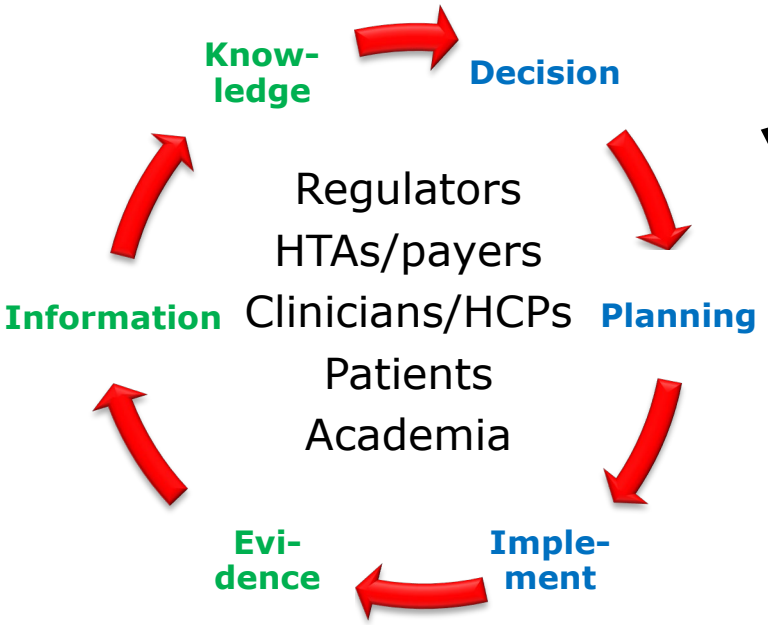
- Medicines regulators (like EMA) assess the benefit/risk of a medicinal product
- HTA bodies contextualise the use of the medicine compared to other technologies

Hypothesis: Alignment of thinking across decision makers should facilitate access → decision makers come together early to discuss

- the planned development including populations / comparators / design of trial / endpoints
- the requirements for post-licensing evidence generation

Expectation: Optimised evidence generation plan meeting the needs for different type (scope) of decision making

The (expected) value of cooperation and how it cascades



Guidelines on development

New endpoints for drug development

Learnings from decision making

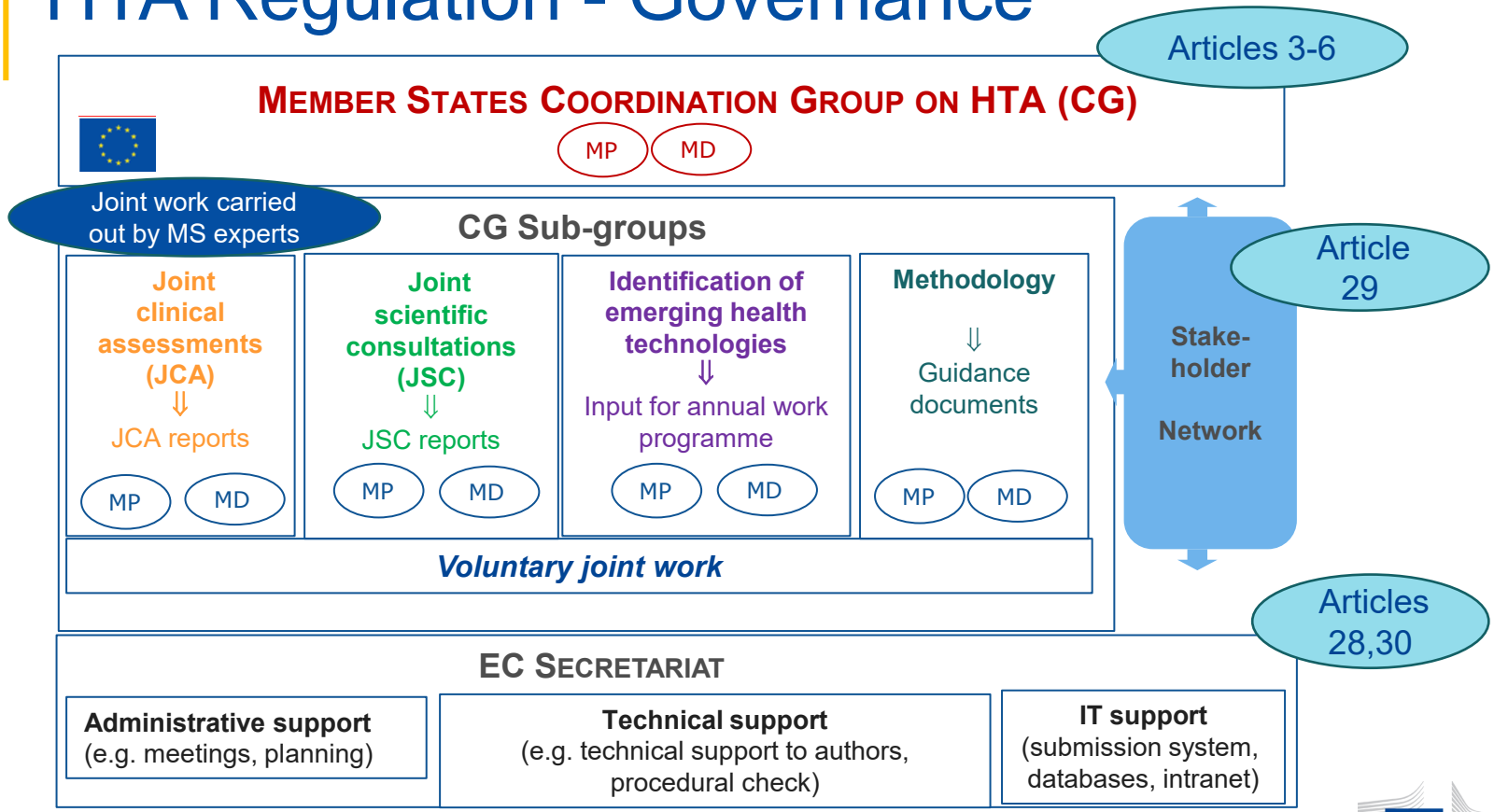
European collaboration between regulators and HTA bodies

- Since 2010, EMA and the European Network for Health Technology Assessment (EUnetHTA) have been working closely on topics of mutual interest
- The cooperation was initially facilitated through coordination of HTA bodies in EU-financed Joint Actions, and now continues under a tender for service
- The aim of this regulatory/HTA cooperation is to build synergies between regulatory evaluation and HTA along the medicine lifecycle
- The new HTA regulation in Europe recognises the value of such collaboration

Highlights of achievements under the EMA/EUnetHTA work plan 2017-2021 (report)

- Single process for Parallel Consultation, with over 60 completed procedures
- Scientific article "Regulatory and health technology assessment advice on PLEG"
- Framework for provision of the final CHMP assessment report in the context of joint REA production developed
- Article "Assessment of significant benefit for orphan medicines by European regulators may support subsequent REAs by HTAs"
- Mutual learning regarding patient engagement practices in assessment
- Joint ATMP workshop to increase mutual understanding of the regulatory process and the reimbursement landscape

HTA Regulation - Governance

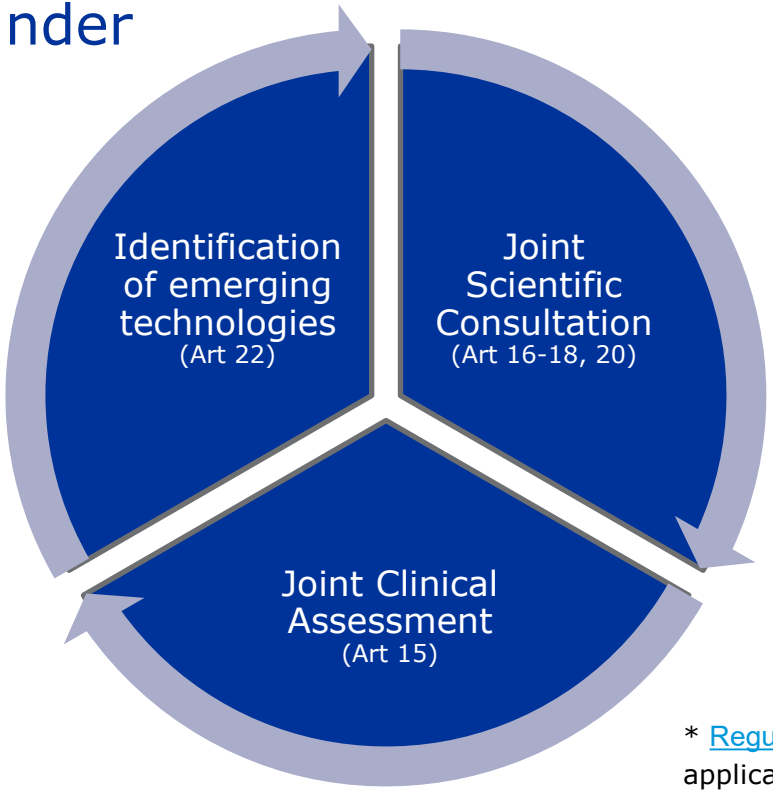


MP = medicinal products, MD = medical devices

Cooperation with EMA under the HTA Regulation*

Further details through Implementing Acts

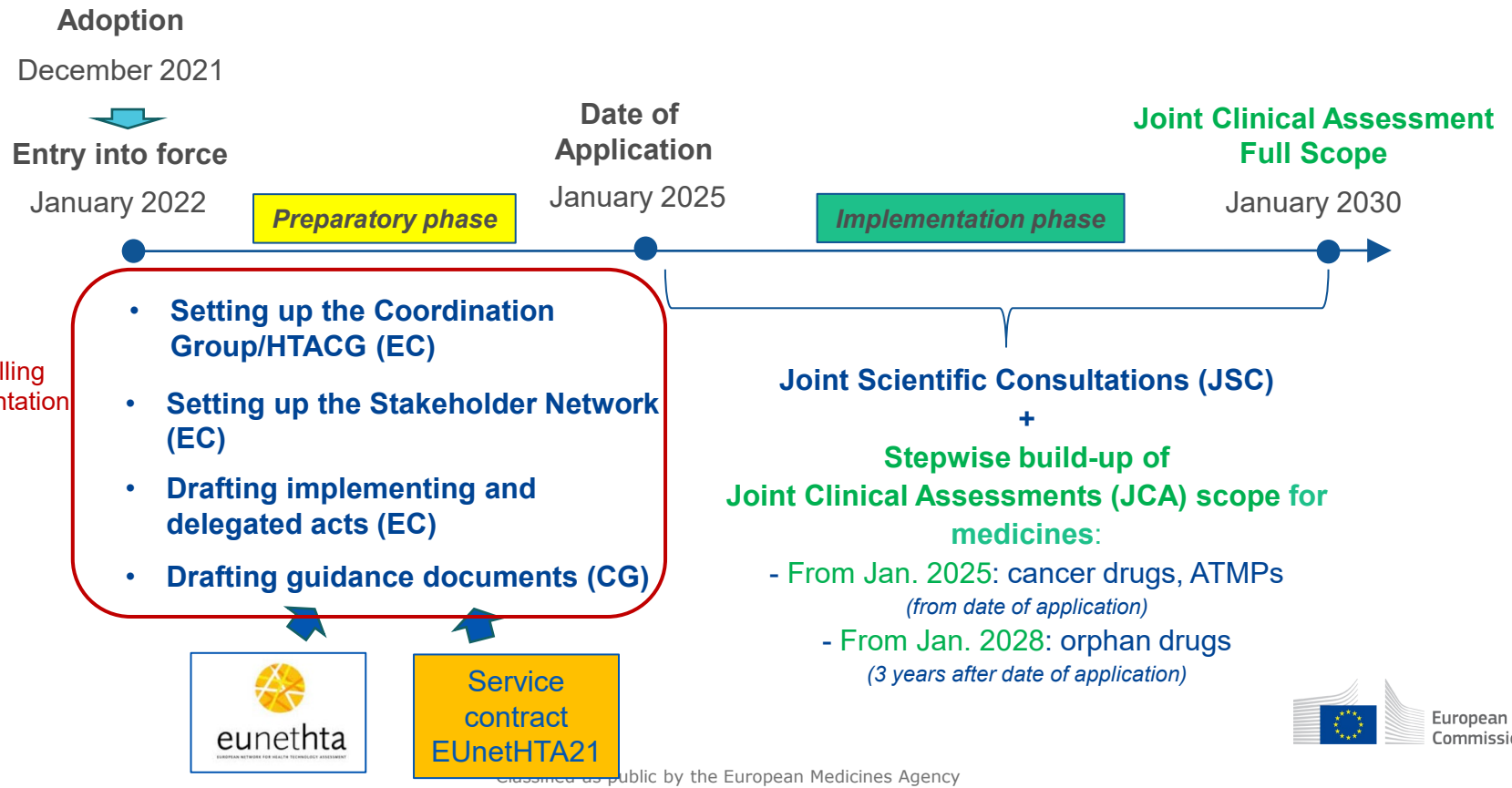
Transversal elements in the Regulation to facilitate such work, supported by the European Commission, include the sharing of confidential information



Note: "Joint" refers to collaborative work amongst HTA bodies

* Regulation (EU) 2021/2282, applicable from January 2025

HTA Regulation
Implementation timeline



Supporting the implementation work together with the EUnetHTA 21 consortium

EMA and the EUnetHTA 21 consortium set priorities for their collaboration

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News 12/04/2022

The European Medicines Agency (EMA) and the European Network for Health Technology Assessment (EUnetHTA) 21 consortium have published a joint work plan until 2023. The focus of the plan is to prepare, from a methodological and operational perspective, for the coming into application of the Regulation on Health Technology Assessment (EU) 2021/228 in January 2025 after a 3-year implementation period.

The work plan continues the close collaboration between EMA and Health Technology Assessment (HTA) bodies in Europe, which began in 2010 through consecutive EUnetHTA Joint Actions of which the last one concluded in May 2021. This collaboration has demonstrated many synergies between regulatory evaluation and HTA along the lifecycle of a medicine and aims to facilitate patients' access to medicines in the European Union.

Contribution through the joint EMA/EUnetHTA21 work plan

Joint scientific consultation on evidence generation, including PLEG Exchange of information on the respective assessments of medicinal products by regulators and HTA bodies Continuous optimisation of regulatory outputs	Study methods and guide-lines of real-world evidence, including for registries Methodologies for engage-ment of patients and HCPs Extrapolation / evidence transfer as tool to support assessment in smaller populations	Generation of patient relevant data / information to support decision making Practices in the context of companion diagnostics Horizon scanning and preparedness of HTA and regulatory systems

Potential to further improve the evidence utilisation across stakeholders

- Pre-approval joint advice procedures were successful and highly valued by all stakeholders
- Information exchange at the time of regulatory decision is coming together, yet the European Public Assessment Report can be further optimised
- Collaboration on post-licensing evidence generation requirements shows potential but needs solidifying

Jansen et al. (valueinhealthjournal.com)

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Strengthening the Interface of Evidence-Based Decision Making Across European Regulators and Health Technology Assessment Bodies

Ella Jansen, MSc, Philip A. Hines, MSc, Michael Berntgen, PhD, Angela Brand, PhD

Table 3. Pairwise comparison of clinical evidence use between 8 EPARs and corresponding rapid REAs.

	EPAR (8)	Rapid REA (8)
Active comparator used	2	6
Active comparator and placebo used	0	0
Surrogate endpoint as primary endpoint in efficacy/effectiveness domain	4	1
QOL measurement present	6	5
Perceived importance of QOL measurement	2 secondary endpoint, 5 exploratory endpoint, 1 not mentioned	6 critical endpoint, 1 secondary endpoint, 1 not mentioned
Subgroup analysis present	8	7
Discussion on reasons to include certain subgroup analyses	2 and 4 only partially	5
Assessment of risk of bias/strength of evidence reported	2	8
Requests for additional information fulfilled by the developer	7 and 1 not applicable	3

EPAR indicates European Public Assessment Report; QOL, quality of life; REA, relative effectiveness assessment.

Take home messages

- Discussions across decision-makers are crucial to better guide on **evidence requirements** throughout the medicine's lifecycle, including post-authorisation evidence
- The **HTA Regulation** will facilitate collaboration at the regulatory/HTA interface – implementation work is ongoing

  *e.g. to gain further experience with **exchange of information** between regulators and HTAs on their respective assessments and to initiate more collaboration on **methodologies** and types of evidence*
- Engagement with **stakeholders** in the context of the respective activities is a focus area of collaborative work