SEED
Shaping European Early Dialogues

SEED Consortium Final Report

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Presented by François Meyer MD

On behalf of SEED coordinating team

HAS
HAUTE AUTORITÉ DE SANTÉ

and SEED Consortium Partners

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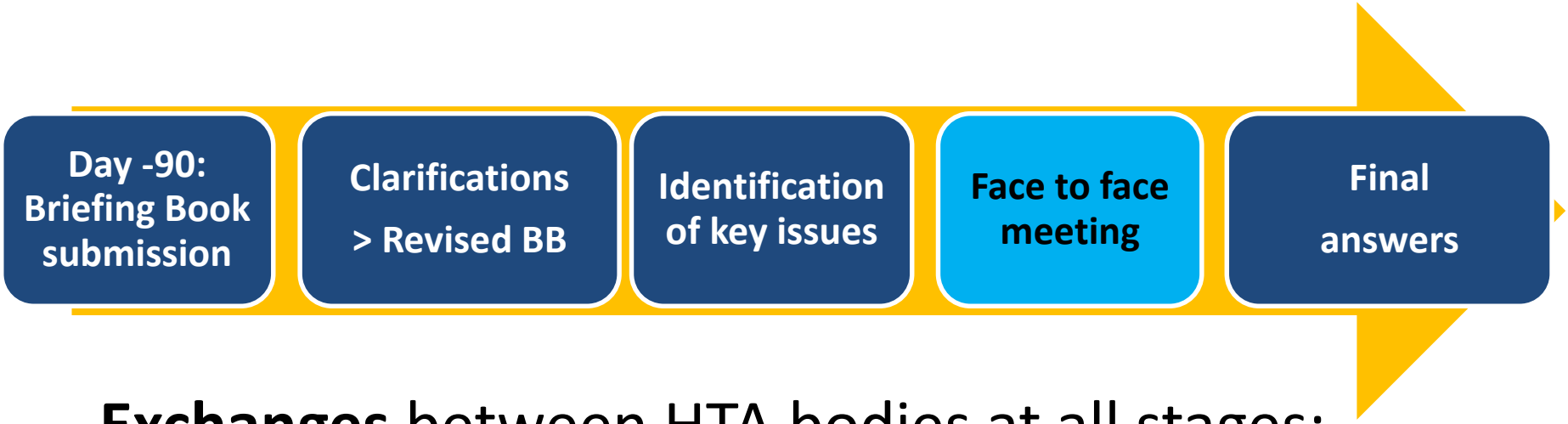
SEED PARTNERS			Number of EDs*	
			MP*	MD*
AETSA	Regional Government- Andalusian Regional Health and welfare Ministry	SP	5	0
AETS-ISCIII	Instituto de Salud Carlos III	SP	0	3
AIFA	Italian Medicines Agency	IT	4	0
ASSR	Agenzia Sanitaria e Sociale Regionale	IT	4	3
AVALIA-T	Galician Health Technology Assessment Agency	SP	7	3
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)	DE	7	2
GYEMSZI	National Institute for Quality and Organizational Development in Healthcare and Medicines	HU	3	1
HAS	Haute Autorité de Santé	FR	7	3
HIQA	Health Information and Quality Authority	IE	0	2
HVB	Hauptverband der Österreichischen Sozialversicherungsträger	AU	7	0
IQWIG	Stiftung für Qualität und Wirtschaftlichkeit im Gesundheitswesen	DE	4	2
KCE	Belgian Health Care Knowledge Centre	BE	4	2
NICE	National Institute for Health and Care Excellence	UK	7	3
ZIN	Dutch National Health Care Institute (formerly CVZ)	NL	5	3

**: Number planned. MP = medicinal products. MD = Medical Devices.*

SEED Collaborative approach



Exchanges between HTA bodies at all stages:

- To identify the need for additional **clarification** of the briefing book
- To identify **key issues** to be transmitted to the company
- To exchange written **draft positions** of each HTA body
- **Final Face-to-face exchange** among HTA bodies
- Final answers with Consortium position

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Briefing book content

- **Background information**
  - **Disease** : Overview / Relevant epidemiological data / information on natural history / Treatment options
  - **Product**: Indication / Form, route of administration, dose, dosage / Characteristics / Mechanism of action
  - Status of the **clinical development programme**/ Clinical development up to date / Planned trials
  - **Economic aspects**
  - Regulatory status of the product / Rationale for seeking advice / Discussion on added benefit
- **Questions and company's positions**
  - Clinical questions
    - Population / comparator / trial design , duration / endpoints..
  - Economic questions (if applicable)
    - Population / choice of comparator / choice of economic model /data used to populate the model / time horizon and extrapolation hypothesis / perspective (societal, healthcare related etc.) / utility values / resource utilisation data
- **Annexes**
  - Referenced articles / Trial protocols, summaries and reports / Relevant clinical practice guidelines / Previous scientific advice received

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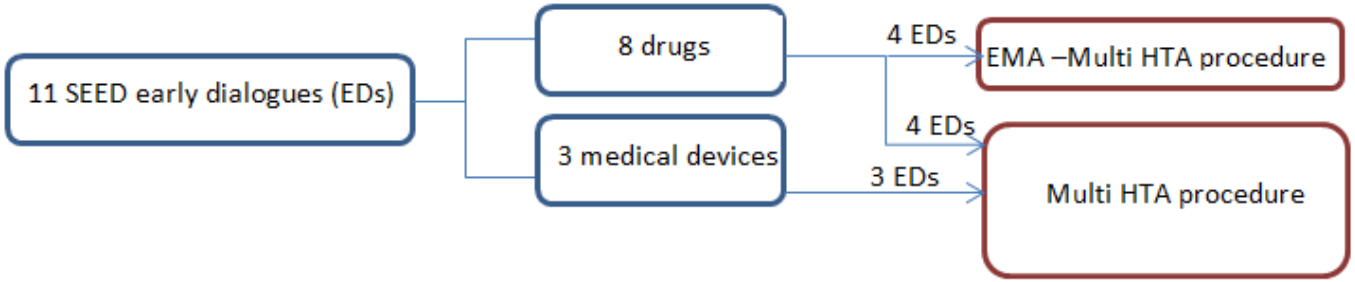
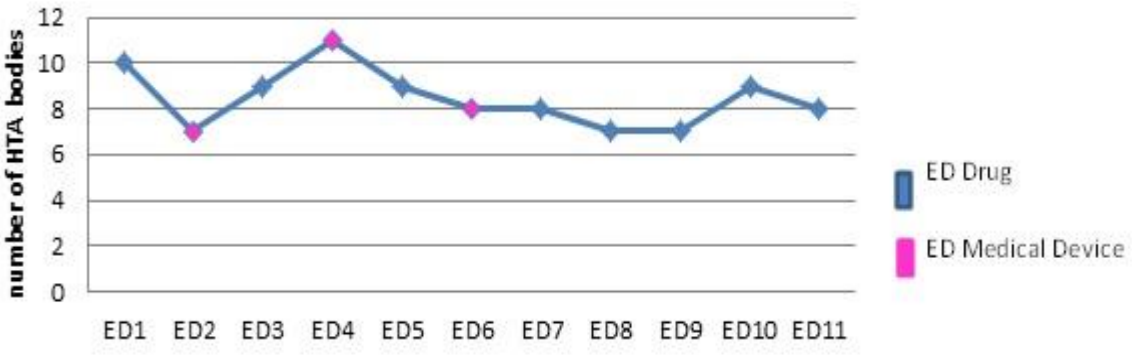
DAYS	PROCEDURE (main steps)
-90:	Company: draft briefing book (BB) ▶ HAS ▶ transmitted to all participating HTA bodies
-75	HTA bodies: written points for clarification ▶ HAS ▶ consolidated list of points for clarification to company
-60	Company: final BB ▶ HAS ▶ consolidated BB to partners involved
-30	HTA bodies: list of key issues ▶ HAS ▶ organises e-meting with all participating partners, produces a consolidated list of key issues to the company. Indicates if written answer needed before meeting.
-15	Company: responses to the key issues ▶ HAS ▶ disseminated to all partners.
-10	HTA bodies: draft written answers to company's questions ▶ HAS ▶ compiled draft document. ▶ all partners
0:	Face-to-face meeting: ⏭ Preliminary discussion among HTA bodies only ⏭ Face-to-face meeting of HTA bodies with the company ⏭ Conclusions among HTA bodies only
+10	Company: detailed minutes of the meeting ▶ HAS ▶ forwarded to the HTA bodies
+30	HTA bodies: final written answers ▶ HAS ▶ releases individual HTA positions + SEED consortium statement, to participating HTA bodies and to the company

Early Dialogues performed

- 29 requests were received, 10 for MDs and 17 for medicinal products: 9 for HTA-only EDs, 8 for parallel advice with EMA.





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EDs for medicinal products

- 8 EDs: 4 in parallel with EMA
  - 7 different companies (2 SMEs with no product on the market)
  - 1 ATMP, 6 biotherapies, 1 small molecule
  - 3 out of 8 had an indication in oncology. 3 Orphans.
  - 1 ED canceled at the request of the company. Other EDs were conducted as planned, with only minor changes.
  - HAS premises for HTA-only EDs and at the EMA premises in London for the EMA-SEED parallel EDs.
- Parallel advice with EMA:
  - No particular difficulty was faced for the conduct of the parallel EDs.
  - Previous experience of EDs involving multiple HTA bodies was useful
  - Excellent dialogue and cooperation between all actors (HTAs, Companies, EMA and SAWP members)
  - The dialogue between HTA bodies and SAWP members was considered very fruitful
  - Experience led to improvement of the SEED procedure

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EDs for medical devices

- **3 EDs** : 1implantable medical device, 1 diagnostic test , 1 MD aiming at enhancing penetration of active products in parts of the body through physical action.
- **Stage of development**: very early for one product, quite late for another. Flexibility accepted to test various cases.
- A suggestion was made by a group of companies to conduct a multi-company **ED for a new category of MDs** (each company developing its own model)
  - Limitations of the data that could be disclosed (companies = competititors)
  - should however be further explored in the future.
- In total, the diversity of the situations in the field of medical devices emphases the need for **further pilots** and for a **in-depth dialogue** with MD developers to define the best way(s) to organise EDs for MDs.
- Diagnostic tests were the type of MDs with the highest number or requests.

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Participation of patients

- EURORDIS accepted to help selecting patients and preparing their intervention

  First questions from patients when contacted by Eurordis
  - Who's EURORDIS? Why are you contacting me and not HTA bodies?
  - What's HTA?
  - What's SEED?
  - What's EMA?
- Each meeting represents ~ 4 work-days for Eurordis
- 5 patients need to be contacted, for 2 to be invited
- Preparation of the participation of Patients : E-meeting with the patients to read the briefing book
  - Key for patients to be well prepared
  - But takes time (2x2 hours minimum)
  - Briefing book: 50 to 80 technical pages, was received late by patients

(Adapted from EURORDIS comments)

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Some issues: training

- EUPATI and other initiatives to train patients on HTA
  - Hundreds of patients trained already
- Yet, in most cases patients invited to SEED/EMA Early Dialogues will not have been trained
  - Training must be ad hoc, few days before the meeting
  - Need for training materials, e-learning, webinars, videos
- Patients may find it intimidating or difficult to express themselves
  - Meeting very “intense”. “Take the floor as soon as you can”
  - Chair could ask for their input more pro-actively
  - Some express a high degree of frustration
    - “not having the opportunity to express my thoughts”
    - or being told “this is not what we expect from you”

(Adapted from EURORDIS comments)

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Going forward: recommendations

Conflicts of interests

- Potential for financial or intellectual conflicts of interests (CI) are part of the public debate
- The prevention, identification and management of CIs should be taken into full consideration for the conduct of EDs.
- It should be acknowledged that the situation currently differs across participating public bodies with regard to the preventive measures to be taken.
- Full harmonization of the processes ?
- *Full transparency and an open dialogue including public consultation should be guaranteed when deciding on the* ***rules of procedures*** *and* ***codes of conducts*** *of future multi-HTA collaborative EDs.*

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Coordination between international Multi-HTA and National Single-HTA Advice

- Offering the possibility of EDs at 2 levels (national/regional and international) provides a welcome flexibility.
- Coherence and consistency should however been ensured.
- *Codes of conducts/rules of procedures for future multi-HTA early dialogues should be transparent with regard to the relationship between multi-HTA and single-HTA ED.*

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Participants in EDs

- HTA bodies
  - Adequate expertise necessary.
    May be more difficult in small agencies.
    Proposal: develop dedicated expertise in small or medium-size agencies.
  - Number of HTA bodies per Member State ?
    Coordination will be needed at national level.
- Regulators
  - Drugs: *The EMA rather than national regulatory bodies*
  - MDs: ?
- Health Professionals:
  - *The conditions for participation of external experts (health professionals, methodologists, health economists, others) should be determined*
  - *The process and procedure for their participation should be developed and made more transparent for future permanent multi-HTA EDs.*

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Strengthening Organization and Value of Multi-HTA EDs

- **Standing Committee:**
  - Aim: optimising the process in terms of scientific value and organisation
  - *Proposal: to gather agencies having both experience and available resources as the "core" permanent members of multi-HTA EDs.*
  - This group will be joined by a number of other HTA bodies having expertise in the concerned therapeutic area.
- **Improving collaborative aspects:**
  - Exchanges among HTA bodies should be reinforced.
  - *In the final document, "consortium statement" to be developed, individual HTA bodies specific answers being limited to justified specific positions*
- **Coordination:**
  - *Organisational coordination: For reasons of efficacy, practical coordination should be put in one single institution, with one unique contact-point.*
  - *Scientific coordination could be rotating between voluntary HTA bodies*
  - *Particular responsibilities could be granted to HTA bodies, such as defining best ways to recruit experts, patients, improvement of the final outcomes of the EDs.*

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Funding

- SEED and EUnetHTA EDs were publicly funded, with no fees to be paid by companies.
- Alternative sources of funding have to be put in place.
- The fee-for-service approach seems appropriate
- Possible difficulties in organizing it from legal and practical points of view.
- *An institution with legal and organisational capacity to collect fees from industry and redistribute it to participating HTA bodies is to be identified.*
- *This question will have to be looked at as rapidly as possible after the start of EUnetHTA JA3, in order to put in place a new financing system not later that two years after the start of this JA.*
- *Fee waivers or reduction in some cases (SMEs) have to be considered.*

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EMA-HTA and EMA-SEED parallel advice

	EMA HTA PARALLEL ADVICE	SEED EMA EARLY DIALOGUES
Choice of HTA bodies involved	Up to the company	Decided by SEED partners
Recruitment of participating HTA bodies	By the company	SEED coordinator
Coordination role among HTA bodies	No	Yes
Fees for HTA bodies	For some HTA bodies.	No fees
Exchanges between HTA bodies	Limited	Developed
Final outcome	Sum of individual HTA bodies position	Compilation of HTA answers with an effort to reach consensus when possible

Toward a single EMA-HTA parallel procedure for ED/SA?

Currently 2 procedures for HTA-EMA parallel EDs coexist : EMA-HTA parallel advice and SEED-HTA parallel dialogues

- *Take full advantage of EMA and SEED experiences and merge the two procedures.*
- *EMA and EUnetHTA, together with involved stakeholders and in cooperation with the European Commission should make proposals for having these two processes merged.*
- *Next future: start of the JA3.*
  - *First two years: EUnetHTA funded EDs will persist*
  - *For debate: possibility during this phase of mixed recruitment (i.e. through EUnetHTA for some HTA bodies and according to the current EMA-HTA parallel advice procedure for additional HTA bodies)*

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Thank you for your attention

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