Spitzenverband

Draft Report on the proposal for a regulation of the European Parliament and the Council on health technology assessment and amending Directive 2011/24/EU, 4.5.2018 [2018/0018(COD)]
European Parliament, Committee on Environment, Public Health and Food Safety
Rapporteur: Soledad Cabezón Ruiz

1) Reflections on the Draft Report

The Draft Report adjusts the COM proposal for a regulation on HTA into the right direction, focusing on the further development of EU cooperation between national HTA bodies and leaving the national HC systems more leeway for integrating joint outcomes into their procedures. From the perspective of the German Health Insurance Funds the following impulses in the Draft Report are especially welcome and should be supported:

- Amendments 89-92: MS institutions will have more freedom in using the joint assessment reports in their respective health technology assessments. While MS shall not duplicate the work done at EU level, they are not prevented from carrying out their own assessments as part of their own appraisal processes.
- Am. 95: Updates of joint clinical assessments shall not only be performed upon request or due to conditional approval but regularly after five years.
- Am. 133, 134: The obligation of MS to use harmonised rules for their own assessment is being relaxed slightly. It must be clarified, however, that HTA institutions will be able to use the methodology needed in their HC system context.
- Am. 51, 84, 145, 163: It is coherent to focus the influence of the COM within the Coordination Group and on the assessment process, as the goal is to strengthen the cooperation between HTA bodies. No voting rights are foreseen for COM in the Coordination Group. Furthermore, less regulatory power is being delegated to the COM.

- Am. 49, 55, 78: The Coordination Group will take its decisions on a two thirds majority basis if not by consensus. This decision making method is necessary to build trust and prevent outcomes at the expense of individual HC systems. However, even if it is "one member state, one vote" it may be necessary that MS send more than one representative into the Coordination Group.
- Am. 139: The Coordination Group will also draw up the methodology to be used for clinical assessments and consultations.
- Am. 57, 76, 160: The highest possible level of transparency throughout the entire EU cooperation on HTA is being welcomed. This will be achieved by making public the work and decisions of the Coordination Group, comments of stakeholders as well as giving full public access to all the information contained in the IT platform.

Further amendments will be needed regarding

- referring to evidence based medicine in the rules for preparing joint assessment reports,
- sanctions in the case of failure of a developer to deliver all the information needed, and
- information that is to be transmitted by the developer for the assessment process.

2) **Proposals for amendments:**

Amendment 49

Proposal for a regulation
Article 3 – paragraph 2

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
2. Member States shall designate ***their*** national ***authorities and bodies*** responsible for health technology assessment as ***members*** of the Coordination Group and its sub-groups ***and inform the Commission thereof and of any subsequent changes. Member States may designate more than one authority or body responsible for health technology assessment as members of the Coordination Group and one or more of its sub-groups.***	2. Member States shall designate ***one*** national ***or regional*** authority or body responsible for health technology assessment as ***a member*** of the Coordination Group and its sub-groups.	2. Member States shall designate ~~one~~ national **or regional** **authorities** or **bodies** responsible for health technology assessment as ~~a~~ **members** of the Coordination Group and its sub-groups.
Justification: Member States need to be able to designate more than one body. Healthcare systems may be organised regionally and HTA split between different bodies in one member State.		

Amendment 68

Proposal for a regulation
Article 6 – paragraph 2

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
2. The designated sub-group shall request relevant health technology developers to submit documentation containing the information, data and ***evidence*** necessary for the joint clinical assessment.	2. The designated sub-group shall request the health technology developer to submit ***all available up-to-date*** documentation containing the information, data and ***studies*** necessary for the joint clinical assessment. ***That documentation shall include the available data from all tests performed and from all the studies in which the technology was used, both being of paramount importance in ensuring that assessments are of high quality. However, assessors can access public databases and sources of clinical information. The reproducibility of the assessment implies that such information has to be public.***	2. The designated sub-group shall request the health technology developer to submit all available up-to-date documentation **as specified in Annex I** containing the information, data and studies necessary for the joint clinical assessment. That documentation shall include the available data from all tests performed and from all the studies in which the technology was used, both being of paramount importance in ensuring that assessments are of high quality. However, assessors can access public databases and sources of clinical information. The reproducibility of the assessment implies that such information has to be public.
Justification: Annex I specifies the information that is to be provided by the developer.		

Amendment 71

Proposal for a regulation
Article 6 – paragraph 5 – point a

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
(a) an analysis of the relative ***effects*** of the health technology being assessed ***on the patient-relevant health outcomes*** chosen for the assessment;	(a) an analysis of the relative ***efficacy and safety*** of the health technology being assessed ***in terms of the clinical criteria relevant to the clinical entity and patient group*** chosen for the assessment;	(a) an analysis of the relative efficacy and safety of the health technology being assessed **on the patient-relevant health outcomes** ~~in terms of the clinical criteria relevant to the clinical entity and patient group~~ chosen for the assessment, **which adheres to the international standards of evidence based medicine**;
Justification: The assessment must focus on patient-relevant health outcomes. Surrogates can only be accepted in exceptional cases and if validated through scientifically validated criteria. Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available evidence from systematic research. As such it is internationally recognised and its standards should be enshrined in the European HTA regulation.		

Amendment 74

Proposal for a regulation
Article 6 – paragraph 8

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
8. The assessor shall provide the draft joint clinical assessment report and the summary report to the ***submitting*** health technology developer ***and set a time-frame in which the developer may submit*** comments.	8. The assessor shall provide the draft joint clinical assessment report and the summary report to the health technology developer ***for*** comments.	8. The assessor shall provide the draft joint clinical assessment report and the summary report to the submitting health technology developer and set a time-frame **with a maximum of 14 days** in which the developer may submit comments.
Justification: As the developer did already provide the assessors with all information available to him at the beginning of the process, it should be ensured that any further clock stop of the clinical assessment remains reasonably short and should not lead to inappropriate delay. It is of uttermost importance to guarantee complete transparency on the involvement of the developer, which highlights the importance of the corresponding changes in Art. 6 paragraph 10.		

Amendment 75

Proposal for a regulation
Article 6 – paragraph 9

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
9. ***The designated sub-group shall ensure that stakeholders***, ***including patients*** and clinical experts***, are given an opportunity to provide*** comments during the ***preparation of the draft*** joint clinical assessment ***report and the summary report and set a time-frame in which they may submit comments***.	9. ***Patients, consumer organisations***, ***healthcare professionals*** and clinical experts ***may submit*** comments during the joint clinical assessment.	**The assessor shall provide the draft joint clinical assessment report and the summary report to stakeholders, including patients and clinical experts and set a time-frame with a maximum of 14 days in which the stakeholders may submit comments.**
Justification: List of stakeholder should not exclude other interest groups, e.g. payers' organisation. To guarantee the necessary transparency and independence of the assessment, all stakeholders should be subject to similar rules regarding submission of comments.		

Amendment 87

Proposal for a regulation
Article 7 – paragraph 5

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
5. If the Commission concludes that the modified approved joint ***clinical*** assessment report and summary report do not comply with the ***substantive and*** procedural requirements laid down in this Regulation, ***it shall decline to include*** the ***name*** of the ***health technology*** in the List. The Commission shall inform the Coordination Group thereof, setting out the reasons for the ***non-inclusion***. The obligations laid down in Article 8 shall not apply with respect to the health technology concerned. The Coordination Group shall inform the submitting health technology developer accordingly and include summary information on those reports in its annual report.	5. If the Commission concludes that the modified approved joint assessment report and summary report do not comply with the procedural requirements laid down in this Regulation, ***the health technology which is*** the ***subject*** of the ***assessment shall be included*** in the List***, together with the summary report of the assessment and the Commission's comments, and all published on the IT platform referred to in Article 27***. The Commission shall inform the Coordination Group thereof, setting out the reasons for the ***negative report***. The obligations laid down in Article 8 shall not apply with respect to the health technology concerned. The Coordination Group shall inform the submitting health technology developer accordingly and include summary information on those reports in its	5. If the Commission concludes that the modified approved joint assessment report and summary report do not comply with the procedural requirements laid down in this Regulation, the health technology which is the subject of the assessment shall be included in the List, together with the summary report of the assessment and the Commission's comments, and all published on the IT platform referred to in Article 27. The Commission shall inform the Coordination Group thereof, setting out the reasons for the ~~negative report~~ **determined noncompliance with procedural requirements**. The obligations laid down in Article 8 shall not apply with respect to the health technology concerned. The Coordination Group shall inform the submitting health technology developer accordingly and in-

	annual report.	clude summary information on those re- ports in its annual report.
Justification: Clarification.		

Amendment 96

Proposal for a regulation
Article 9 – paragraph 1 – subparagraph 1 (new)

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
	In the cases referred to under points (a) and (b), the technology developer shall submit the additional information. In the event of a failure to do so, the earlier joint assessment would no longer fall within the scope of Article 8.	In the cases referred to under points (a) and (b), the technology developer shall submit the additional information. In the event of a failure to do so, the **sanctions mechanism according to Article 22 (1) b applies.**
Justification: Sanctions must be deterrent.		

Amendment 108

Proposal for a regulation
Article 13 – paragraph 8

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
8. ***The designated sub-group shall ensure that stakeholders***, ***including patients*** and clinical experts ***are given an opportunity to provide*** comments during the ***preparation of the draft*** joint scientific consultation ***report and set a time-frame in which they may submit comments***.	8. ***Patients, consumer organisations***, ***healthcare professionals*** and clinical experts ***shall submit*** comments during the joint scientific consultation.	**No change to COM proposal.**
Justification: List of stakeholder should not exclude other interest groups, e.g. payers' organisation. COM proposal is clear about the procedure and should be kept.		

Amendment 133

Proposal for a regulation
Article 20 – paragraph 1 – point b

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
b) clinical assessments of medicinal products and medical devices ***carried out by Member States***.	b) clinical assessments of medicinal products and medical devices ***falling within the scope of this Regulation and not included in the annual work programme***.	**Point b is deleted.**
Justification: Clinical assessments carried out by Member States should be flexible to meet national healthcare systems' needs. The proposed regulation results in a higher hurdle to adapt HTA to national necessities for products that (although eligible) were not chosen for a joint assessment than for products that underwent a joint assessment.		

Amendment 139

Proposal for a regulation
Article 22 – paragraph 1 a (new)

Text proposed by the Commission	*Amendment by Rapporteur*	*New Amendment*
	(1a) The coordination group shall draw up the methodologies to be used to carry out joint clinical assessments and consultations and shall define the content of these assessments and consultations. In any case: ***(a) the methodologies shall be based on high standards of quality, the best available scientific evidence, stemming primarily from double-blind randomised clinical trials, meta-analysis and systematic reviews;*** ***(b) the assessment of relative effectiveness shall be based on end-points which are relevant to the patient with useful, relevant, tangible and specific criteria suited to the clinical situation concerned;*** ***c) the comparators shall be the reference comparators for the clinical entity concerned and be the best and/or most commonly used technological or process based comparator;*** ***d) the technology developers shall for the***	(1a) The coordination group shall draw up the methodologies to be used to carry out joint clinical assessments and consultations and shall define the content of these assessments and consultations. In any case: (a) the methodologies shall be based on high standards of quality, the best available scientific evidence, stemming primarily from double-blind randomised clinical trials, meta-analysis and systematic reviews; (b) the assessment of relative effectiveness shall be based on end-points **according to international standards of evidence based medicine** which are relevant to the patient with useful, relevant, tangible and specific criteria suited to the clinical situation concerned **and shall display the specific outcomes for different subgroups**; c) the comparators shall be the reference comparators for the clinical entity concerned and be the best and/or most com-

	purpose of its clinical assessment provide the coordination group with the complete dossier in eCTD format submitted to the European Medicines Agency for centralised authorisation. This package shall include the Clinical Study Report and the data of individual patients in all clinical trials; ***e) the information to be provided by the health technology developer shall relate to the most up-to-date and public research. Failure to comply with this requirement may trigger a sanctions mechanism.***	monly used technological or process based comparator; d) the technology developers shall for the purpose of its clinical assessment provide the coordination group with the complete dossier in eCTD format submitted to the European Medicines Agency for centralised authorisation. This package shall include the Clinical Study Report and the data of individual patients in all clinical trials; e) the information to be provided by the health technology developer shall relate to the most up-to-date and public research. Failure to comply with this requirement may trigger a sanctions mechanism.
Justification: It's important to refer to the internationals standards of evidence based medicines within a regulation on HTA; in addition, assessments need to be fit for purpose, taking into account differences within the more general authorised populations.		

Amendment 172 (new)

Proposal for a regulation
Article 22 – paragraph 1 a (new)

New Amendment
Annex I **Content of the submission informing the assessment of relative effectiveness of a health technology** **Introduction and General Principles** The particulars and documents constituting a submission for an assessment of relative effectiveness shall be provided in accordance with the requirements below. In assembling the submission file for a relative effectiveness assessment the applicants shall take into account the corresponding submission templates published by the Commission. All information which is relevant to the assessment of the health technology concerned shall be included in the submission file, whether favourable or unfavourable to the health technology. All methods used to generate the submission shall be described in sufficiently precise detail so as to be assessable with regard to scientific appropriateness and validity. All methods used shall correspond to the state of scientific progress at the time. **Part 1 Summary of the Dossier** Administrative information identifying the responsible developer of the technology and a comprehensive summary of the information

supplied in parts 2, 3 and 4.

Part 2 Characteristics of the Health Technology under Assessment

Features of the technology

General information on the technology, such as its characteristics and mode of action.

Regulatory status of the health technology

The current EU regulatory status, with relevant dates (date of approval) and type of regulatory procedure shall be described.

Therapeutic indication under assessment

The therapeutic indication(s) under assessment shall be described.

Further therapeutic indications approved in the EU

Further therapeutic indication(s) in the EU shall be described.

Requirements for use of the technology

If any special conditions for use of the health technology are part of the regulatory authorisation (e.g. relating to settings for use or restrictions on professionals who can use or may prescribe the technology), these shall be described.

Part 3 Characteristics of the Health Problem

Overview of the disease or health condition

The disease/condition for which the health technology is indicated shall be described briefly.

Target population (including prevalence and incidence)

The patient population covered by the approved indication shall be described specifically.

The prevalence and incidence of the disease/condition for which the health technology is indicated shall be described and an estimate of the size of the patient population in the Member States shall be provided. The submission shall address possible differences in prevalence and incidence between Member States.

Diagnosis

The requirements for diagnosis of the health problem shall be described briefly. If a companion diagnostic is required for use of the health technology under assessment, this shall be characterised.

Treatment strategies (across disease stages)

The current clinical pathway and treatment options of the disease/condition for which the health technology under assessment is indicated shall be described. The submission shall address possible differences in clinical pathways and treatment options in the Member States.

Comparators used in the assessment

The comparator(s) used in the assessment shall be described.

Part 4 Documentation of Effects for Benefits and Harms versus Comparator(s)

General requirements

The particulars and documents constituting a submission for an assessment of relative effectiveness shall be provided in accordance with the requirements below. The submission must enable a sufficiently well-founded and scientifically valid opinion to be formed as to which effects the health technology under assessment provides in relation to relevant comparator(s).

The submission shall include the results of comparisons of the health technology under assessment versus one or more relevant com-

parator(s). The relevant comparator(s) shall be defined by the Member States.

The assessment must be based on the complete relevant data set. The compilation of this data set and the data set itself shall be described transparently in the submission file. If a data set is incomplete with regard to a research question of the assessment, no conclusions on relative effectiveness of the health technology shall be drawn for this research question.

The submission shall also include the assessment reports prepared by the regulatory authorities (Rapporteurs' Day 150 and Day 180 Joint Response Assessment Reports, the European Public Assessment Report (EPAR) or the CHMP Assessment Report if the EPAR is not yet available).

Systematic review of available studies

The assessment shall be based on a systematic review of the studies performed with the health technology under assessment and relevant comparator(s).

The developer of the technology must provide information (a list of studies, study protocols and study reports) on all studies performed with the health technology under assessment which were sponsored or otherwise supported by the MAH. In addition, relevant studies shall be identified by systematic searches of bibliographic databases, study registries, websites of regulatory agencies and other relevant data sources. The selection of studies for inclusion in the assessment shall be presented transparently and exclusions of studies shall be justified.

Presentation of results

The particulars of each study must contain sufficient detail to allow an objective judgement to be made:

- detailed description of planned and conducted study procedures and analyses

- summary results characterising the relevant patient population for the assessment
- summary results on study outcomes addressing the research question of the relative effectiveness assessment
- the corresponding source documentation: the Clinical Study Reports (according to ICH E3) including appendices (appendices covering personal data, e.g. data on investigators, do not need to be submitted); a documentation to a comparable level of detail for studies for which no Clinical Study Report is available

The study results shall be presented for each study individually and combined using suitable statistical methods, as appropriate.

Any secondary analyses based on primary studies shall be presented to the same level of detail.

Effects for benefits and harms versus comparator(s)

Patient population

The patient population included in the assessment shall represent the patient population for which the health technology under assessment is authorised. The patient population shall be characterised. In addition, relevant subpopulations shall be covered by the assessment, as appropriate. If part of the authorised patient population is not covered by the available studies, this shall be described.

Intervention

The intervention included in the assessment shall correspond to the authorised application. The intervention shall be characterised.

Comparators

The comparator(s) included in the assessment shall meet the requirements of the Member States. The Member States shall define the relevant comparator(s) ahead of the assessment.

Outcomes

The assessment shall be conducted according to the standards of evidence-based medicine. It shall be based on patient-relevant endpoints. The assessment shall describe the effect sizes for endpoints describing added benefits and harms and the certainty of the effects of the health technology under assessment versus the comparator(s). The assessment shall include the effects in relevant patient subpopulations, as appropriate, to investigate possible differences in outcomes for patients.
Justification: A clear set of requirements is needed. It is up to the coordination group to regulate the details within the framework set by the regulation.