Department of Political Sciences

Chair of Health Care Policy

Proposal for a Regulation of the European Parliament and of the Council on the Health Technology Assessment and amending Directive 2011/24/EU: stakeholders' qualitative analysis.

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INTRODUCTION

Health Technology Assessment is defined

«*a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective health policies that are patient focused and seek to achieve best value*»[1]».

An example of health technologies includes medical products, medical equipment, diagnostic and treatment methods, rehabilitation, and prevention methods. In recent years, Health Technology Assessment have increasingly been performed by European countries. EU-level collaboration on HTA has been ongoing for years, in the form of a number of projects as well as Joint Actions. It was one of the areas for the future collaboration for which the Cross-Border Healthcare Directive (Directive 2011/24/EU) created a legal basis through Article 15. However, the wide variety of procedures and methodologies, among Member States, results in significant differences in how data and evidence are assessed. Thus, in its 2017 working programme, the European Commission announced that it would introduce

[1] EUnetHTA Joint Action definition.

an initiative on strengthening EU cooperation on HTA in order to improve the functioning of the single market for health products. The Commission's proposal was adopted on 31 January 2018 and has been sent to the Council and the European Parliament for their consideration under the ordinary legislative procedure. In the preparation of this proposal an extensive consultation with stakeholders has been made. In order to reach all interested stakeholders and to ensure a high quality and balance input a combination of consultation methods was used. However, after the proposal's publication there were divergent opinion among stakeholders.

The aim of this dissertation is to give an overview of the current European Commission proposal for a Regulation on Health Technology Assessment, with a specific focus on the Stakeholders' Network through a qualitative analysis.

The thesis is divided in four parts, and its aim is to understand which the stakeholders' position on this proposal are, as well as the main concerns which might have influenced the drafting of the legal text. The first part will be an overview of the several interpretations given by analysts and researches over the years on this topic. Starting with the numerous definitions of health technology assessment, it will be described its origins and development in different countries, moving from the first assessment degree in 1972 in US to the European scenario with Sweden, Netherlands, France, Germany, UK and Italy. Remaining at European level, in second chapter there will be an historical overview of the EU cooperation on HTA, from the first project (1993), the EUR-ASSESS, to the third one, the EUnetHTA Joint Action 2016-2020. This part will be essential in order to understand the main reasons beyond the initiative on strengthening EU cooperation on HTA, explained in the third chapter together with the legal proposal. Before moving to the stokeholds' analysis. The purpose of these chapters is to give a background with an open-mind attitude in order to understand the main differences among the interested parties.

Finally, the last chapter is the heart of this thesis as it focuses on the stakeholders' qualitative analysis. With the aim of making clear their position on this proposal in the preparatory phase and in the post adoption, it will be used a computer software QRS named "NVivo". It is the most advance computer tool for qualitative analysis and it helps to systematically record and to organize data. The version used in this thesis is "NVivo 12". The fourth chapter is structured in five parts. While in the first part the methodology used in the analysis will be explained, the others four paragraphs focus on each stakeholder's category: health providers, patients and consumers, payers and industry. For each of them there will be the description of their position on the pre-adoption and post-adoption phases as well as the main findings emerged from the "NVivo 12" (analytical method/computer software nive/ tool ect), through the use of the "Word Frequency Criteria".

FRIST CHAPTER

HEALTH TECHNOLOGY ASSESSMENT:

FUNDAMENTAL CONCEPTS

1.1 From Technology Assessment to Health Technology Assessment

In the last five decades, technology innovation has yielded truly remarkable advance in the health care. Technological innovation has taken a strategic role in transforming the economy of industrialized countries from manufacturing economy into service economy.

Its introduction in the health sector will lead to a higher operating cost. However, rather than costs, it should be a strategic investment to an overall improvement of the system, in medium and long run.

Before giving a comprehensive definition of Health Technology Assessment, it is important mention the several interpretations given by analysts and researches over the years. First of all, the term "Assessment" is referring to any process of analysis, which underline the characteristics of specific technology. These

characteristics can be related to safety, efficacy, flexibility, cost-benefits relation, and they may cover social, ethic and economic aspects.

Furthermore, as D. Banta explained, technology can be defined as "the systematic application or other organised knowledge to practical task"[2], emphasising the pervasiveness and the heterogeneity of this phenomenon.

This focus on technology innovation is also present in the healthcare service sector, as the implementation of new technologies can offer a better level of diagnosis, treatment and of better effectiveness[3]. By definition health technology "is the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and system developed to solve a health problem and improve quality of life[4]". Therefore, it is possible say that health technology is the application of knowledge to improve and maintains individual or population health. Thus, a cardiac monitor, for example, is a technology, and at the same time, an intensive care unit – one of its component parts being the monitor- is it also a technology.

The healthcare technology concept is kind of open to interpretation. The Office of Technology Assessment (OTA) include in the definition given by the World Health Organization, also intangible elements, such as a system of support and organization under which health care is provided[5].

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[2] Banta, David. *"The development of health technology assessment*". Health policy 63.2.121-132. (2003).

[3] Effectiveness in this context means the success of the medical service and consequently complete satisfaction and well-being of the patient. It is important make a difference between efficacy, that is, the ability to achieve the desired results, and effectiveness the ability to achieve the excepted results under real conditions in the given time.

[4] http://www.who.int/en/

[5] Cicchetti, A., and M. Marchetti. *"Manuale di Health Technology Assessment."* Il Pensiero Scientifico Editore (2010).

However, the definition given by OTA is in contrast with the one given by CIVAB[6], which does not consider the medical products as elements that could be correlated to health technology.

Goodman[7] sums up the notion of health technology with twofold interpretations. The first one refers to its physical nature: drugs; biologic; devices, equipment and supplies; medical and surgical procedures; public health programs; support system and organizational and managerial system.

While with the second interpretation technologies can also be grouped according to their healthcare purposes, such as prevention, screening, diagnosis, treatment, rehabilitation and palliation[8].

Another interpretation, categorised health technologies on the stage of diffusion.

- *Future* that is the earliest stage of development or the conceptual stage;
- *Experimental*, the undergoing bench or laboratory experiments using animal;
- *Investigational* as the undergoing initial clinical evaluation of a particular condition;
- *Established* when a particular health technology is diffused into general use;
- *Obsolete/outmoded/abandoned* when it is suspended by other technologies or demonstrated to be infective[9].

Therefore, it is also interesting to mention a particular case study conducted by Mikhail and his team, at the end of 90's. They made the so-called "technology spectrum" to classify health technologies. The technology spectrum is a useful construct to position a technology in terms of its "evolution" or "life cycle" and to

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[6] Centro informazione valutazione apparecchiature biomediche di Trieste – Ministero della Sanità.

[7] Goodman, C. *"HTA 101: Introduction to health technology assessment."* US National Library of Medicine, National Institutes of Health, National Information Centre on Health Services Research and Health Care Technology (NICHSR). (2004).

[8] Ibidem

[9] Ibidem

characterize its rate of development. In positioning a technology on the spectrum, the focus is not only on where the technology happens to be at a given point in time, but also on how quickly the technology is moving along the spectrum[10].

Moreover, as it is possible see in the Figure 1.1, with this method the life cycle of technology is divided in five phases:

1. *Virtual edge*: refers to technologies that are still in the conceptual phase.

2. *Cutting edge*: refers to technologies that are experimental or those that are just emerging from the realm of basic research into the very beginning of applied research.

3. *Leading edge*: technology is within the realm of applied (medical) research, while emerging with limited viability in clinical practice. Its cost-effectiveness and role in clinical practice is not yet fully established.

4. *Standard edge*: the technologies becomes broadly demonstrated with routine, with sufficient evidence of proven cost-effectiveness for reimbursement.

5. *Trailing edge*: when a new standard of are emerges, the old technology transitions into this phase. It is use is limited to setting that ten to lag behind standards of care clinical practice.

[10] Mikhail, O., Swint, J. M., Brinker, M. R., Moye, L. A., & Sabino, M. *"Technology evolution: the technology spectrum and its application to orthopaedic technologies."* International journal of technology assessment in health care.15(1), 254-263. (1999).

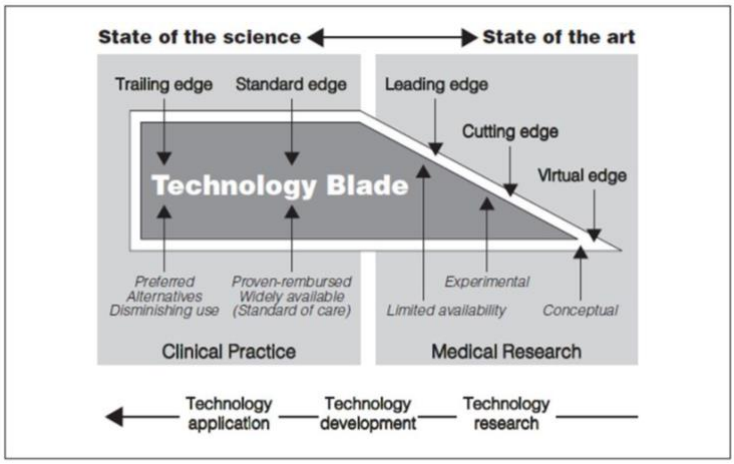

Figure 1.1 Technology Spectrum[11]

All these categorisations are not strict. For example, vaccines are biologists that are used in immunization programs, and screening test for pathogens in donated blood is used by blood banks. Moreover, the different stages of diffusion are not clearly defined, and technologies do not develop through them in a linear fashion. Many technologies undergo multiple incremental innovations after their initial acceptance into general practice or technology that was once considered obsolete may return to established use for a better-define or entirely different clinical purpose[12].

The adoption of new biomedical technology in the healthcare system is the result of a long process based on the interaction between the three following elements and their associated "initial role": universities engaging in basis research, industries producing commercial goods and governments that are regulating markets. This interaction is known as "Triple Helix of innovation model"[13] and it

[11] Mikhail, O., Swint, J. M., Brinker, M. R., Moye, L. A., & Sabino, M. *"Technology evolution: the technology spectrum and its application to orthopaedic technologies."* International journal of technology assessment in health care.15(1), 254-263. (1999).

[12]Goodman, C. *"HTA 101: Introduction to health technology assessment."* US National Library of Medicine, National Institutes of Health, National Information Centre on Health Services Research and Health Care Technology (NICHSR). (2004).

[13]Etzkowitz, H., & Leydesdorff, L. *"The dynamics of innovation: from National Systems and "Mode 2" to a Triple Helix of university–industry–government relations*". Research policy, 29(2), 109-123. (2000).

is the key to innovation susses in biomedical field. According to Etzkwitz and Leydesdorff[14], a scientific research becomes a good innovation, when the industry can identify and finance it in an early stage. At the same time the public institutions, through specific policies, should boost the interaction between research and industry. Nevertheless, in the biomedical sector the institution has a double role: on one hand they encourage the innovation – as in the Triple Helix model- but on the other hand they regulate and assess new technologies.

In the healthcare system the innovation has to be safe, it has to make an advantage in terms of healthcare and at the same time it has to be cost effective[15].

However, in the biomedical sector, according to Cicchetti[16], the innovative process is the synthesis of three processes: innovative, regulative, and innovative.

The first process which concerns the innovation leads to the creation of a new solution through the combination of different assets: intellectual, relational, and financial[17]. This process is complex due to the involvement and the interaction of several actors, such as researches, doctors, patients, and technology manufacturers. Moreover, this process is a cyclical due to the ongoing interaction of main actors and it is subject to technical and regulatory risks[18].

The second process is the regulative and its aim is to assess the safety and the marginal utility of new product than other already in the system.

Furthermore, there is the assessment process which is managed by specific agency which decides on principles and tools of the Health Technology Assessment[19]. In this step should be stressed, that the advantage of new technologies in the health

[14] Ibidem

[15] Cicchetti, A., and M. Marchetti. "Manuale di Health Technology Assessment." Il Pensiero Scientifico Editore (2010).

[16] Ibidem

[17] Ibidem

[18] Ibidem

[19] Cicchetti, A., and M. Marchetti. *"Manuale di Health Technology Assessment."*, cit (LO HAI GI° CITATO).

care fields has, unfortunately, been accompanied by an increase in costs, as a consequence of scarce resources in nature. For this reason, more and more information is requested to sustain decision on development, adoption, acquisition and the use of new technologies: the Health Technology Assessment (HTA) served this purpose.

1.2 Health Technology Assessment

Over the years, there have been several definitions of Health Technology Assessment and all emphasize its role, as tool supporting decision making at different level of the healthcare system, its multidisciplinary nature, and its strong reliance on transparent scientific rigours methods[20].

Therefore, it is a process that takes advantages of and adopts both the techniques of research, that are strictly scientific and the managerial ones, focusing more on the decision-making analysis and creating a link between the scientific model

[20] WHO Definition (EB 134/30): " Health technology assessment is the systematic evaluation of properties, effects and/or impacts of health technologies and interventions. It covers both the direct, intended consequences of technologies and interventions and their indirect, unintended consequences. The approach is used to inform policy and decision-making in health care, especially on how best to allocate limited funds to health interventions and technologies. The assessment is conducted by interdisciplinary groups using explicit analytical frameworks, drawing on clinical, epidemiological, health economic and other information and methodologies. It may be applied to interventions, such as including a new medicine into a reimbursement scheme, rolling-out broad public health programmes (such as immunization or screening for cancer), priority setting in health care, identifying health interventions that produce the greatest health gain and offer value for money, setting prices for medicines and other technologies based on their cost–effectiveness, and formulating clinical guidelines."
EUnetHTA definition " Health technology assessment is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective, health policies that are patient focused and seek to achieve best value"

oriented on the performance analysis technology and decision-making activities (policy paradigm) aimed at evaluating the effective and efficient use of resources[21].

Thus, researches who deal with "assessment", differently from other health sectors, are concerned with producing information that can direct decision makers towards health care policy choices that comply with the optimal allocation of resources.

However, one of the best explanations of the role of HTA has been given by Battista and Hodge in 1995 as a bridge between research and decision-making[22]. Fig.1.2 illustrates the close relation between HTA and policy-making ad depicts the interdependence and separation between research-based assessment and decision-making. A successful process from a policy question to an HTA report that informs policy will span paradigms in a conscious and transparent way.

[21] Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessment*." Springer. (2014)

[22]Nolte, E., & Knai, C. "*Managing chronic conditions: experience in eight countries"* (No. 15). WHO Regional Office Europe. (2008).

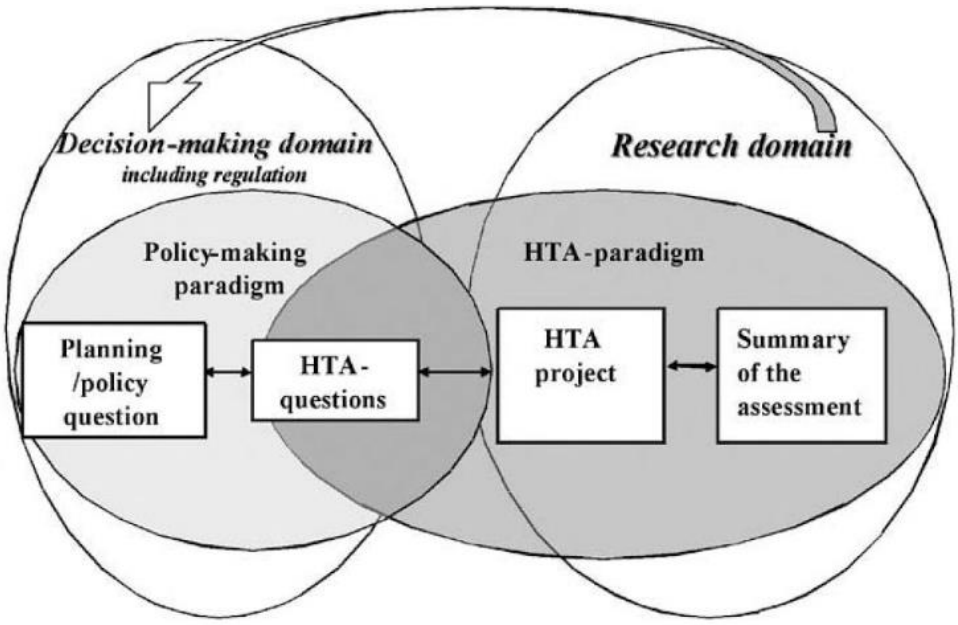

Figure 1.2: relation between HTA and policy-making[23]

From all these definitions examined it is possible underline the main characteristics of HTA. Frist of all its multidisciplinary and multidimensionality. In fact, this explain all the possible impacts and consequences that the adopted technology can have on Hospital-Based level as well as on patients. Matching different levels, the HTA creates an assessment process, involving several actors with heterogeneous expertise.

Therefore, when a new technology has to be evaluated to access into the market, the main dimensions that the assessor should take into account are: clinical safety, efficacy, the economic impact, organizational aspects as well as socials, legal, ethic and politics. Moreover, for having a comprehensive study of HTA, expertise from different field, such as doctors, economists, biomedical engineering, pharmacist, lawyers, and sociologists, are grouping in team. In this way the HTA can give to the policy makers, a comprehensive overview.

[23] Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessment*." Springer.(2014)

1.3. Evidence Based Medicine

Health technology assessment needs to be understood in the context of evidence-based health delivery and policy, which calls for decision making in the healthcare sector and beyond to be based on a systematic analysis of scientific evidence of the effects of interventions. Health technology assessment parallels and overlaps with evidence-based medicine (EBM)[24]. While EBM tries to integrate individual clinical expertise with the best available external clinical evidence from systematic research[25] HTA incorporates the aims of EBM and refers to systematic research with broader goals: to offer guidance to decision making at all levels (including health policies at a macro level) and to assess interventions from a larger societal perspective to include economic, social, ethical, and organizational impacts. Health technology assessment is also indebted to the Cochrane Collaboration (CC) and the development of methods to summarize scientific evidence. The CC is a large international network of scientists who critically review health intervention literature with the goal of improving health policy and practice. CC can be considered a main facilitator to bridge scientific evidence with decision makers. It is clear that "HTA, EBM, and the CC are natural allies, albeit with somewhat different foci"[26]. The CC works to summarize evidence, the EBM movement works to use scientific evidence to improve medical and healthcare practice, and HTA encompasses the scope of the analysis to offer guidance for health policy. Despite these different foci, there is an overlap between the three. 'Together, they are beginning to lead to significant changes in how policy and practice decisions are made.'[27]

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[24] Fattore, G., Nikos M., Lorenzo G., and Boriani. L. *"Health technology assessment: what is it? Current status and perspectives in the field of electrophysiology." Europace* 13, no. suppl_2 (2011).

[25] Gray J. *"Evidence Based Health Care."* New York: Churchill Livingston; (1997).

[26] Banta, D. "*The development of health technology assessment*". Health policy 63.2.121-132. (2003).

[27] Ibidem

Hence, scientific evidence justifies political decisions on a more neutral and non-ideological ground and it takes centre stage in the decision-making process.

1.3.1 Basic HTA Orientations

In the 1970s, the approach used was mainly *technology-oriented assessment,* in which the principal goal was assess the safety and the efficacy of technology and then establish all the possible impacts that the application of that technology could have on clinical, procedural, and professional level. For example, a government agency may want to determine the clinical, economic, social, professional, or other impacts of cochlear implants, cervical cancer screening or widespread adoption of electronic health record system.

Since the '90, however, there was a shift to *problem-oriented approach* where the economical, ethical, and social dimension was replacing the main point of the previous approach, such as safety and efficacy. During these years, the economic weight that a specific technology could have been became essential to considered, and for this reason team of people with different competence started to analyse different variable[28]. At the beginning of 2000 there was the need to introduce different technologies also in a restricted reality, such as hospitals or ASL. It was important, the adaptation of the problem-oriented approach and its dimension to the small reality, shifting into a *project-oriented approach.*

Notwithstanding, the evolution of the assessment orientation it is also possible say that these basic assessment orientations can also overlap and complement one another. In fact, for example, the information used in a project-oriented assessment by a particular hospital may include findings of pertinent technology- and problem-oriented assessment, local data collection and analysis may be required

[28] Lorusso S., "*Health Technology Assessment come strumento di supporto al managment: aspetti cognitivi e metodologici*, Mecosan," Vol. 53. (2005).

to determine what is appropriate for that hospital. Thus, many HTAs will blend aspects of all three basic orientations.

1.3.2 The pillars of Health Technology Assessment

There are different points of view regarding the number of the pillars in HTA. Cicchetti and M. Marchetti[29] to define the main characteristic of the HTA approach, they taken into account the summary that where included in The Trento Charter, in which is analysed the principles of health technology assessment highlighting: who does what, where, when, why and how.

The evaluation of health technologies should involve all the parties interested in health care (who) must take care of all elements that resort to health care assistance (what) and all levels of health systems and structure management that are part of it (where) must be an ongoing activity, carried out prior to the introduction of technologies and persisting through its cycle (when), it is a necessity and an opportunity for the integrated governance of health care systems and structures that they are part of (why) it is a multidisciplinary process that should be conducted in a consistent manner with other welfare and technical-administrative processes of health systems and structures that they are part of (How).

1.3.3 HTA and Decision-Making Process

Define problems and find the most appropriate solutions for achieving long-term goals is often a difficult experience, in particular in health care. The discomfort related to sharing is even more evident in this field due to the different cultures involved characterized by considerable autonomy that affects every collaborative situation. An example of problems of integration between different cultures are found where examining the collaboration between technicians and mangers in

[29] Cicchetti, A., and M. Marchetti. *"Manuale di Health Technology Assessment."* Il Pensiero Scientifico Editore (2010).

healthcare organizations, when, for fear of losing autonomy, some request from the other party are practically not implemented[30]. Nowadays the collaboration between engineers and managers within an HTA program is of fundamental importance, in particular considering HTA as a bridge between science and politics.

All of this is strictly connected to a decision making-processes, which act as operational mechanism and are characterized by information input from a system of choices and an output of actions and information.

The level of HTA is directly proportionate to the dimensions of decision-making space, because "the effect of the evaluation process on the decision- making function is greater if the decision-making space available is large"[31]. This means that the information useful for all decision-making process is produced through HTA.

Health technology Assessment process consist of several steps, liked to each other.

The first step of the process is the identification and explanation of clinical needs [32]. In this phase a key role is playing by medial, which are in close contact with patients, and for this reason they perceive better the need of the community.

The second phase is clinical applicability that is; a macro-analysis designed to identify potential technological solutions, compare them, and identify, the optimal

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[30] Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessmen"t*. Springer. (2014).

[31] Ibidem

[32] In the context of this clinical need, the potential to improve the benefits must be represented by three factors:

a) Potential relative to the impouvement of health care outcomes
b) Potential for reducing costs
c) C9 potential relative, to the simplification of the healthcare service supply process.

Briganti, Ferrara, Salvatore *Temi emergenti negli studi di organizzazione sanitaria,* 2011, G. Giappichelli, cap. VIII.

technology area, if there is one[33]. In fact, in this phase there is a selection of the potential new alternative technologies in order to transfer the clinical needs into operating parameters.

The third step is concerned with the evaluation of the alternatives in the technology field identified in the clinical applicability analysis. It is a very sensitive stage, in which the process is very empirical: it requires accurate assessment to be carry out under standard operating conditions.

The fourth phase is the approval by the authority. However, in this point most of the initiatives are blocked due to the difficulties that arise. In this case the multi-professional team have to develop an appropriate implementation plan in order to introduce the technology.

Lastly there is a follow-up phase in which the team, that deals with the technology assessment, observes the introduction of the technology and tries to resolve problem, when are observed[34].

Following this process, HTA performs a function of "organizer" as it identifies the lines of action to achieve goals as effectively as possible. There are, three main aspect that characterize HTA:

1. Identification of different alternatives possible;
2. Evaluation of the pro and cons of the alternatives considered;
3. Evaluation and comparison of expected results and objectives

[33] Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessmen"t*. Springer. (2014).

[34]Briganti, P., Ferrara, M., Salvatore D.."*Temi emergenti negli studi di organizzazione sanitaria",* G. Giappichelli, cap. VIII. (2011).

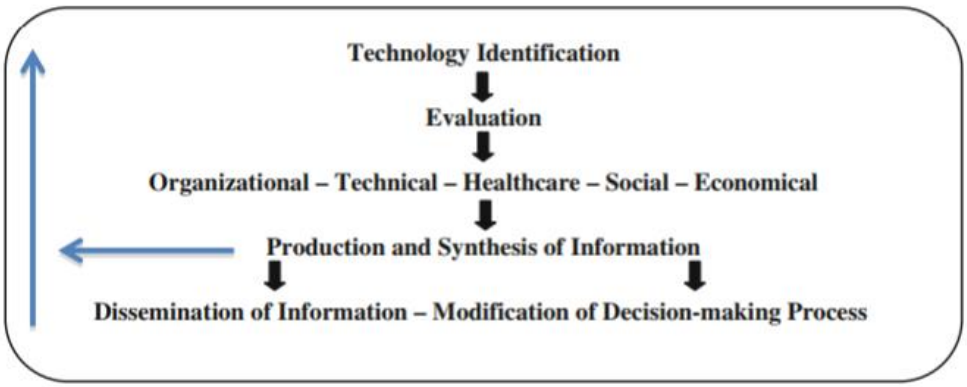

Figure 1.3 Bureaucratic process of HTA[35].

1.3.4 The implementation of HTA Process

There are three main levels of development and dissemination of HTA process (Fig1.4):

- **Macro,** in which HTA supports policy making and the research for appropriateness of clinical practice, serving as a bridge that connects science and research to centralized decision making;
- **Meso** that is also the level represented by individual companies that provide welfare services. In this level HTA support managerial decision-making research of efficient and effectiveness when providing healthcare services, in order to reduce the high variability of clinical practice and organizational innovation at processes, technology and infrastructure level;
- **Micro** or the level of clinical practice. In this level there is the interaction between medical, practitioners and patients.

[35] Briganti, P., Ferrara, M., Salvatore D..“*Temi emergenti negli studi di organizzazione sanitaria”,* G. Giappichelli, cap. VIII. (2011)

Figure 1.4 HTA and decision-making levels[36]

Moreover, each level is characterized by the working of different actors:

- National Government (Macro);
- Regions and Hospitals' outpatient (Meso);
- Practitioners and scientific societies (Micro).

1.4 Origins and Development

The aging population, the expanding use and the number of new and expensive technologies have contributed to burgeoning health care cost. In this purpose several counties have implemented health technology assessment as a means of informing the decision process basic on clinical and economic evidence[37].

The first assessment decree[38] was issued in the USA, in 1972, with which the Office of technology Assessment was established (OTA) to develop and demonstrate how much the HTA is usefulness to the political representatives[39].

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[36] Cicchetti, A., and M. Marchetti. *"Manuale di Health Technology Assessment."* Il Pensiero Scientifico Editore (2010).

[37]Kanavos, P., Nicod, E., Van Den Aardweg, S., & Pomedli, S. "*The impact of health technology assessments: an international comparison."* (2010).

[38] Public Law 92-484

[39]Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessmen"t*. Springer. (2014

In the European scenario, the importance of assessment started to be understood about a decade later respect to the USA, when the WHO (World Health Organization), within the program "Health for Hall", suggest that European states identify a formal mechanism for an efficient assessment of the use of medical technologies to determine their effectiveness, efficiency, safety and acceptability[40].

The response of the governments was to introduce policy to control the spread of technologies with the logic of cost containment. This first phase did not produce significant results in term of technology management, while allowed the introduction of economic assessment methods and in the particular the concept of cost-effectiveness in health care. In particular, as Archie Cochrane stated, selecting a technology based on effectiveness[41] is also a way of allocating resources efficiently[42]. In that period born the Cochrane Collaboration[43] with the aim of systematically recording and updating a database of experimental clinical studies (trials) and systematic reviews based on them, in support of empirical evidence.

Most of HTA agencies were born between 80s and 90s, and consist of technical structures, financed through public resources, that issue government authority.

The first national HTA agency was founded in Sweden in 1987 establishing the Swedish HTA Council (SBU) due to the high expenditure for health care, the visibility of new technologies, and the necessity to begin to rationalise health care

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[40]Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessmen"t.* Springer. (2014).

[41] Ability to benefits from the patient

[42]Cochrane, A. L. Archie Cochrane in his own words: Selections arranged from his 1972 introduction to "*effectiveness and efficiency: Random reflections on the health services".* Controlled clinical trials, 10(4), 428-433. (1989).

Kanavos, P., Nicod, E., Van Den Aardweg, S., & Pomedli, S. "*The impact of health technology assessments: an international comparison."* (2010).

[43] The first centre opened in the United Kingdom and since than the collaboration has grown into venture of about 15 centres in some 12 counties.

technology[44]. In 1997 Sweden was followed by Denmark with the "*Danish Institute for Health technology Assessment"* (DIHTA). The aim of these organizations is the promotion and dissemination of HTA information and the promotion and the use of health care resources, thought the evaluation of clinical, economic and ethical issues related to the use of new and well-established technologies[45].

Other than Sweden and Denmark, also Holland, France, and Spain are considered to be the cradle of HTA. In particular, in Netherlands, the process of planning and remuneration of activities take place on the bases of HTA activities in both public and private sector. In fact, in 1988 the Sickness Funds Council, with the collaboration of the Ministries of Health and education and Science agreed to setting up of a National Fund for Medical Research which became the national HTA program[46]. The fund covers technology assessment activities and the analysis of the main health care policy issues. Furthermore, in 1998 on request of the Ministry of Health, a national core was created for the coordination of HTA activities in Netherlands[47].

In France, in 1989 an independent association, ANDEM, was establish by law, commissioned to conduct HTA programs, with an impact on public health care, that did not involve drugs. However, the greatest propagation of HTA came in 1996 after the health care reform, when it was decided to replace the ANDEM with ANAES[48] in which the fundamental innovations represented by the agency's involvement in the process of hospital accreditation[49]. Therefore, ANAES is nowadays personally involved in all decision-making: health structure

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[44]Banta, D. "*The development of health technology assessment*". Health policy 63.2.121-132. (2003).

[45] Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessmen"t*. Springer. (2014).

[46] Banta, D. "*The development of health technology assessment*". Health policy 63.2.121-132. (2003)

[47] Ibidem

[48] *Agence National d'Accreditation et d'Evaluation en Santé*

[49] Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessmen"t*. Springer. (2014).

accreditation, processing of refund fees for outpatient services, and the planning of investments in technology.

Another country with growing HTA interest is Germany[50]. The idea of using the HTA also in healthcare system arose in the mid-90s, with a research program founded by BMG. Following the results of this project, in 1969 was founded the HTA reference point in Germany: DIMDI (Deutshe Institut fur Medizinische Dokumentation und In-formation). It is responsible for implementing and managing an information system of health care-economic evaluations on medical records and technologies[51]. DIMDI is involved in other initiative, such as the creation of the "German Working Group of Technology Assessment in Health Care" that has implemented a series of HTA studies on different technologies.

On the same line of Germany, it is possible find the UK, thanks to the birth of NICE (National Institute for Clinical excellence), founded in 1999. At international level, NICE is an innovative experiment. In fact, it is the first national agency capable of producing analysis and guideline covering the entire spectrum of health care technologies[52]. In preparing the assessment NICE take into account the aspect of both clinical effectiveness and cost-effectiveness of the new technologies, which are selected[53] by two authorities, such as The Department of Health and the National Assembly for Wale.

In Italy, the main concepts of HTA were cast for the first time, within the Italian Network of Health Technology Assessment born in 2003 as a research project titled "promotion of network for dissemination of Health Technology Assessment

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[50] Fricke, F. U., & Dauben, H. P. *"Health technology assessment: a perspective from Germany."* Value in Health, *12*, S20-S27.(2009)

[51]Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessment*." Springer. (2014).

[52]Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessment*." Springer. (2014).

[53] On the basis of four criteria: possible clinical benefits, involvement in specific health care policy, programmes, the possible impact on NHS resources, possible added value produced by NICE guidelines.

for the management of information technology within healthcare organization. The aim of this project was to bring together the Italian NHS companies with HTA experience, in order to promote a sample model for technology assessment to sustain managerial decision, thus favouring the extension of HTA knowledge[54].

HTA is mentioned for the first time at national policy document in the 2006-2006 National Healthcare Plan: "…It is necessary for HTA to be recognized as a priority also in Italy, as it is necessary to promote the use of HTA tools, gathering all knowledge on the subject, some of which already exists in a number of regions and Trusts..."

Following this statement, the Standing Conference between State, regions, and autonomous provinces gave the National Agency for Regional Healthcare Services (AGENAS) the task of supporting the regions for the development of current HTA, in connection to the national Ministry of Health[55].

AGENAS started the production of HTA report for the General Directorate of Medical Devices of the Ministry, through an ad hoc working group. In September 2008, AGENAS began a project to create a monitoring system of emerging technologies, link with the European project EUROSCAN. With COTE[56] project it is possible mobilise a national "alert" network that involves regions, university and scientific bodies[57]. Additionally, a great step was made by the so called "Green paper on the future of welfare", published by the national Ministry of Welfare,

[54]Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessment*." Springer. (2014).

[55]Favaretti, C., Cicchetti, A., Guarrera, G., Marchetti, M., & Ricciardi, W. "*Health technology assessment in Italy*." International Journal of Technology Assessment in Health Care, 25(S1), 127-133. (2009)

[56] Observation Center for Emerging Biomedical Technologies

[57]Cicchetti, A. and M. Marchetti. "*Manuale di Health Technology Assessment*." Il Pensiero Scientifico Editore (2010).

giving the possibility that HTA process will further institutionalize itself in a model comparable to those in other countries[58].

However, HTA is a broad concept with many facets and vague boarders and it differs from country to country, both in its foci and methods. As Banta wrote[59] a considerable part of these differences in HTA by countries has depended on the interests of particular societal groups, stakeholders. Hence, differences hamper HTA development internationally. An HTA might be a technical evaluation of medical device done for regulatory purposes; it could be a prospective academic study of the health consequences of particular health care practice or it could be a systematic review of any all aspects of a particular healthcare practice carry out by an HTA agency. So, this diversity has strengths, but it also makes generalisation difficult and certainly hampers change[60].

[58] "The process HTA allows rational and economic programming when distributing equipment, according to appropriate catchment areas, avoiding waste of human and material resources and to induce new questions"

[59] Banta, D. "*The development of health technology assessment*". Health policy 63.2.121-132. (2003)

[60] Ibidem

SECOND CHAPTER

EU COOPERATION ON HEALTH TECHNOLOGY ASSESSMENT

2.1 The European Union health policy

Since the establishment of the first national HTA agency in Sweden in the 1980s, the number of the institution involved in the assessment of health technologies has multiplied within the member states of the European Union. Some of them have also been institutionalized within the country's health system.

During the years the European Union and the European Commission have gradually become more active in health care. Initially, health policy was so high

in the political agendas that most of the governments did not want the union interfering in it. Notwithstanding, in 1991 the Health Ministers have asked the European Commission for help in dealing with strategic issues[61] that affect all Europeans. One of these issues was "value for money in health care". In the same year the Health Ministries identified HTA as a key tool to improve the management of scarce resources. For the first time, in 1992 with the Maastricht Treaty, the public health was included as a task of the European Commission, including a special section to regulate the public health (TITLE X). According to the treaty, the EU has a mandate of "encouraging cooperation between member states" and "if necessary, leading support to their actions" in public health (article 129(1))[62]. Moreover, the EU was given the power to spend money on European level health projects but forbidden to pass laws harmonising health measures in the member states (article 129 (4))[63]. Therefore, this article reflects the complex drafting, in which the issue with EU powers on health has been striking a balance potential common interest in working on health and the high degree of national sensitivity and specify about health matters.

The mandate was significantly strengthened in the Amsterdam Treaty, in which the EU's powers over the health policy was revised. In fact, according with article

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[61] Cranovsky, R., Matillon, Y., & Banta, "*D.EUR-ASSESS Project Subgroup Report on Coverage.*" International Journal of Technology Assessment in Health Care, *13*(2), 287-332. (1997).

[62]The Conmunity shall contribute towards ensuring a high level of human health protection by encouraging cooperation between the Mernber States and, if necessary, lending support to their action.

Community action shall be directed towards the prevention of diseases, in particular the major health scourges, including drug dependence, by promoting research into their causes and their transmission, as well as health information and education. Health protection requirements shall form a constituent part of the Community's other policies.

[63] In order to contribute to the achievement of the objectives referred to in this Article, the Council:

- acting in accordance with the procedure refenced to in Article 189b, after consulting the Economic and Social Committee and the Committee of the Regions, shall adopt incentive measures, excluding any harmonization of the laws and regulations of the Member States;

- setting by a qualified majority on a proposal from the Commission, shall adopt recommendations.

152 of the European Community Treaty, the EU was ruled to ensure "a high level of human health protection" in the "definition and implementation of all [union] policies and activities" and to work with member states to improve public health, prevent illness and "obviate sources of danger to human health". None the less, as defined in paragraph 4 and 5 of article 152, harmonization of member states' public health legislation, with two small exceptions, continued to be prohibited and the EU was mandate to "fully respect" the member states' responsibilities for "the organization and delivery of health services and medical care".

In 1999 the then president of the European Commission, Romano Prodi decided to create a directorate general for health and consumers protection: giving a new profile to EU health policy[64].

Moreover, the real division of competencies is summarized at the start of the TFEU which came into force in 2009. The only relevant are of shared competence between the EU and the Member states is *«common safety concerns in public health matters[65]»*; for the wider objective of the «*protection and improvement of human health[66]»*, the EU may only *«support, coordinate or supplement»* Member Sates' action[67]. It is also important underline that the art 168 of the TFEU is not an article on health, but on public health. This was deliberate attempt by the drafters to align EU action towards population-level measures and away from action on health service. Moreover, the powers given to the EU to achieve these public health objectives are very limited. Indeed, the only area where binding legislation is provided covers concerns of quality and safety standards for substances of human origin, blood and blood derivates[68].

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[64] Duncan B. *"Health policy in the European Union: how it's made and how to influence it."* BMJ : British Medical Journal. 1027-1030. (2002)

[65] TFEU; Article 4, paragraph 2 (k).

[66] TFEU; Article 6, subparagraph (a).

[67] TFEU; Article 6.

[68] http://www.euro.who.int/__data/assets/pdf_file/0008/259955/Everything-you-always-wanted-to-know-about-European-Union-health-policies-but-were-afraid-to-ask.pdf

There are also some additional and unusual tools provided in Article 168. One of this is the power for the Council of Ministry to adopt recommendation in support of the objective of the Article. Another power is the provision for the member states to coordinate their own policies on areas too sensitive for legislation or outside their scope, working through the establishment of the establishment of guidelines and indicators, the organization of exchange of best practice, and the preparation of the necessary elements for periodic monitoring and evaluation"[69].

The European Community Treaty may forbid the union from using its health policy to cuts across member states' rights to run their own healthcare system. However, the health care systems of European Member states are not isolate from the effect of EU law in other areas[70]. B. Ducan, in his paper[71] illustrates three types of EU health policy making:

1. **Directorate health policy making**: identification of health objective and seeks to realise it by EU action, either law making or funding or cooperation between the member state.
2. **Indirect health policy making**: when EU is pursuing an objective other than health, but health is considering an important part in determining the final outcome.
3. **Unintentional health policy making**: pursuing an economic or social policy objective but it affects health in an unplanned manner, or a law, or article produces unforeseen effects on health policy. An example of this would be the

[69] TFEU; Article 168, paragraph 2

[70] European Health Management Association. Impact of European Union internal market regulations on the health services of member states. Dublin: EHMA; 200

[71] Duncan B. Health policy in the European Union: how it's made and how to influence it. *BMJ : British Medical Journal*. 2002;324(7344):1027-1030.

common agricultural policy, which public health advocates see as having negative impacts on diets[72].

2.2 Projects: HTA cooperation at EU level

The Commission of the European Union, since the early 1990s, is supportive of health technology assessment as a means of establishing the best health practice in the member states. At international level, during the 1970s and 1980s, it starts to think about international cooperation on Health Technology Assessment. This thought became reality in 1985 with the first meeting of the International Society for Technology Assessment in Health Care (ISTAHC) in Copenhagen, followed by the International Network of Agency for Health Technology Assessment (INAHTA), created in 1993. Moreover, in those years annual meeting of ISTAHC have allowed those working in the field to identify gaps and duplication in coverage of technology assessment. There were several examples of useless duplication such as the myopia treatment by excimer laser that has been necessary by five or more agencies or the carrying out of similar studies on heart transplantation in the United States, the United Kingdom, the Netherlands, and Sweden. As a result of all of these, in Europe a group of agency heads and others, including Egon Jonsson (Sweden), David Banta (the Netherlands), Michael Peckham and Chris Henshall (UK), Yves Matillon (France), Alicia Granados (Catalonia), and Richard Cranovsky (Switzerland) began to talk about the need for coordination of HTA activities in Europe[73]. These discussions ended up in a decision apply to the BIOMED Programme of Directorate General XII of the European Commission for support to establish a coordinating network[74]. The result

[72] Duncan B. Health policy in the European Union: how it's made and how to influence it. *BMJ : British Medical Journal*. 2002;324(7344):1027-1030.

[73] Cranovsky, R., Matillon, Y., & Banta, D. *"EUR-ASSESS Project Subgroup Report on Coverage".* International Journal of Technology Assessment in Health Care, *13*(2), 287-332. (1997)

[74] Ibidem

of its first application, in 1992, was unsuccessful, however the partners decide to persevere aided by informal contract with the Commission. In 1993 a second proposal was submitted and to the funding of the project EUR-ASSESS**.** The oversight of the project was carried out by a Steering Committee representing the major partners in the projects, especially representing the ten countries[75]. However, during the course of the project, new contracts were made, and new agency were established. Therefore, by the third year of the project almost every country of the European Union participated in the Steering Committee.

Since the beginning, the European Commission had made it clear that it would not support a coordination mechanism per se. for this reason, it was necessary to have substantive tasks. Therefore, four subgroups were setting to carried out four issues of importance to HTA:

1. Priority setting;
2. Methods of HTA;
3. Dissemination and implementation of HTA;
4. Health insurance coverage of HTA.

The chair of each subgroups was those who had supported the attempt to gain support for the project. Moreover, each subgroup, at the end of the work wrote its own report. This report was then exanimated by the Steering Committee and revise before being accepted for the final report. The report, themselves were useful. However, the most important result of the project achieved was that people from several disciplines and nationalities, worked closely together successfully for several years, and the result reflected the diversity of Health Technology Assessment approach in Europe[76].

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[75] Italy, Germany, Denmark, Spain, Greece, Netherlands, Sweden, France, the UK and Switzerland.

[76] Banta, D., Finn Børlum K., and Egon J... *"A History of Health Technology Assessment at the European Level."* International Journal of Technology Assessment in Health Care 25. S1. 68–73. (2009)

At the end of the project the Steering Committee for the EUR-ASSESS project made several recommendations:

1. The European Commission should make funds availed to support activities aimed at fostering communication on HTA among different countries, including conference and meeting;
2. The EC should support activities aimed at development of robust and reliable system for sharing information on HTA in Europe;
3. The EC should devote resources to studying the relationships between HTA and health system in the member states of the European Union.

The Steering also recommended that

« each country should have at least one organization (or a coordination body) that can serve as a contact for technology assessment activities, including priority setting, dissemination, and implementation[77].»

The EUR-ASSESS project was followed by a European Commission-sponsored activity named HTA-Europe, from 1997 to 1998. The aim of this new project was to develop paper on HTA and health system of all members of the European Union. The papers, commissioned from all countries of the European Union in a common format, were published in the HTA journal[78]. The general structure of the project was similar to that of the EUR-ASSESS project. However, the Steering Committee now represented all member states of the European Union[79]. At the end of the project, staff of the European Commission invited the coordinators of the project to produce a document developing the case of a better coordination of HTA in Europe. As a result of this initiative, the European Commission decide to publish

[77] Banta HD. *"Introduction to the EUR-ASSESS report*." Int J Technol Asseess Health Care. 13:133-143. (1997)

[78] Banta HD, Oortwijn W. "*Health Technology assessment in the European Union."* Int J Technol Asseess Health Care. 16:626-635. (2000)

[79] Banta, D., Finn Børlum K., and Egon J... *"A History of Health Technology Assessment at the European Level."* International Journal of Technology Assessment in Health Care 25. S1. 68–73. (2009).

the result of the paper as a policy document[80]. The Steering Committee of the HTA Europe Project recommended that "It would be beneficial for health care system of European Union countries for the European Commission to assist the establishment of coordinating mechanism for HTA at the European Level.[81]"

In 2000, the European Commission strongly supported a third major project in the field named *The European Collaboration for Assessment of Health Intervention and Technology* (ECHTA/ECAHI) and led by Egon Jonsson[82]. As well as the previous European projects there was a Steering Committee representing all member states and a series of six subgroups, covering the following topics:

1. Assess health promotion and disease prevention activities in terms of benefits, risks, and economic, social, and ethical implications as a complement to community health indicators;
2. Develop system for routine exchange of information between programs on emerging technology issues, priorities for future evaluation, and performance and timing of ongoing evaluation including findings from evaluations;
3. Identify possible joint evaluation and to coordinating findings and existing resources within the community to support joint assessments;
4. Develop and disseminate best practices in undertaking and reporting assessments, and identify needs for methodological development;
5. Develop and coordinate education and support networks for individuals and organizations undertaking or using assessment of health interventions and to identify needs in the field;

[80] Ibidem.

[81] Ibidem.

[82]Banta HD, Oortwijn W. "*Health Technology assessment in the European Union."* Int J Technol Asseess Health Care. 16:626-635. (2000).

6. Identify and share the successful approach that lead link findings of assessment to health policy and practice, that contribute to health indicators and health care decision making[83].

A key challenge for the working groups of the ECHTA/ECAHI project was to take all the advantage from the relevant expertise within Europe. However, the main goal of this project was to promote evidence-based health care in European Community, promote the cooperation and to explore opportunities to reinforce the network throughout the member states. At the end of the project was published in IJTAHC the Steering Committee conclusion

«There is now a need to strengthen this collaboration and create a sustainable Network within the European Union. The objective of the Network would be to assist the European Union, its member states and the candidate countries to plan, deliver and monitor health services effectively. Strong commitment and funding from the Commission would allow such a Network to achieve this objective. The Network should involve those working actively on assessments in health care in Europe, focusing on those in the public sector, but welcoming those working in other settings. The Net- work should be based on an agreed work plan, developed within the ECHTA/ECAHI project. A Steering Committee should oversee the Network, which should be supported by a Secretariat, initially placed in an existing HTA agency in a member state. The Network should work closely with global efforts of collaboration in the area, such as with INAHTA.[84]»

After the end of the ECHTA/ECAHI Project at least two European policy processes brought forward the political basis for European HTA. In May 2002, the High-Level Group on Innovation and Provision of Medicines in the EU (G10) recommended that the European Commission organize a European process to

[83] Banta, D., Finn Børlum K., and Egon J... *"A History of Health Technology Assessment at the European Level."* International Journal of Technology Assessment in Health Care 25. S1. 68–73. (2009)

[84] Jonsson E, Banta HD, Henshall C, Sampietro-Colom L. Euro- pean collaboration for health technology assessment: Develop- ing an assessment network. *Int J Technol Assess Health Care.* 2002;18:213-455.

reflect on how Member States could improve ways of sharing information and data requirements. With the aim to achieve greater certainty and reliability for all involved, even if their policy decisions might differ[85]. One objective was to foster the development of HTA, including clinical and cost-effectiveness, in the Member States and the EU. This would improve the value of HTA by sharing national experiences and data while recognizing that relative evaluation should remain a responsibility of Member States. As a conclusion of the Health Council (Health Ministries from EU Member States) was presented a paper in 2003[86]. This document stated that HTA could assist policy makers in making informed decisions by providing evidence on medical, social, economic, and ethical issues concerning healthcare policy and practice. The report recommended inviting the European Commission to consider how a sustainable network and coordination function for health technology assessment could be organized and funded and to make an appropriate proposal[87].

In 2004 the European Commission established a High-Level Group on Health Service and Medical Care (HLG) consisting of high-level officials from Member State ministries of health to endorse and implement the recommendations issued from the patient mobility reflection process[88]. The HLG established different groups in which one of them on HTA. The group, involving six Member States was able to draft a report after few months. The report stated that should be create a network in order to address:

1. Methods to develop common core information packages;

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[85] Kristensen, Finn Børlum, et al. "European network for Health Technology Assessment, EUnetHTA: Planning, development, and implementation of a sustainable European network for Health Technology Assessment." *International journal of technology assessment in health care* 25.S2 (2009): 107-116.

[86] http://ec.europa.eu/health/ph_overview/Documents/key01_mobility_en.pdf

[87] Ibidem

[88] Finn Børlum K.,. "*European network for Health Technology Assessment, EUnetHTA: Planning, development, and implementation of a sustainable European network for Health Technology Assessment."* International journal of technology assessment in health care 25.S2 (2009).

2. Support transferability of assessment;
3. Help member state to identify and prioritize topics;
4. Commission reports tailoring common core information to national health policy process;
5. Share methodologies, expertise, and practical issues[89].

In the same year, the HLG work resulted in a report that identifies an urgent need to establish a sustainable network for HTA and proposed several steps, starting with a three years project supported by the EU Public Health Program. This was approved by the Council of Ministers and follows by a call for proposal in SANCO's work program for 2005 aiming at projects to establish a European network for HTA (EUnetHTA)[90].

In the same period, the Commission call was answered by a group of 35 organizations throughout Europe, and the activities of the EUnetHTA Project were led by the Danish Centre for HTA (DACEHTA) in Copenhagen. The consequent activities oh European network of Health Technology Assessment were organised throughout the establishment of the EUnetHTA Collaboration 2009, the EUnetHTA Joint Action 2010-2012. EUnetHTA Joint Action 2 2012-2015 and EUnetHTA Joint Action 3 2016-2020.

[89] Jonsson E, Banta HD, Henshall C, Sampietro-Colom L. "E*uro- pean collaboration for health technology assessment: Develop- ing an assessment network*". Int J Technol Assess Health Care.;18:213-455. (2002)

[90] Finn Børlum K.,. "*European network for Health Technology Assessment, EUnetHTA: Planning, development, and implementation of a sustainable European network for Health Technology Assessment."* International journal of technology assessment in health care 25.S2 (2009).

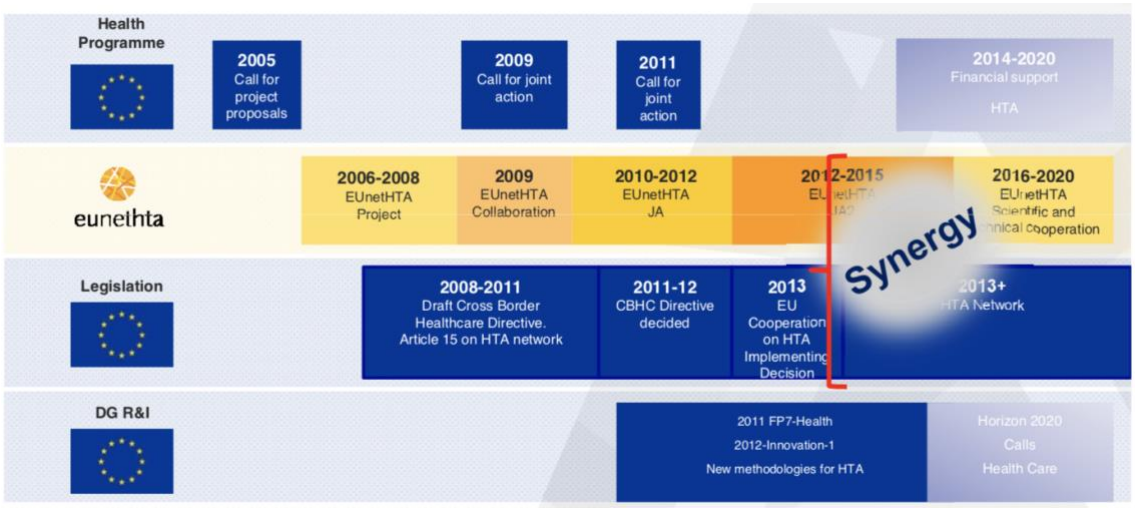


FIG. 2.4 The timeline of reaching a sustainable and permanent HTA network in Europe[91].

2.3 EUnetHTA Project

Whereas EUnetHTA is a voluntary association of organisations involved in HTA with a clear focus on scientific aspect of HTA, the so called Cross Border Directive the Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 provides the legal bases for a European HTA network with an overall mandate concerning HTA cooperation in Europe[92].

The Article 15 (1) "Cooperation on health technology assessment" of the latter stated that

> *«The Union shall support and facilitate cooperation and the exchange of scientific information among Member States within a voluntary network connecting national authorities or bodies responsible for health technology assessment designated by the Member States. The Member States shall communicate their names and contact details to the Commission. The members of such a health technology assessment network shall participate in, and*

[91] http://www.who.int/medical_devices/Sat_am_HTA_3_CERBO.pdf

[92]https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2014_strategy_eucooperation_hta_en.pdf

contribute to, the network's activities in accordance with the legislation of the Member State where they are established. That network shall be based on the principle of good governance including transparency, objectivity, independence of expertise, fairness of procedure and appropriate stakeholder consultations.[93]*»*

Moreover, as defined by the Directive, the objective of the HTA networks shall be supporting cooperation between national authorities or bodies as well as supporting Member States in the provision of comparable and transferable information. The final goal is to avoid duplication of assessments, and above all, to enable Member States to develop and share methodologies[94].

In line with the Directive, the strategic objective of the EUnetHTA Project were to:

- Reduce overlap and duplication of effort and hence promote more effective use of resources;
- Increase HTA input to decision-making in Member States and the EU and hence to increase impact of HTA;
- Strength the link between HTA and Health care policy making in the and its Member States;
- Support countries with limited experience with HTA.

EUnetHTA Project spanned 3 years, from January 2006 to December 2008, and included eight Work Packages (WPs):

1. WP1- Coordination
2. WP2- Communication
3. WP3-Evaluation
4. WP4-Common Core HTA
5. WP5-Adapting HTA

[93] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:088:0045:0065:en:PDF

[94] Ibidem

6. WP6-HTA and Health Policy
7. WP7-New technologies
8. WP8-System to support HTA

The Work Packages were aligned with specific objectives and each was expected to produce substantial deliverables (TAB 2.1). The individual Work Package reports will include the lists of the individuals that were involved in the WP work from each of the participating organizations[95]. Moreover, for the development of the Work Package were used a variety of scientific approaches, such as literature searches, survey questionnaires, Delphi surveys, pilot and applicability testing of tools structured reviews and several meetings and other collaboration in order to build consensus.

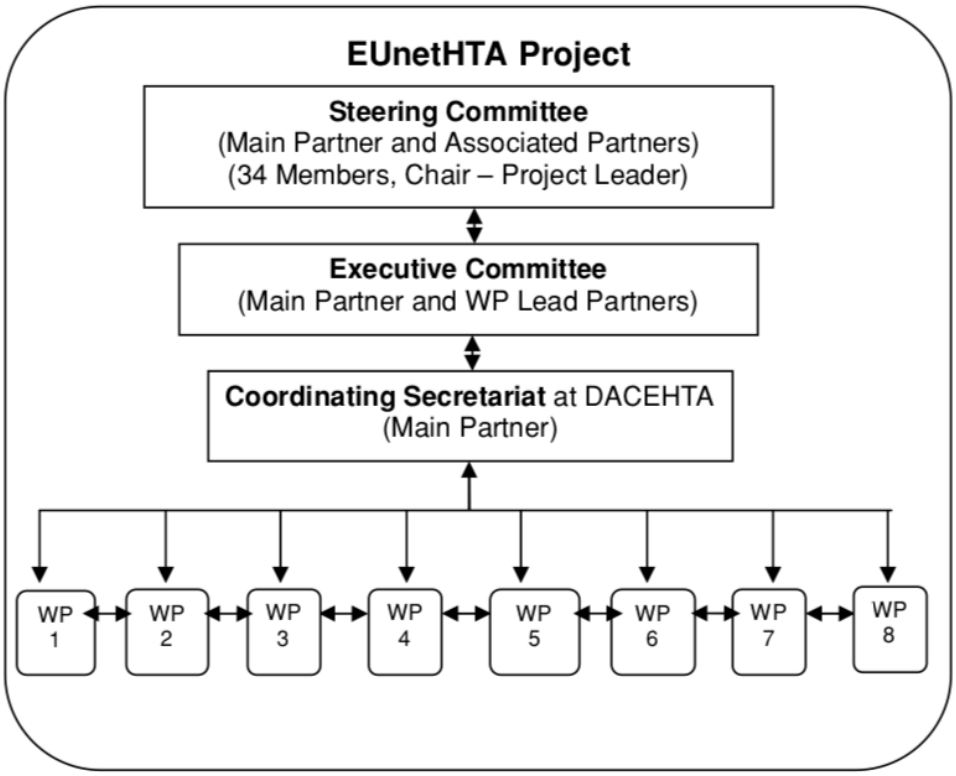
[95] The EUnetHTA Project involved a multidisciplinary staff of 64 organizations in 33 countries across the world.

Specific Objectives	Key Deliverables	Work Package
To establish the organisational and structural framework for the network with a supporting secretariat	• The EUnetHTA organisational structure including a supporting Secretariat • Final report from the project • EUnetHTA conference presenting the project results	1 Coordination
To effectively disseminate and handle HTA results, information sharing and coordination of HTA activities through the development and implementation of elaborate communication strategies and description of Clearinghouse functionality	• Communication strategy • A clearinghouse functionality - detailed identification of the clearinghouse needs of different target groups and consecutive structure development to be ready for practical application after 3 years • EUnetHTA conference presenting the project results	2 Communications
	• Internal evaluation of the project • Framework for external evaluation	3 Evaluation
To produce generic Core Models for HTAs on two essential categories of health technology questions: interventions and treatment, as well as Core HTAs on selected topics for each category	• Core HTA structure/model • 2 pilot examples of Core HTAs for different types of questions (e.g. diagnosis and treatment) • A handbook on Core HTA.	4 HTA Core Model
To develop and implement generic tools for adapting assessments made for one country to new contexts	• A toolkit for adapting Core HTA results from existing HTAs into other contexts including a HTA Glossary of adaptation • Applicability testing of core information from 2 existing HTA reports in various national environments using the toolkit	5 HTA Adaptation Toolkit
To develop and implement effective tools to transfer HTA results into applicable health policy advice in the Member States and EU – including systems for identification and prioritisation of topics for HTAs and assessment of impact of HTA advice	• EUnetHTA Open Forum for stakeholders to exchange views and expectations/feedback on HTA • A book containing a systematic overview of the HTA & healthcare policy links in selected Member States & EU representing different health systems, remuneration systems, etc	6 Transferability of HTA to health policy
To structure prioritisation for HTA and provide health care decision makers with policy relevant information on new and emerging technologies	• A prototype of a structured information service on high volume, costly, rapidly developing, emerging technologies	7 Monitoring development of emerging and new technologies and prioritisation of HTA
To provide tools to monitor the development of health technologies and to share data and results of this monitoring	• A set of monitoring tools for emerging/new technologies	7 Monitoring development of emerging and new technologies and prioritisation of HTA
To establish a support system for countries without institutionalised HTA activity	• Handbook on HTA organisations. The handbook will compile the results and information extracted from the review and the survey of HTA organisations	8 System to support HTA in Member States with limited institutionalisation of HTA

TAB 2. 1 Objectives and planned deliverables for each Work Package[96]

[96] https://www.eunethta.eu/wp-content/uploads/2018/01/Overview-of-the-EUnetHTA-Project-Results-2006-2008_0.pdf

To ensure the achievement of objectives and consistence and high-quality work was needed a clear management and coordination restorability. FIG 2.2 shows the organizational structure of the Project.



TAB 2. 1 EUnetHTA Project Organizational Structure[97]

The engagement of stakeholders was an important element of building the knowledge base about HTA collaboration across Europe. Hence, the Work Package 6 (WP6) identified five stakeholder groups at the European level as potentially sharing an interest in EUnetHTA and its products[98]:

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97 https://www.eunethta.eu/wp-content/uploads/2018/01/Overview-of-the-EUnetHTA-Project-Results-2006-2008_0.pdf

98 Finn Børlum K.,. "*European network for Health Technology Assessment, EUnetHTA: Planning, development, and implementation of a sustainable European network for Health Technology Assessment."* International journal of technology assessment in health care 25.S2 (2009).

1. Policy makers at national and regional levels;
2. Policy makers at the institutional level;
3. Patient organizations;
4. Healthcare professionals;
5. Industry.

Furthermore, WP& developed a Stakeholder Open Forum on the EUnetHTA Web site[99] with a "Frequently Asked Questions" section and links to important stakeholder policy statements on HTA[100]. Additionally, to facilitate the discussion plans for future HTA collaboration across Europe many face-to-face meetings were planned, in which it presented a draft stakeholder policy[101]. The participants agreed that this policy should be forwarded to those responsible for taking forward collaboration in EUnetHTA in the future along with notes from the meeting and a discussion topic catalogue, which reflected the issues that stakeholders found unclear or problematic.

Moreover, it is important underline that The EUnetHTA Project aimed to build on all previous work that sought to improve approaches to HTA by the development of practical tools for information sharing. The key elements of this were the HTA Core Model, the HTA Adaptation Toolkit and the system for monitoring new and promising health technologies.

The HTA Core Model is a novel approach to HTA. It should define a clear structure for HTA information and provide guidance on the content, i.e. the elements to go in the structure[102]. Standardisation of the individual elements in an HTA report in this way should not only facilitate transparency, improved quality

[99] http://www.eunethta.net/Stakeholder_ Forum/Home/

[100] http://www.eunethta.eu/Stakeholder_Forum/ Activities_for_Stakeholders/

[101] https://www.eunethta.eu/wp-content/uploads/2018/01/Overview-of-the-EUnetHTA-Project-Results-2006-2008_0.pdf

[102] Banta, D., Finn Børlum K., and Egon J... *"A History of Health Technology Assessment at the European Level."* International Journal of Technology Assessment in Health Care 25. S1. 68–73. (2009)

and comprehensiveness in the development of reports, but it should allow the individual elements of information to be extracted from the report.
Furthermore, the HTA Core Model was developed on the basis of nine domains:

1. Health problems and current use of technology;
2. Description and technical characteristics;
3. Safety;
4. Clinical Effectiveness;
5. Cost and economic evaluation;
6. Ethical analysis;
7. Organizational aspects;
8. Patients and social aspects;
9. Legal aspects.

On the other side there is the JTA Adaptation Toolkit sought "*to facilitate better use of existing HTA reports by developing a toolkit to use parts of HTA reports that could be adapted to inform policy in other countries or context*[103]".
According to a survey on HTA agency/networks, the majority of respondents felt that work in technology use, safety, effectiveness, economic evaluation and organisational aspects would be more applicable and adaptable across different countries. Consequently, these domains were taken forward into the HTA.
Adaption Toolkit which has divided in two sections:

1. Speedy sifting – a screening tool to enable rapid sifting of existing HTA reports to assess their possibility for adaptation; and
2. Main toolkit – more comprehensive tool with questions on reliability and transferability.

[103] https://www.eunethta.eu/wp-content/uploads/2018/01/Overview-of-the-EUnetHTA-Project-Results-2006-2008_0.pdf

The main outcome of the EUnetHTA Project was the result achieved in developing tools aims at providing a common methodology with the intent to establish a suggest standard for conducting and reporting HTA and facilitating increased collaboration between agencies.

- As a result, eunethta members have noted many elements of added value from their collaboration in the Project, including[104]:
- Advancing methodological developments in the practical application of HTA;
- Discussion about the content of HTA;
- Providing an arena for increased international collaboration between agencies, institutions, and individuals
- Working with HTA;
- Increased international visibility and credibility through participation in the eunethta;
- Challenge to thinking about current working processes;
- Improved understanding of the role of HTA in relation to other processes in healthcare policy making;
- Better connected to HTA colleagues in Europe;
- Better informed about HTA processes in Europe;
- Increased attention to stakeholder involvement.

Additionally, at the conference at the end of the EUnetHTA Project, stakeholders were given the opportunity to comment specifically on the added value of EUnetHTA. In particular, industry representative focused on the value of HTA Core Model to support collaboration about the requirement element of HTA, which will increase the efficiency and quality of the process. Hence although, this Project has been highly successful, there was a need to continue collaboration in HTA across Europe to ensure that all the good work is put into practice, used and

[104] https://www.eunethta.eu/wp-content/uploads/2018/01/Overview-of-the-EUnetHTA-Project-Results-2006-2008_0.pdF

developed further[105]. The consequent activities of the European network for Health Technology Assessment were organize through the establishment of the EUnetHTA Collaboration 2009, the EUnetHTA Joint Action 2010-2012, EUnetHTA Joint Action 2 2012-2015 and EUnetHTA Joint Action 3 2016-2020.

2.4 Joint Action

As a result of the EUnetHTA Collaboration, in early 2009, between EU and Member-States-appended HTA bodies and representatives, 3-years Joint Action (2010-12) under the EU Health Program (2008-13) will be the bases for continuation of European networking in HTA and further work on relative effectiveness assessment of pharmaceuticals[106].

As stated at the conference in Stockholm in December 2009[107], "*EU cooperation added value is significant to address clinical issues, where substantial scientific questions are at stake[108]*". Moreover, core methods and data can be jointly developed for possible reuse at national level. In order to avoid the duplication of efforts and resources for industry, HTA bodies and payers were established a polling of expertise. In this way, all Member States should benefit from HTA expertise.

2.4.1 The Joint Action 2010/2012

The EUnetHTA Joint Action 2010-2012 redefine the structures and tools with attention to global developments in the field. The objective and the governing rules were defined by the Member States (24 involved) and the European Commission which financed the 50% of the project.

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[105] https://www.eunethta.eu/wp-content/uploads/2018/01/Overview-of-the-EUnetHTA-Project-Results-2006-2008_0.pdf

[106] European network for Health Technology Assessment EUnetHTA: planning, development and so on.

[107] P7R network of competent authorities, European Commission, DG SANCO.

[108] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20091215_co01_en.pdf

The strategic objectives of the JA1 were to develop principles, methodological guidance as well as functional online tools and policies for: producing, publishing, storing and retrieving structured HTA information and Core HTAs (including a new application of the Core HTA Model structure in screening);improved Relative Effectiveness Assessment (REA) by identifying areas where methodological guidance is needed and by providing it, suggesting ways to integrate REA[109] of pharmaceuticals as a special version of the HTA Core Model (JA WP5) and structured exchange and storage of information on evidence generation on new technologies (JA WP7)[110]. Moreover, to test implement was needed a web- based toolkit for structured exchange and storage of information on evidence generation on new technologies and the application of the Core HTA model in common production and a real-life support of information flow on new technologies prompting those where parallel assessment of the same technologies is detected and alerting on opportunities for information sharing and closer collaboration.

Furthermore, a core principle for stakeholders' involvement in the EUnetHTA Joint Action was provided, together with an internal Standard Operating Procedures (SOP) which stipulated procedures for all types of stakeholder involvement. The EUnetHTA Joint Action defined stakeholder: "*Groups or organisations which provide considerable insight into views of the groups they represent, and which will be affected by, or have an interest in, and may in a consultative role contribute to the actions or aims of an HTA organisation, project or policy direction.".*

[109] The Rapid Relative Effectiveness Assessment (REA) covers and limited to the clinical domains and measures the medical/therapeutic added value of a technology. It is also called clinical assessment.

[110] https://www.eunethta.eu/ja1-archive/

Based on this definition four types of stakeholder group have been identified as particularly important for the interaction with the EUnetHTA Joint Action:

1. Patient and healthcare consumer organizations
2. Healthcare providers (professionals and hospitals)
3. Payers
4. Industries

However, the involvement of stakeholder representatives and involvement of experts are differentiated both in criteria and procedures for their identification and provision of input into the work of the EUnetHTA Joint Action[111]. In particular, the involvement of stakeholders consists of participation in the EUnetHTA Joint Action Stakeholder Forum, public consultation on deliverables, participation in the EUnetHTA Joint Action Work Packages through advisory groups and with the provision of specific subject-matter information/knowledge on specific technical questions.

Hence, The EUnetHTA Joint Action recognises that different groups and organisations bring key information and experience on the producing of concrete Health Technology Assessments (HTAs). It further recognises the impact of HTA on the development, use and funding of various health interventions that could be subject to an HTA. Therefore, the EUnetHTA Joint Action Stakeholder Policy was developed to facilitate a transparent, responsible, accountable, participative and responsive stakeholder involvement process.

2.4.2 Joint Action 2 (2012-2015)

As described above the JA1 developed the methodology for joint HTA assessments, while JA2 developed ten pilots to follow for testing methodology and

[111] https://www.eunethta.eu/wp-content/uploads/2018/01/EUnetHTA-JA-Stakeholder-Involvement-Policy.pdf

procedure of joint assessment. Specifically, the JA2 was to develop a general strategy, principles and implementation proposal for a sustainable European HTA collaboration according to the requirements of Article 15 of the Directive for cross-border healthcare. Hence, the strategical objectives from 2012-2015 were to strengthen the practical application of tools and approaches to cross-border HTA collaboration and bringing the collaboration to a higher level resulting in better understanding for the Commission and Member States (MS) of the ways to establish a sustainable structure for HTA in the EU.

For what concern the stakeholder involvement, the EUnetHTA Stakeholders Involvement Policy, developed during EUnetHTA Joint Action 1 continued to apply during the JA2. Furthermore, some adjustments in the procedures were agreed and approved by the Plenary Assembly to be applicable in the EUnetHTA JA2 stakeholder involvement activities, such as:

1. The incrementation in number of organisations per stakeholder group from 4 to 6 in the eunethta stakeholder forum meeting;
2. All applying organisations found eligible for participation in the eunethta stakeholder forum received a status of a stakeholder forum member;
3. The stakeholder group members were responsible to organise themselves for the participation in the stakeholder forum meetings (with the maximum number of meeting participants per stakeholder group limited to 6);
4. New forms of stakeholder involvement (in addition to the stakeholder forum and stakeholder advisory groups (sags) as expert meetings, was introduced;
5. Earlier involvement of stakeholder expertise was to be considered;
6. Adequate time to provide input was to be allowed[112].

[112] https://www.eunethta.eu/ja2-archive/

2.4.3 Joint Action 3 (2016-2020)

Previous European projects have demonstrated that collaboration and information sharing is facilitated with an organizational structure and common tools for HTA production. As a progress continuum, the EUnetHTA JA1 refined the collaboration structure and tools with attention to global developments in the field. EUnetHTA JA2 extended this by strengthening the practical application of tools and approaches to cross-border HTA collaboration, further supporting and redefining a system of collaboration in HTA[113]. So, these experiences have proven the ability of HTA bodies to work together, to develop Joint Tools and at the same time piloting joint work. Another strong achievement has been the well-defined interactions with other stakeholders and other organisations, within a structure for collaboration with regulators in pharma (EMA) and the interactions with other stakeholders, such as technology procedures and patients in assessments, early dialogue, preparation of methodology.

Additionally, the directive on cross-border healthcare (CBHC, 2013) demand the establishments of a permanent network on HTA in Europe. On one side the Council of European Union has pointed out the need to strengthen activities with the aim of ensure financial sustainability of health system and at the same time, ensure equitable access to quality care. The Health Technology assessment is under financial pressure as the health system and for this reason is important to use its resources efficiently. On the other side, the European Commission ant he HTA-scientific community pointed out the need to enhance the use of HTA.

On this purpose the Joint Action 3 is now proceeding with the final step of establishing this permanent sustainable network on HTA in Europe[114]. In fact, the

[113] https://webgate.ec.europa.eu/chafea_pdb/health/projects/724130/summary

[114] Ibidem

general objective for EUnetHTA JA3 is to increase the use, quality and efficiency of joint HTA work at European level to support evidence-based, sustainable and equitable choices in healthcare and health technologies and ensure re-use in regional and national HTA reports and activities, in order notably to avoid duplication of assessments. An overarching objective is to develop a general strategy, principles and proposal for a scientific and technical mechanism of permanent sustainable European Collaboration on HTA in the light of the Directive on CBHC[115].

For what concern the governance structure and the stakeholder involvement in EUnetHTA Joint Action 3 will be, in general, in conformity with EUnetHTA JA Stakeholder Involvement Standard Operating Procedures and Policy. The main change where the classification of stakeholders, six groups instead of four:

1. Patients & consumers
2. Regulators
3. Technology Produces
4. Payers/Decision-makers
5. Providers
6. Research &Academia

2.5 Achievements and shortcoming of the current EU cooperation

Trying to sum up the main evidence at the end of this chapter, it is possible affirm that at EU level, cooperation on HTA has been ongoing since 1980s, and the European Commission made great efforts and investment to support the cooperation between HTA bodies. The first two Joint Action were followed by a number of projects, and the third Joint Action was launched in June 2016 and runs until 2020, with a total budget of EUR 20 million. The participation in the Joint

[115] https://www.eunethta.eu/ja3-archive/

Action has been very high, including participation from all EU Member States. In addition, following the Directive CBHC, the HTA Network was established in 2013 to provide strategic and political guidance to the scientific and technical cooperation at Union-level. Notwithstanding the achievements of the current EU cooperation, a number of shortcoming have been identified, which cannot be sufficiently addressed by continued project-based voluntary cooperation on HTA. The main problem results after a deep analysis regards the low uptake of joint which lead to the duplication of work by HTA bodies and industries, the difference in the procedural framework and in national methodologies.

THIRD CHAPTER

Proposal for a Regulation of the European Parliament and of the Council on health technology assessment and amending Directive 2011/21/EU

3.1 Context of the proposal

In the last years, several key players have been called for the reinforcement of EU cooperation in the area of HTA. In particular the EU total, public and private, health care expenditure amounts to around EUR 1 300 billion per annum, according to Eurostat. Health care expenditure thus accounts on average for about 10% of the EU GDP. The expenditure is likely to increase in the coming years, considering inter alia Europe's ageing population, the increase of chronic diseases, and complex new technologies. At the same time, Member States are increasingly confronted with budgetary constraints. These developments will require Member

States to further improve the efficiency of health budgets – focusing on effective technologies whilst maintaining a stimulus for innovation[116]. However, in order to address to the above-mentioned challenges, the health technology assessment has become an important tool used to assist Member States in creating and maintaining sustainable health care system.

This was analysed for the first time in the "Inception impact assessment" (IIA), published in 2016 and considered as the first key milestone in HTA initiative. In the same document was summarize the political context and the view of Member States, the EU institutions and the key stakeholders to strength the HTA cooperation.

Member States, expressed their opinion clearly in a document called "Strategy for EU Cooperation in HTA"[117]. In this document the HTA network called upon the European Commission to explore how to secure support for the joint work in the long-term[118]. Moreover, in the Council conclusion on "Personalised medicines for patients" of December 2015[119], the Member States and the European Commission were invited to reinforce HTA methodologies[120]. Additionally, the Council conclusion on "Strengthening the balance in the pharmaceutical system" in June 2016[121] confirmed that the Member States see a clear added value on EU HTA

[116]http://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf

[117]https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2014_strategy_eucooperation_hta_en.pdf. This document was adopted by the Member States representatives in the HTA Network in October 2014.

[118]http://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf

[119]http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1473406227181&uri=CELEX:52015XG1217%2801%29

[120]http://ec.europa.eu/smart regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf

[121]http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1473409810047&uri=CELEX:52016XG0723(03)

cooperation[122]. At the same time the European Parliament also asked for a reinforcement of the HTA cooperation and in 2016 the Parliament commissioned a study on HTA, highlighting its interest in the subject. On the other side, the Commission often referred on HTA, including as a key part of supporting other important EU/Commission initiatives. Additionally, throughout a stakeholder's public consultation, that will be analysed in the next chapter, it was possible collect the stakeholders' view on EU cooperation on HTA beyond 2020. The main result was the highlight of the usefulness of EU cooperation on HTA.

However, taking into account the stakeholders view and concerns, the European Commission draft the legal proposal with annex the Impact Assessment in line with the calls of key stakeholders and in line with the position expressed by the EU institutions/Member States[123].

3.2 Problem definition

Whilst HTA is considered an important tool for ensuring sustainability of health systems and stimulating innovation and cooperation at EU level, evidence shows that several shortcomings, affect the development of the benefits for Member States, with consequences also for EU patients and healthcare providers[124].

The main problems identify by the European Commission and analysed in the Impact Assessment, published the 31st of January of 2018, are three:

1. Impeded and distorted market access
2. Duplication of work for national HTA bodies
3. Unsustainability of HTA cooperation

[122]http://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf

[123] Ibidem

[124] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf

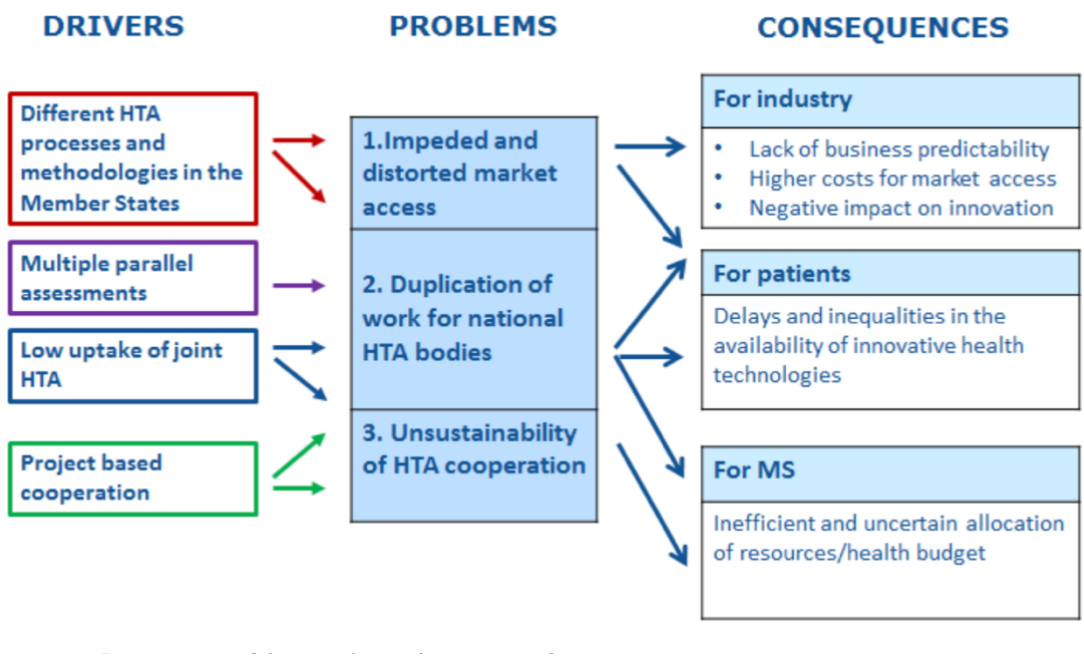

Figure3.1. Main problems, their drivers and consequences[125]

3.2.1 Impeded and distorted market access

As explained in the second chapter, in the last 20 years, all Member States have started to introduce HTA process ay national or regional level[126]. Nowadays, there is some convergence in national HTA system but at the same time there are significant discrepancies. Throughout the Impact Assessment it is possible see clearly which the main differences in the procedural framework and the main differences in methodologies are. The first differences, for what concern the procedural framework, lies in the scope of health technology that has to be assessed[127]. In fact, 20 Member States and Norway have declared to use HTA

[I0] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf

[126] Patient Involvement in Health Technology Assessment in Europe. Results of the European Patient's Forum Survey. 2013.

[127] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf

system for medical device, while 17 Member States and Norway indicate that they have an HTA system for other technologies[128].

Looking at the tasks allocated[129], the main role of the most of HTA body is to *"carry out assessment and provide recommendations for decision making[130]".* However, in addition to this role, some HTA organizations develop quality standard, perform horizontal scanning[131] , manage register or offer early dialogues/scientific advice to health technologies developers. Moreover, the study mapping on HTA process across EU shows that there are also significant differences concerning the resources available. Another example of difference in the Member States is that some HTA organizations consider a dossier submitted by industry in their assessment. Additionally, it is possible find[132] differences in the type and number of assessment as well as in the time needed to complete a health technology assessment process and in the stakeholders' involvement.

There are also divergences in the methodologies used by different HTA bodies. Could be possible that HTA organization, for example, can take different methodological approaches when assessing the acceptability of particular types of studies and study design issues such as the comparator used, endpoints measured, the type of patients enrolled and the duration of the study.

Therefore, all these differences illustrated above mean that economic operators who want to introduce a health technology in multiple Member States are confronted with various data requests. This in turn contributes to an impeded and distorted market access, higher cost and in the long-run negative effects on

[128] Mapping of HTA national organisations, programmes and process in EU and Norway. 2017.

[129] Mapping of HTA national organisations, programmes and process in EU and Norway. 2017.

[130] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf

[131] Horizon scanning refers to the systematic identification of emerging technologies that could have significant effects on health care, and which might be considered for health technology assessment (WHO definition)

[132] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf

innovation[133]. The effects of these divergences were underlined by different stakeholders in the public consultation, in which the most significant was reported by pharmaceutical industry. They pointed out that this diversity continued a hurdle for companies, as they have to adapt to multiple and various national requirements. Moreover, duplication of assessments increases cist for industry which need to prepare dossier for multiple national system with potentially different data requirements. Requirements for additional evidence are a key cost component, with potential delays/risks in market access[134]. The small companies with limited resources may face difficulties in put in place such alternatives. This situation was confirmed in the online public consultation and in a special report from EuropaBio in which is explained how the SMEs have limited experience in working with HTA bodies and may not have staff dedicated to HTA work. All this poor business predictability and high fragmentation of Health Technology Assessment system across Europe constitute barriers to investment by industry in development programmes for innovative technologies[135]. Finally, the high variability in the timing of assessment and the divergences in the conclusion of HTA reports on added value, contribute to differences in availability of medicines to EU patients. These divergences are illustrated in the Table1, for a sample of cancer drugs. As it is possible see in the table, there are common trends but also discrepancies in the conclusion reached by different HTA body due to differences in the clinical part of HTA (REA) and/or the economic part of HTA[136].

[133] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf

[134] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf

[135] GÖG-LSE Study, Section 7.1.13

[136] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf.

Abbreviated indication	Brand name (generic)	HTA recommendation					
		GEMANY	THE NETHER-LANDS	FRANCE	ENGLAND/ WALES	SCOTLAND	POLAND
Bone metastases from solid tumours	1. Denosumab	Not assessed	Equal benefit	Added benefit Equal benefit	Positive	Not assessed	Negative
Breast cancer	2. Eribulin	Equal benefit Equal benefit	Added benefit	Added benefit	Negative	Negative	Negative
	3. Pertuzumab	Added benefit	Not assessed	Added benefit	Not assessed	Negative	Positive
Colorectal cancer	4. Aflibercept	Added benefit	Not assessed	Equal benefit	Negative	Negative	Positive
Gastric cancer	5. Tegafur / gimeracil / oteracil	Not assessed	Lesser benefit	Lesser benefit	Not assessed	Positive	Negative
Melanoma	6. Ipilimumab	Added benefit	Added benefit	Added benefit	Positive	Negative	Positive
	7. Vemurafenib	Added benefit	Added benefit	Added benefit	Positive	Negative	Positive
	8. Dabrafenib	Equal benefit	Not assessed	Equal benefit	Positive	Positive	Positive
Non-small-cell lung cancer	9. Afatinib	Added benefit Added benefit Equal benefit Lesser benefit	Not assessed	Equal benefit	Positive	Positive	Positive
	10. Crizotinib	Equal benefit	Not assessed	Added benefit	Negative	Negative	Negative
Prostate cancer	11. Cabazitaxel	Added benefit Added benefit	Added benefit	Added benefit	Negative	Negative	Negative
	12. Enzalutamide	Added benefit Added benefit	Not assessed	Added benefit	Positive	Positive	Positive
	13. Abiraterone	Added benefit	Equal benefit	Added benefit	Positive	Negative	Positive
Renal-cell carcinoma	14. Axitinib	Added benefit	Not assessed	Added benefit	Positive	Negative	Positive

Table 3.1 Conclusion of HTA reports across a sample of cancer drug[137]s

3.2.2. Duplication of work for national HTA bodies

The duplication of work refers to assessments of the same technology being conducted in parallel or with a similar time frame by HTA bodies in different Member States[138].

According to the survey carry out by GOG-LSE study,

«costs for HTA bodies range from an average of EUR 35 000 for a REA produced mainly by an HTA body and EUR 20 000 per REA produced by industry and reviewed by an HTA body to EUR 95 000 for a full HTA produced by an HTA body and EUR 40 000 for the cases in which the full HTA is produced by industry and reviewed by HTA body."

Moreover, the current low uptake of joint REA undertaken by EUnetHTA influences on the results in duplication and incurs additional work and costs. As

[137] GÖG-LSE Study, Section 7.1.13

[138] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf.

described in the Impact Assessment, in a sample of 20 pharmaceuticals, 8-15 reports were conducted by different Member States for each individual product[139]. Different outcomes/conclusions negatively affect business predictability and contributes to delays and inequalities in patient access.

In the public consultation, several Member States confirming the increasing trend towards applying HTA to support decision-making for medical technologies. One of these Member States is Italy which expressed concerns in this field also in the post adoption meetings with the European Council and Member States' Health Attaches. In response to the growing need of HTA for medical technology in Italy was adopted "national programme for HTA on medical technologies". As described on the Ministry of Health web site, the programme has established a Steering Committee, coordinated by the Ministry of Health and gathering key national agencies and the regional HTA bodies, which have expertise and perform HTA[140]. The final aim of the projects to increase the availability of HTA for medical technologies in order to provide *"guidance to decision makers, increase consistency and avoid duplication of assessment for better use of resources[141]"*. The same path was followed by the United Kingdom that in last year has established a special programme for assessment of medical technologies.

However, despite the fact that a joint European report was done, most Member States still performed the assessment of the same technology at national level. Due to this the uptake of joint EU outputs at national level remain low. The low uptake was confirmed by evaluation report of EUnetHTA Joint Action 2[142] as well as by the HTA GOG-LSE Study which points out that the most national HTA organizations did not make the correct use of the resulting output. Across the

[139] Ihttps://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf.

[140] http://www.salute.gov.it/portale/temi/p2_6.jsp?id=1202&area=dispositivi-medici&menu=tecnologie

[141] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf.

[142] EUnetHTA JA2. WP3 DELIVERABLE Report on evaluation of project completion including assessment of impact on secondary users of HTA information p.23.

above-mentioned studies and the online public consultation[143] has been outline the main hurdles to uptake.

Legal uncertainty is identifying as the main element hindering the uptake of the joint work. Uncertainty around the status/relevance of the joint outputs in the context of national HTA frameworks constitutes a major reason for the current low uptake[144]. In each of 26 Member States there is a particular legal/procedural framework that regulate the HTA within preparation and uptake. National law gives the key provision related to the roles and responsibilities of the HTA bodies and the HTA assessment while further details are provided by the administrative provision. Oppositely, the legal status of joint outputs coming from the EUnetHTA Joint Action and their relevance from national HTA process is not defined, making difficult for national decision maker to adapt their national framework to joint outputs[145].

The timely availability of the joint uptake make for national decision making has been underlined as another important limitation leading to the low uptake. In fact, for Member States timelines are enforced by legal procedure HTA framework while the EUnetHTA Joint Actions have so far not been able to ensure timeliness of joint outputs to meet Member States need[146]. Additionally, Member States will only use a joint REA report if the quality of the report is high. In this regard, in the online consultation some respondent highlight that the first reports prepared under the first two EUnetHTA Joint Actions were of suboptimal quality. Moreover, there are others issues such as the topic prioritization for the joint work and the language barrier. Several Member States have noticed that there have been insufficient for topics prioritization in the EUnetHTA Joint Actions so far. In fact, some topic has been relevant for the authors of the work package but have not met the needs and priorities of all HTA bodies. In addition to above, as it is mentioned in the Impact

[143] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

[144] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf.

[145] Ibidem

[146] Ibidem

Assessment, the low uptake decreases the readiness of industry to submit new technologies for the joint assessment. Therefore, the preparation of a submission file costs financial and human resources, and such investment cannot be done if the joint assessment has not relevance for the national procedures.

In conclusion, the current duplication of works and the low uptake imply that investment into the cooperation both in terms of resources from EU budget and the human resources from Member States are not used optimally[147].

3.2.3 Unsuitability of HTA cooperation

Nowadays the EU cooperation on HTA is project-based. This means that every financial cycle its funding needs to be secured, re-negotiated and there is no guarantee for continuing the activities in a long-term. In these large projects substantial resources and time are spent on organizational issue[148]. Among the limitations of the current model of cooperation most cited by the public consultation were the lack of flexibility of the framework for EU-funded projects which require high efforts for the preparation of the proposal, delays in performing joint work which effected the availability of joint reports, insufficient commitment from all partners to use the output, uncertainty about the quality of joint works and lack of knowledge on the impact on decision-making. Moreover, organizations representing stakeholders such as academia, stakeholders and consumers representatives expressed their concerns on the limited duration in time and the lack of a sustainable funding mechanism of the current EU cooperation on HTA[149].

[147] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf.

[148] The Joint Action 3 involves 81 participants and benefits from an EU contribution of approximately EUR 16.000.000.

[149] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf.

3.3 Policy objectives

As described above, the diversity and multitude of approach to HTA across the Member States means that, due to their scale and effects, only action at European Level can eliminate the obstacle described. In fact, as described by the European Commission press realised, while the on-going cooperation (i.e. EUnetHTA Joint Actions and HTA Network) has illustrated benefits of EU cooperation, the current model has not contributed to the removal of the fragmentation of the internal market, or the duplication of assessments[150]. Without an EU initiative, it is unlikely that long-term cooperation on HTA between Member States would be strengthened, with a potential risk of losing the results achieved until now. By carrying joint clinical assessments, economies of scale, greater business predictability, increased quality and consistency and improved transparency for patients would be achieved in the long run[151].

The Impact Assessment report has identified two domains of the Health Technology Assessment (FIG. 3.2): clinical domain and non-clinical domain. The first one lends themselves to a common assessment at EU-level, while the non-clinical assessment have more country-specific elements. Making this distinction, this initiative

«*will maximise the EU added value while at the same time ensuring an approach to HTA assessment that is proportionate and in keeping with the principle of subsidiarity by leaving Member States to continue carrying out the parts of HTA better achieved at national level*[152]»

[150] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_exefinal_en.pdf

[151] Ibidem

[152] Ibidem

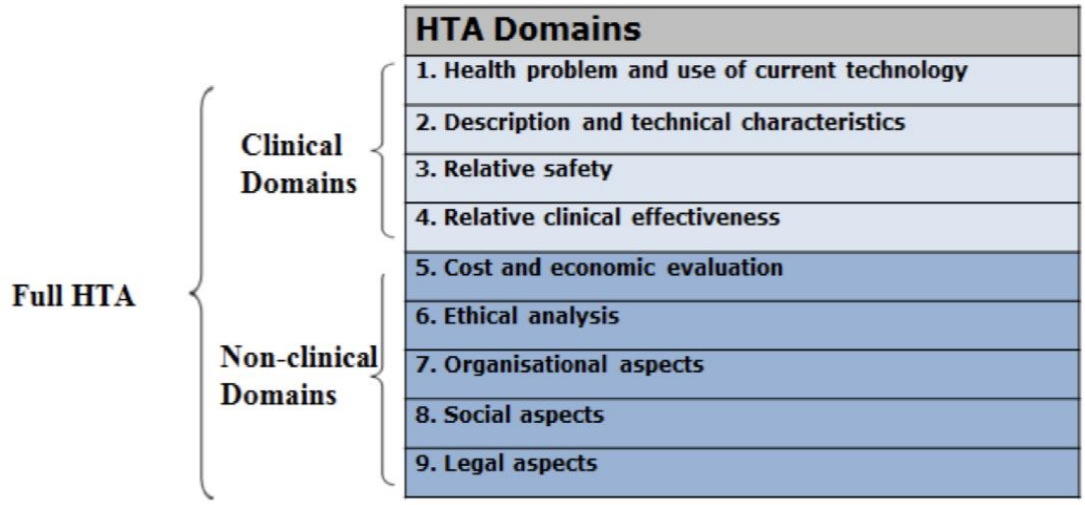

Figure 3.2 HTA domains (based on EUnetHTA HTA Core Model[153]

Moreover, it was underline the differences between the pharmaceutical and the medical technologies sectors, in particular in relation with the role that the HTA plays in the two sectors and the lower level of duplication/parallel process compared with pharmaceuticals. Thus, in order to ensure that a proportionate approach is taken, such differences are reflected in the policy options design and comparison. Finally, before to describe the policy objectives, it is important underline that the principle of subsidiarity is ensured in the initiative by fully respecting Article 168(7) TFEU according to which

«*Union action shall respect the responsibilities of the Member States for the definition of their health policy and for the organisation and delivery of health services and medical care. The responsibilities of the Member States shall include the management of health services and medical care and the allocation of the resources assigned to them. The measures referred to in paragraph 4(a)*[154] *shall*

[153] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf.

[154] Measure setting high standards of quality and safety of organs and substances of human origin, blood and blood derivatives; these measures shall not prevent any Member State from maintaining or introducing more stringent protective measures.

not affect national provisions on the donation or medical use of organs and blood[155]».

In the Impact Assessment the policy objectives, what this initiative expected to achieve, were divided in three categories: general, specific and operational. The general objectives of the initiative are to ensure a better functioning of the internal market of health technologies and to contribute to a high level of human health protection[156]. The specific objectives are to improve the availability of innovative health technologies for EU patients, to ensure efficient use of resources and strengthen the quality of HTA across the EU and to improve business predictability[157]. Finally, the operational objectives (FIG. 3.3) are focus on promote convergence in HTA tools, procedures and methodologies, reduce duplication of efforts for HTA bodies and industry, ensure the uptake of joint outputs in Member States and ensure the long-term sustainability of EU HTA cooperation[158].

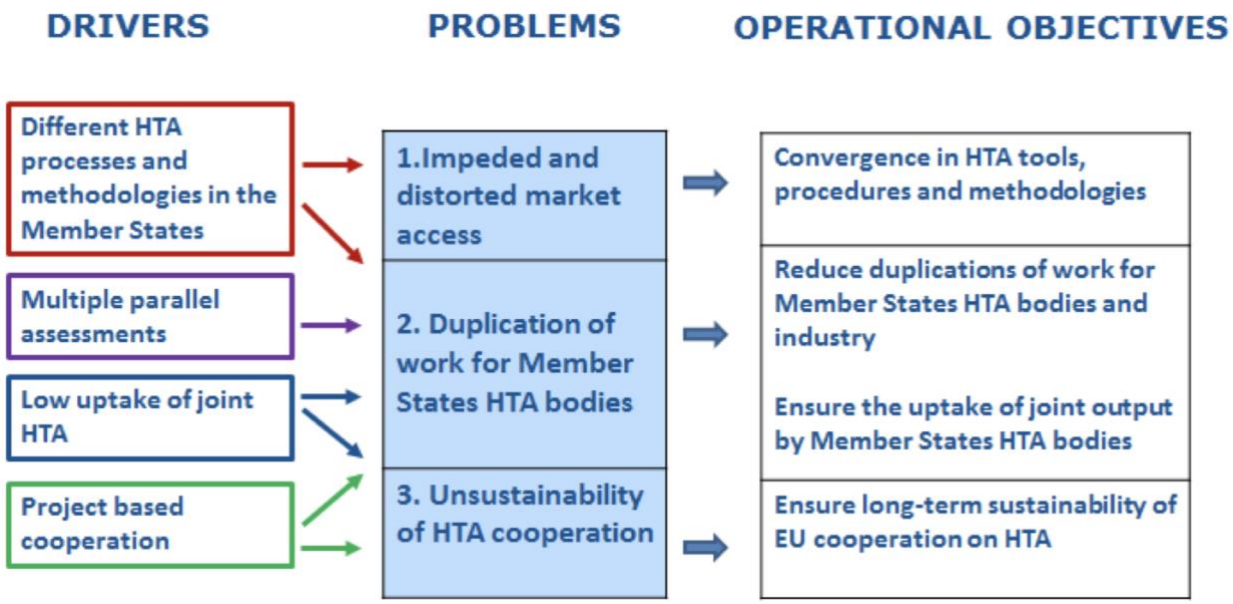

Figure 3.3 Intervention logic.

[155] The Lisbon Treaty. Treaty of the Functioning of the European Union. Part 3, Title XIV, Art 168 (7).

[156] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf.

[157] Ibidem

[158] Ibidem

3.4 Policy Options

In conformity with the identified shortcoming, experiences with the current cooperation and stakeholders' consultation, were identified five key principle for constructing the policy options[159]:

- The need to build on existing structures, activities and achievements and maintain a Member States driven approach;
- The need to address the specificities of the different sectors: pharmaceuticals, medical and other technologies;
- Ensure a high level of quality, transparency and independence (scientific and financial);
- Ensure the engagement of stakeholders, in particular patients, health care professionals and payers;
- Support the development of HTA capacities at national level.

In the Inception Impact Assessment[160] the policy options identified were five (PO 1-5). However, on these, policy option 5 was discarded upfront. The legislative option which includes joint full HTA repots[161] was included in the analysis of options conducted in the GOG-LSE Study and in the public consultation. Therefore, form the input received in several fora as well as in the online consultation, become clear that such an option is not realistic. Notwithstanding, there is a broad agreement that voluntary cooperation would be useful to increase consistency and predictability of the assessment, the development of EU legislation mandating joint full HTA reports at EU level would bring more

[159] http://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf

[160] Ibidem

[161] Joint production of HTA reports which cover clinical and non clinical domains.

challenges than benefits[162]. Moreover, "option 5" was discussed in the GOG-LSE study, in which raised concern as regards its proportionality, Member States' responsibility under the above-mentioned Art 168(7) TFEU and its feasibility. Thus, this option is not discussed in the Impact Assessment.

		Non-legislative		Legislative		
		PO 1	PO 2	PO 3	PO 4	
		No EU action after 2020 (baseline)	Project-based cooperation on HTA activities	Permanent cooperation on common tools, procedures and Early Dialogues	Permanent cooperation on common tools, procedures and Early Dialogues and REA	
					4.1 REA (MS opt-in)	4.2 REA (all MS)
Joint outputs	Common tools and procedures					
	Early dialogues					
	Joint REA					
	Joint Full HTA					
Technologies covered			Pharmaceuticals, medical and other technologies	Pharmaceuticals, medical and other technologies	Pharmaceuticals, medical and other technologies	
Governance		No EU support	Project based cooperation	Permanent structure	Permanent structure	Permanent structure
Financing		No EU support	EU+MS	EU+MS+fees from industry (for early dialogues depending on chosen governance model)		

Table 3.2 Overview of policy options[163]

3.4.1 Policy Option 1 (Baseline scenario). No joint Actions After 2020

The baseline scenario assumes that after the current EUnetHTA Joint Action 3 will end in 2020 there would be no further Joint Action in this topic. This choice is the consequences that although the Joint Actions have been successfully demonstrated a proof of concept, a continuation on fourth Joint Action is considered to be both ineffective and unrealistic[164]. Moreover, it was also indicated by the Court of

[162] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[163] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[164]Ivi pp. 70.

Auditors which considered that this type of actions or projects is not supposed to be renewed too many times[165].

Thus, under the policy option 1, the European cooperation would be limited to the high-level strategic policy discussions within the HTA Network, which mainly consist of meetings between Ministries of Health and national HTA organizations in order to discuss the policy developments which are relevant to HTA both a national and European level[166]. However, without EU stable cooperation, joint early dialogues would be limited to HTA bodies to HTA bodies participating to the parallel scientific advice procedure offered to developers by EMA. At the same time regional cooperation is expected to continue on a voluntary basis, particular in relation to the production of some joint assessment to be used in joint price negotiations and procurements efforts. On the other side, different HTA regional cooperation are developed across the EU, duplication between those are likely to occur as well as divergences as regards process and methodologies, in addition to the continued national divergences [167]. However, the HTA Network[168] is expected to continue to meet twice per years to share high level national experiences.

[165] European Court of Auditors, Special Report Dealing with serious cross-border threats to health in the EU: important steps taken but more needs to be done, 2016 https://www.eca.europa.eu/Lists/ECADocuments/SR16_28/SR_HEALTH_EN.pdf

[166] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[167] Ibidem

[168] Established under the Directive 2011/24/EU

3.4.2 Policy Option 2. Project-based cooperation on HTA activities

As described in the Impact Assessment, this option foresees voluntary cooperation supported by the EU funding organised in the form of project(s)[169] other than Joint Actions[170]. The project would finance by the Health Programme or any other EU financing instruments. Such a model would implement by project(s) through competitive calls for proposal in line with the priorities and Eu added value criteria identified by the European Commission. Differently from EUnetHTA Joint Action it would be based on competitive calls which may result in more than one group (Consortia) of Member States competition with each other. The calls would support the enhancement of a define number of joint outputs in a given timeline. The selected project is supposed to be 38-48 months, during which it would need to deliver the planned out[171]. Moreover, in order to facilitate the commitment from technology developers, their European trade associations could be included in the project. Through the project SEED (2012-2015) was tested a similar project-based model for Early Dialogues and it could address some of the shortcoming identified in the Joint Action EUnetHTA such as delays, high number and heterogenous profile a number of participants and the inconsistency of the quality[172]. Therefore, Policy Option 2 foresees no EU legal framework and the governance model would be a project secretariat manged by one of the beneficiaries of the winning consortium or consortia. It is expected that national HTA bodies would take up the coordination role and distribute and monitor tasks and responsibilities between partners to ensure the delivery of the agreed joint outputs[173]. This option expects also a top-down approach with the Commission in the led, identifying priorities,

[169] This could be done as one project, subsequent projects or multiple parallel projects. The assessment of Policy Option 2 in this report based on the assumption of one project in line with the GOG-LSE study.

[170] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[171] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[172] Ibidem

[173] Ibidem

monitoring the projects and disseminating the results. In conclusion, the financing of this option is expected to rely on the EU budget and Member States' co-financing.

3.4.3 Policy Option 3. Permanent cooperation on common tools, procedures and early dialogues.

JOINT OUTPUTS	TECHNOLOGIES COVERED	INSTRUMENT	GOVERNANCE	FINANCING
Technology specific reports • **Early dialogues** with health technology developers **Common tools and procedures** • Methodologies • Horizon scanning • Procedural framework • Submission and other templates • Database • IT tools • Training and capacity building	• **Pharmaceuticals** • **Medical technologies** • **(Other technologies)** Early dialogues would be initiated by the industry. In case the number of requests exceeds the Member States capacity to respond to the requests, prioritisation criteria are needed (e.g. unmet medical; potential impact on patients, public health, or healthcare systems; significant cross-border dimension/major Union-wide added value)	**Legislation** Mandatory Uptake by HTA bodies of joint outputs	**Permanent structure**	**EU budget** **+** **MS in kind contributions** **+** **Industry fees for early dialogues** (depending on the governance structure chosen)

Table 3.3 Overview of policy option 3[174].

As it is possible to see in the Table 3.3, in the policy option 3 the joint outputs would include early dialogues with health technology developers and several common tools and procedures specified in the table. In particular, common procedures will be aimed to ensure the involvement of patient and external expert in the HTA process, avoiding conflicts of interest and ensuring transparency. In this option, all types of health technologies[175] would be covered and as early

[174] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[175] Subject to selection and prioritization criteria in accordance with the needs of Member States.

dialogues would be initiated by the industry, it cannot be guaranteed that all technologies will benefit from them.

Moreover, the instrument used to implement PO3 would be a "new" EU legislative framework which would ensure the mandatory uptake by HTA bodies of the common tools and procedures and of joint early dialogues[176]. These tools, procedure and early dialogues would have related to the clinical aspects of HTA and supporting the assessment at Member State level of clinical domain of HTA (REA). Moreover, there would be the mandatory uptake of both common procedures/tools and early dialogues. This imply that on one side Member States shall use these basic tools and procedures to conduct joint early dialogues and clinical HTA work at national level to facilitate the cooperation and to ensure a high quality. On the other side Member States shall use the joint early dialogues in the same way that they would use a national early dialogue[177].

The governance model would be ensured by a central structure which could provide: Administrative, scientific and ITA support to deliver joint outputs of high quality, in a transparent, independent and timely way, with appropriate involvement of stakeholders. The financing of this option foresees the EU budget, some kind contributions from Member States and for the early dialogues a fee from industry would cover the costs of the experts and the overhands needed to support the production of this specific joint outputs[178].

Therefore, an important new element of this policy option is the abrogation of Article 15 of Directive 2011/24/EU, since it would not be compatible with the legislative approaches described above[179]. As described in the Impact Assessment "*The HTA Network foresees fully voluntary cooperation, the output of the cooperation has no legal status. While Art 15 would be deleted from Directive*

[176] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[177] They should not repeat at national level an early dialogue which has already been conducted jointly.

[178] Industry fees would only be possible if the tasks are carried out by an EU agency.

[179] Ihttps://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

2011/24/EC, the foreseen new Legal framework would maintain and further develop the objectives defined by the article, and add provisions to ensure their achievements, which is currently limited. It will also re-introduce key elements already foreseen by the article such as the involvement of stakeholders in the cooperation and it will use similar working methods already applied such as the setting up of dedicated Member States experts' groups/subgroups to develop the specific outputs, it will further develop its good governance principles in a dedicate governance structure. In addition, the new Legal framework would provide a more stable framework for granting aid to support the cooperation.[180]*''*

3.4.4 Policy Option 4. Permanent cooperation on common tools, procedures, early dialogues and joint REA.

JOINT OUTPUTS	TECHNOLOGIES COVERED	INSTRUMENT	GOVERNANCE	FINANCING
Technology specific reports • **Early dialogues** with health technology developers • **Relative Effectiveness Assessment (REA)** **Common tools and procedures** • Methodologies • Horizon scanning • Procedural framework • Submission and other templates • Database • IT tools • Training and capacity building	• **Pharmaceuticals** (centrally authorised pharmaceuticals + other pharmaceuticals prioritised by Member States) • **Medical technologies** (prioritised by Member States based on : - potential high risk (i.e. devices undergoing the EU scrutiny mechanism) or - potential impact on public health and health systems (e.g. addressing unmet medical need, potential to transform the organisation of care, high budget impact) • **(Other technologies)**	**Legislation** Mandatory Uptake by HTA bodies of joint outputs	**Permanent structure**	**EU budget** **+** **MS in kind contributions** **+** **+** **Industry fees for early dialogues** (depending on the governance structure chosen)

Table 3.4 Overview of policy option 4[181].

[180] Imphttps://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[181] Ibidem

Policy option 4 foresees the same joint outputs included in the policy option 3 plus the joint REAs. The scope of the Joint REAs are different for pharmaceuticals and medical technologies.

Pharmaceuticals' joint REAs would comprise centrally authorised pharmaceuticals and other pharmaceuticals prioritised by Member States due to their high value. Therefore, for medical technologies the scope of the joint REAs comprises those that are prioritised by Member States based on their potential risk or potential impact on public health[182].

As in the previous policy option, the instrument used to implement this option would be a new EU legislative legal framework with the addition of the mandatory uptake of joint REAs. This implies that Member States would use the joint assessment reports in the same way as a national assessment is used nowadays and that REAs should not repeated at national level.

However, Member States would be free to assess other non-clinical HTA domains at national level and would continue to draw the overall conclusion on the basis of the joint clinical and national, non-clinical, assessment parts.

The governance structure would be similar to OP3 but taking into account the extended scope in terms of joint outputs, joint REA. In fact, for the joint REAs, Member States experts, as described in the Impact Assessment, would act as author/rapporteur and co-author/co-rapporteur would carry out the clinical assessment of the application/dossier submitted by industry and prepare a joint assessment report. A committee/group including experts nominated by Member States would thereafter examine the draft and approve the joint report which would then be incorporated in national HTA processes[183]. Moreover, Option 4 could be divided in two sub options:

[182] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[183] Ibidem

1. PO 4.1- an "opt-in" system. With respect to joint REA, this system would allow Member States some flexibility to decide if or when start participating in the EU-level system of joint REA, depending on their situation in terms of needs of adjusting national law, practice and so on. Moreover, if Member States decide to not participate to joint REA system they would still obliged to use their common tools and procedures (PO3) when carrying out their own REA.
2. PO 4.2 is basically the same of option 4.1 with the differences that this option would be applicable to Member States with no possibilities to opt in later or stay out[184].

3.5 Preferred policy option

After an in deep analysis of each policy options described above, the impact assessment reports present the preferred policy option, which has provided the basis for the contest of the proposal. This preferred policy option was carry out comparing against the criteria of effectiveness[185], efficiency[186] and coherence[187], while also respecting the principle of subsidiarity and proportionality. The result of this study shows that option 4.2 receives the highest scores when comparing with the other options. However, this option implies certain risk considering the view of the Member States which need adequate time to adapt to the system. This is addressed by integrating elements from other policy option, as policy option 2 and 4.1 and allowing for some adjustments based on the comments received from the stakeholders. In fact, the EU legislative framework foreseen by this option will include provision to ensure that Member States have adequate time to adapt their national HTA framework to the new EU system[188]. The aim of this adjusted is to

[184] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

[185] The extent to which the option would achieve the objective.

[186] Balance between cost vs benefits.

[187] With the overarching objectives of EU policies.

[188] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

take into account the diversity of HTA frameworks across the EU and the view of the public administrations[189]. Thus, after the date of application, a transitional period is foreseen during which Member States can delay their participation in joint REA and joint early dialogues. There would also be a progressive implementation of the joint work. In particular, the product scope for pharmaceuticals foreseen by the preferred option will be implemented in a progressive manner and this implies that "all pharmaceuticals identified in the scope are expected to go through a joint REA once the system is fully operational[190]". While for the medical technologies the system will remain based on a prioritization mechanism ensuring that joint REA are only performed on medical technologies selected by Member States.

The governance of this option, described in the figure below, is central secretariat hosted by the European Commission. Compared with the other governance option, it will offer a solution for san initial phase characterised by a limited number of human resources and at the same time a stable structure for the EU cooperation on HTA.

[189] https://ec.europa.eu/health/technology_assessment/eu_cooperation_en

[190] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

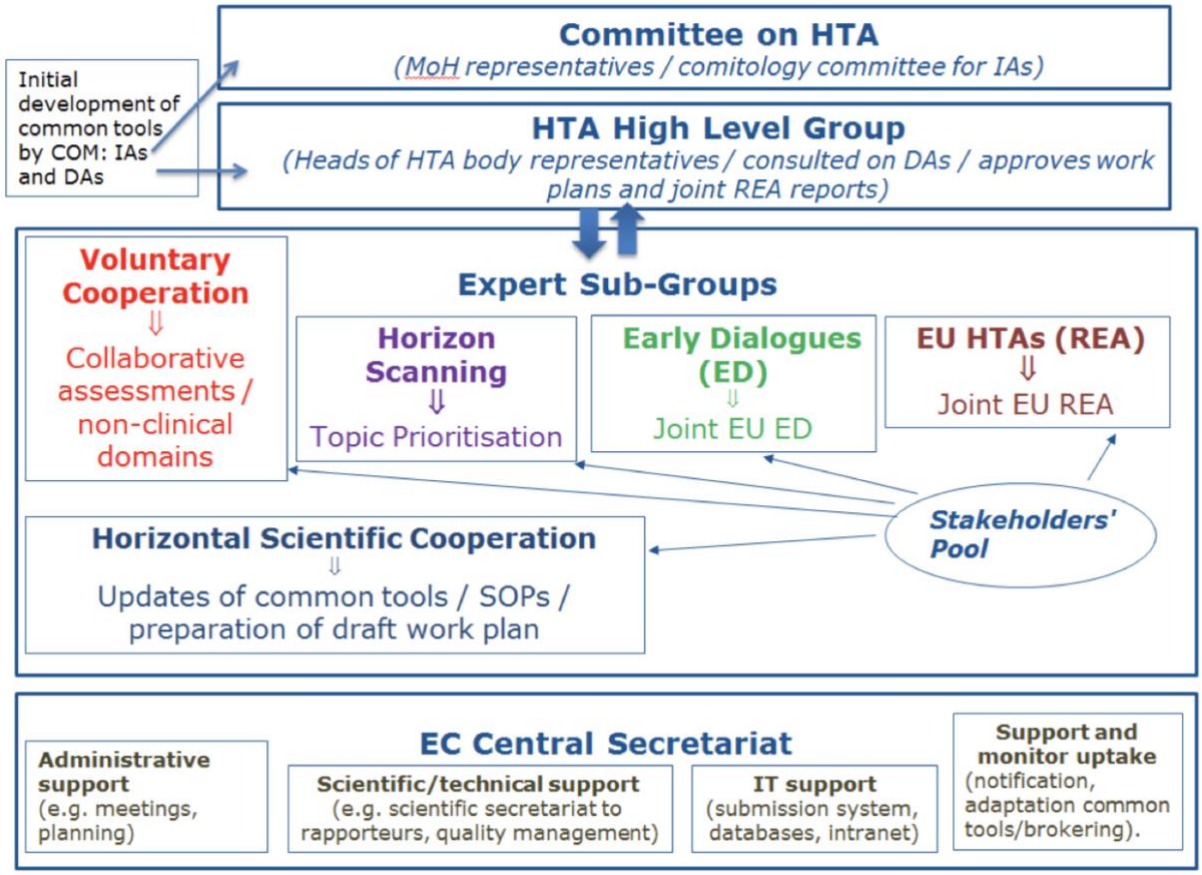

Figure 3.4 Diagram of the governance arrangement for the preferred option[191].

The main task of the centre secretariat will be:

- Administrative support
- Scientific/technical support
- IT support

The HTA high level group broad representatives of Member States' HTA bodies would manage the overall governance and would meet regularly to discuss the annual work programme, provide guidance and steer the cooperation[192].

[191] Ivi, pp 78.

[192] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

Moreover, the scientific-technical work of producing the joint outputs would be carried out by experts nominated by Member States' authorities organised in Committees/groups dedicated to the various types of joint work[193].
In conclusion the preferred option foreseen a review clause. This will allow a review of the new system once it has been fully operational for a sufficient period of time.

3.6 Legal Proposal

The proposal for a regulation of the European Parliament and of the Council on health technology assessment and amending Directive 2011/24/EU was presented by the European Commission the 31st of January 2018. It aims, as declared by the Commissioner Andriukaitis is

« *to ensure patients will have a timely access to innovative health technologies and to improve the sustainability of health system in the EU.* »

The proposal is based on Art 114[194] of the Treaty on the Functioning of the European Union (TFEU). This choice was based on the fact that health technologies such a medicines and medical device are products which benefit from the principle of free movement of goods within the internal market, while the current lack of sustainable EU cooperation on HTA contributes to distorted market access for health technologies. However, this article is used due to both the objectives and contest of the proposal. The main objectives of the proposal are to ensure a better functioning of the internal market and contribute to a high level of human health protection. This is to be achieved by improving patients' access to the most innovative health technologies in a more timely and equitable manner across EU. Moreover, in line with Art. 114(3) TFEU, a high level of human

[193] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_report_en.pdf

protection has been considered in the preparation of the proposal which is expected to improve the availability of innovative health technologies for EU patients.

The proposal takes the form of a new Regulation. As explained in the explanatory memorandum of the proposal, this type of instrument is considered to be most suitable considering that a key element of the proposal is the establishment of procedures and structures for the cooperation on joint work at Union-level[195].

To sum up the key elements of the proposal it is important to underline that the system envisage by the Commission's proposal will be a Member States driven. Member States HTA organizations will coordinate the work and jointly develop outputs while the Commission will play a supportive role. Transparency plays an important role in the proposal, for this reason the Commission shall develop and maintain an IT platform to facilitate information sharing. It will be publishing on the IT platform, which would also include tools for HTA bodies to share early information on their planned and on-going assessment, the lists of both completed joint clinical assessment and assessed health technologies. However, transparency[196] is also about involvement of stakeholders and this should happen at technical level, during the presentation of the Joint Clinical Assessment and Joint Scientific Consultations reports, and at strategic level, when horizontal documents and reports such as the work programme, guidance documents.

[195] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/com2018_51final_en.pdf

[196] Article 7 and Article 22 provide the legal basis of transparency and independence

3.6.1 Detailed explanation of the provision of the proposal

Chapter I	General Provision
Chapter II	Joint Work on HTA at Union Level

Section 1	Section 2	Section 3	Section 4
Joint clinical assessment	Joint scientific consultation	Emerging health technologies	Voluntary cooperation on HTA

Chapter III	Rules for Clinical Assessment
Chapter IV	Support Frameworks
Chapter V	Final Provision

Tab. 3.5 Framework of the Proposal

As describe in table above, the proposal is divide in five chapters consisting a total of 36 articles. In chapter I is outline the subject matter of the proposal and defines the key terms used in the Regulation[197]. In particular, the Article 3 formally established the Members States Coordination Group on Health Technology Assessment, along with its composition, role and responsibilities to oversee the joint work. This Joint work is based on the annual work programme of the Coordination Group which is describe in the Article 4.

[197] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/com2018_51final_en.pdf

The joint work is outline in the chapter II (Art.5-Art.17), which establishes the four pillars of the of the future cooperation between Member States at Union level, in other words, joint clinical assessment, joint scientific consultation, emerging health technologies and voluntary cooperation on HTA. As explain above, the work will be Member States driven through the Coordination Group. In the last section of this chapter (article 19), the proposal provides the

«*cooperation and the exchange of scientific information among Member States*[198]» on four particular situations:

1. Non-clinical assessment;
2. Collaborative assessment on medical device;
3. HTA on health technologies other medicinal product and medical device;
4. The provision of additional evidence necessary to support the HTA.

The third chapter lays down common rules for carrying out clinical assessments at Member States level which will then be developed in detail in tertiary legislation[199], with the aim of harmonize the clinical assessment approach across Member States.

Chapter IV, on the other hand, designs the support framework which will support the joint work at EU-level. It is also established a stakeholder network (Article 26). According with the article, this network is established by the Commission through an open call for applications and a selection procedure. Moreover, the stakeholder network will support the Coordination Group in the identification of patient and clinical expertise for the work of its subgroups. The last chapter outlines the timeline for the implementation of the regulation (FIG.3.5).

[198] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/com2018_51final_en.pdf

[199]Ibidem

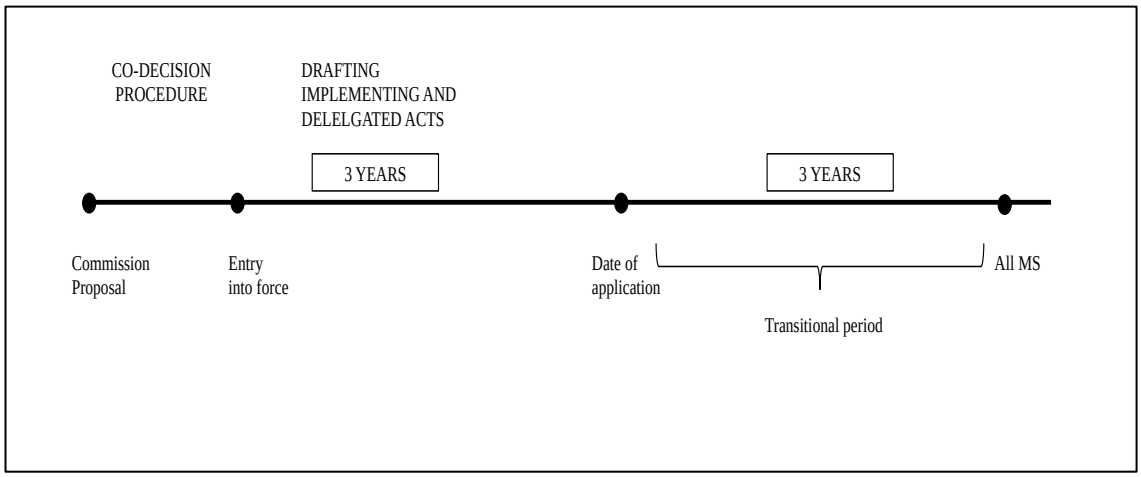

Figure 3.5 Phase-in approach

Following the entry into force, it is proposed a period of three-years in order to allow the development of all tertiary legislation provided for in the proposal for the joint work. After the date of applications, a further three years transitional period is necessary to allow for a phase-in approach in terms of the work undertaken and to allow Member States to fully adapt to the new system[200]. However, during this transitional period Member States have the possibility to delay their participation of joint work. Additionally, in this chapter also includes the safeguard clause (Article 34) and in the following article the amendment of the Directive 2011/24/EU.

3.7 Expected results

Starting from Member States authorities, they will benefit from a better evidence for a national decision-making, due to the high quality and timely joint clinical assessment reports. Moreover, as described in the legal proposal[201], focusing joint assessment on clinical data makes them relevant to all decision-makers without affecting national competence. There will be also a cost saving as well as an

[200] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/com2018_51final_en.pdf

[201] Ibidem

optimization of resources. Finally, a pooling of resources and expertise to address more health technology.

For patients and consumers, an EU HTA system would increase the transparency through the publication of the joint clinical reports and the involvement of patients in the HTA process[202].

As regards healthcare providers, an EU HTA system would provide, as well as in the patients and consumer, for a framework for their involvement in the HTA process. At the same time, the publication of the joint assessments reports would facilitate access to

«reliable, timely and objective information on health technologies allowing for better informed decisions on the best treatment for their patients[203]».

For industry the proposal would be a positive impact on business predictability through innovation investments. Moreover, it could increase the efficiency of evidence generation and submission, reducing duplication of work.

[202] Common procedure for involving healthcare professionals and providers.

[203] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/com2018_51final_en.pdf

FOURTH CHAPTER

THE STAKEHOLDERS' VIEW ON THE PROPOSAL IN THE PRE AND POST ADOPTION:

A QUALITATIVE ANALYSIS

Operating Procedures, which stipulates procedures for all types of stakeholder involvement. Moreover, it has given an official definition of stakeholder:

"*Groups or organisations which provide considerable insight into views of the groups they represent, and which will be affected by, or have an interest in, and may in a consultative role contribute to the actions or aims of an HTA organisation, project or policy direction*[204]*".*

The Health Technology Assessment Network Stakeholder pool was divided in the following four categories: Patients/consumers, health providers, Payers and Industry. Policy maker and mangers can use stakeholder analysis to identify these key players, predict whether they might support or block the implementation of

[204] https://www.eunethta.eu/ja2-archive/

health reforms; develop strategies to promote supportive action and decrease opposing action before attempting to implement major reform at national, regional local level.

4.1 Methodology

The aim of this chapter is to investigate through a qualitative analysis how each different category of stakeholder perceives the new legal proposal. In particular, which is their position, how it changes from the pre to the post adoption and which are the general main concerns on the proposal.

The permission to conduct the study was obtained from the European Commission, DG SANTE, Unit B4, HTA team. During my internship in the HTA team[205] I had the opportunity to interact with the HTA stakeholder's pool (ANNEX 1) and collect data. The literature used to describe the stakeholder's position before the implementation of the proposal included the public consultation[206] and several bi-lateral meetings[207] held from October 2016 and January 2018. On the other hand, to analyse the stakeholder position on the proposal after the 31st of January, it was used the official statement or official position that nearly every stakeholder published.

Before moving to the analysis of data result, a definition of content analysis should be provided. A content analysis is defined (Berelson, 1952) as

"A research technique for the objective systematic and quantitative description of the manifest content of communication[208]".

[205] From February 2018 to May 2018

[206] The Public Consultation was launched on 21 October 2016. The consultation, which run until 13 January 2017, gathered opinion on the future of EU cooperation on HTA. https://ec.europa.eu/health/technology_assessment/eu_cooperation_en

[207] https://ec.europa.eu/health/technology_assessment/events_en#anchor3

[208] Berelson, B."*Content analysis in communication research."* (1952).

This type of analysis assumes that groups of words reveal underlying themes, and that for instance, co-occurrences of key words can be interpreted as reflecting association between the underlying concepts[209]. The software program named NVivo12. was used in order to conduct this qualitative examination and find out the main groups of words. Based on the above-described division of documents, it was used the "Word Frequency Criteria", of the 100 most frequent words, in order to find out the key words for any categories in each phase. The main groups of words, highlight by NVivo12 programme, would have been the starting point to explain their calls of the preparatory period and the main concern of the post-adoption.

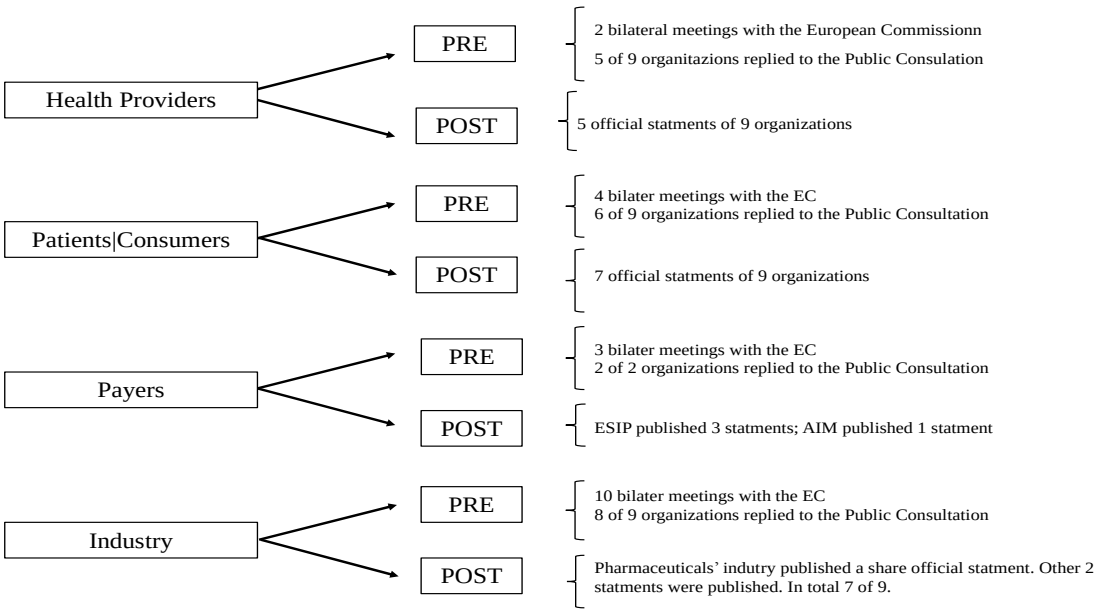

Figure 4.1 overview of all data collect.

[209] Duriau, V. J., Reger, R. K., & Pfarrer, M. D. "*A content analysis of the content analysis literature in organization studies: Research themes, data sources, and methodological refinements."* Organizational Research Methods, 10(1), 5-34. (2007).

4.2 Healthcare Provider

Looking at the data collect of health providers, it is possible to notice that they have not been very active in the preparation phase. Five of nine replied to the Public Consultation and there have been just two bilateral meetings with the European Commission. However, Healthcare providers' official positions on the legal proposal, published after the 31st of January 2018, are five on nine organizations. These statements were published by: European Public Health Association (EUPHA)[210], European Association of Hospital Pharmacists (EAHP)[211], European Forum of Primary Care (EFPC)[212], Comité Permanent des Mèdecins Européens (CPME)[213] and the European Hospital and Healthcare Federation (HOPE)[214]. The Council of European Dentist (CED) was the only that have not contributed to the consultation or given any statement post adoption.

4.2.1 Pre-Adoption

The analysis of the above described documents through QSR Nvivo12 (FIG. 4.2 and ANNEX 2) shows which are the top hundred words with the higher weighted percentage.

[210]https://eupha.org/repository/advocacy/EUPH_Statement_on_EU_Commission_Legislative_Proposal_on_HTA.pdf

[211] http://www.eahp.eu/press-room/eahp-response-proposal-regulation-hta

[212]http://www.euprimarycare.org/news/efpc-invited-eu-commissioner-health-food-safety-dr-andriukaitis-editorial-diederik-aarendonk

[213] Request through email

[214]http://www.hope.be/wp-content/uploads/2018/07/HOPE-Position-Paper-on-Health-Technolgy-Assessment.pdf

Figure 4.2 Word Frequency Query. Health Providers. Pre-adoption.

All these key words are liked to each other by bigger themes. *Participation* and *involvement* are related to stakeholders and health providers, such as medical doctors, in the HTA process. The cooperation between the interest part and the governance has to be sustainable over time in order to ensure a transparent system[215]. The importance of *independence* and *transparency*, which have to lead and characterize all the HTA process, was stresses alsol in the public consultation. They welcome the proposal that would help healthcare providers to have access to innovative treatments with the add of a therapeutic value. In relation to the potential funding mechanism of the future EU cooperation on HTA, healthcare providers' associations observed that a mix of EU budget and national

[215] Bilateral meeting CPME 24042017

contributions could provide for stability and predictability[216]. Many respondents were against a funding mechanism based on *industry fees*, due to the high risk of conflicts of interest. They strongly believe that in order to endure the independence of the process, it has to be disconnected from industry fees. This aspect was also highlight in the meeting between CPME and DG SANTE

> *"The independency of HTA EU-wide agency should be ensuring, by disconnecting industry fees from the assessment process"*[217].

with respect to the governance mechanism, the consultation shows that from healthcare providers point of view there is no existing EU agencies suitable for hosting EU cooperation on HTA, however a new agency could be the perfect solution even if it would be too expensive. It was also underlined that the *coordination* should be as concentrated as possible. For this reason, the solution "Member States HTA bodies on rotation basis" would increase the risk of discontinuity[218]. Finally, with regard to the *policy* option for the future EU cooperation on HTA, in the online public consultation, the preferred choice from this category was the voluntary participation with the *voluntary* uptake (Figure 4.1). Subsidiarity of Member States on healthcare system organization and funding is key to ensure the best care to national citizens. Nevertheless, sharing of best practice between Member States are needed in order to innovate and make sure that the health system is able to respond to challenges and future health needs. If it is based on a *voluntary* international cooperation, Member States could build transparent, comprehensive and robust HTA framework.

However, after the consultation, they expressed interest in voluntary participation with mandatory uptake policy option in bilateral meetings with the Commission

[216] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

[217] SANTE meeting with CPME, 24-04-2017, DG SANTE office https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170424_en.pdf

[218] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

consequently , in this way, HTA would come close to Member States competences notwithstanding the several differences among them.

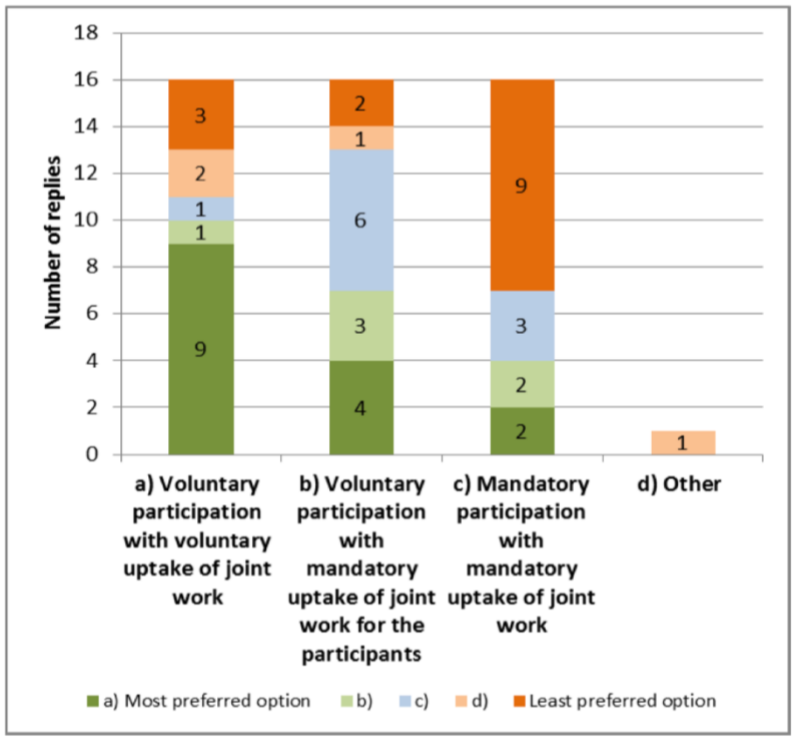

Figure 4.3 Healthcare providers policy option. Public Consultation[219].

[219] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

4.2.2 Post-adoption

Figure 4.5 Word Frequency Query. Health Providers. Post-adoption.

Health providers' organizations welcome the legislative proposal and the intention of the European Commission to further structure the current cooperation, but at the same time they regret that

«*essential aspects are not sufficiently outlined in the proposal regulation but left to implementing and delegating act*[220].»

In particular, there are not clear rules for the joint clinical assessment (in terms of requirements and timeline for the initial assessment). Some of them believe that it is premature to take mandatory for all Member States to participate in the

[220] CPME statement on the European Commission for a Regulation on Health Technology Assessment (HTA) 2018/0018 (COD)

process[221]. Moreover, there is the need to be a *time* limit and more precision on the documents requested. The *timing* of the Joint Clinical Assessment (JCA) is a crucial issue, if the JCA is to be must useful in subsequent decision-making process[222].

From the words' cloud is clear as the stakeholders' involvement is stressed point in their position paper. Provision on transparency and independence are insufficient to guarantee trust in the system as well as the effective involvement of healthcare professionals under each pillar of HTA cooperation. In particular, article 26 on the *stakeholder* network, comma 3 states that:

"The Commission shall organise ad hoc meetings between the stakeholder network and the Coordination Group".

In order to strength the role of the *stakeholder network* and the role of healthcare professional, the Commission shall organise "regular" meetings instead of "ad hoc" meeting. Moreover, the difference nature and resources between European stakeholders should also be taken into consideration.

Transparency as well as independency are the main points mentioned by healthcare providers. Transparency is required in the whole HTA process. In fact, they strongly believe that transparency principle should not be applying only to the results of the joint work but also to methodologies and process in place under each pillar. However, stringent rules on independence are a prerequisite to ensure trust in the system and for this reason it is important to keep industry funding away from all processes of HTA. Regarding the long-term financing of the EU framework on HTA, any shift towards an industry-funded mechanism must be prevent.

[221] CPME statement on the European Commission for a Regulation on Health Technology Assessment (HTA) 2018/0018 (COD)

[222]https://eupha.org/repository/advocacy/EUPH_Statement_on_EU_Commission_Legislative_Proposal_on_HTA.pdf

On the basis of these concerns, several *amendments* were suggested, As it is possible seen in the figure 4.5 and in the Annex 3, the words *"article"* is at top of the list, it was count 79 times. It is followed *by "amendment"* in the third position. Taking into account their participation in the preparatory phase, the number of amendments suggest are pretty high. These evidences were highlighted by the word "welcomes" in the 76th position. Following the main amendments suggest, in particular by HOPE and CPME.

-Article 3 (Points 6 and 7)[223] – The Member States Coordination Group on HTA. For comma (6) a high degree of independence is expected from the member of the Coordination Group. They shall be requested to make a declaration of their direct and indirect interest. While in comma (7) the list of members of the Coordination Group, their appointed representatives and other experts should be made public in order to guarantee transparency.

- Article 6 (Point 1 and 12)[224]- Preparation of the joint clinical assessment. In the Regulation should be a specific time limit for the joint clinical assessment and more precision on the documents requested.

-Article 9 (Point 1)[225] – Update of Joint Clinical Assessment. At the time of marketing authorization, only limited evidence on the added therapeutic values of

[223] *(6) Members of the Coordination Group, and their appointed representatives shall respect the principles of independence, impartiality, and confidentiality. (7) The Commission shall publish a list of the designated members of the Coordination Group and its sub-groups on the IT platform referred to in Article 27.*

[224] *(1) The Coordination Group shall initiate joint clinical assessment of health technologies on the basis of its annual work programme by designating a sub-group to oversee the preparation of the joint clinical assessment report on behalf of the Coordination Group. (12) The Coordination Group shall approve the final joint clinical assessment report and summary report, wherever possible by consensus or, where necessary, by a simple majority of Member States.*

[225] *(1) The Coordination Group shall carry out updates of joint clinical assessments where: (a) the Commission Decision to grant the marketing authorisation of a medicinal product referred to in Article 5(1)(a) was conditional on the fulfilment of additional post-authorisation requirements; (b) the initial joint clinical assessment report specified the need for an update once additional evidence for further assessment is available.*

a medical product is available. Thus, health technology developers should therefore be requested by the Coordination Group to collect data evidence.

Article 11 (Point 1)[226] – Adoption of detailed procedural rules for joint clinical assessment. The tertiary legislation should be limited

Article 34 (Point 1)[227]- Safeguard Clause. In this case Member States should have the possibility to preform they own clinical assessment at national level.

[226] *The Commission shall develop, by means of implementing acts, procedural rules for: (a) submissions of information, data and evidence by health technology developers; (b) the appointment of assessors and co-assessors; (c) determining the detailed procedural steps and their timing, and the overall duration of joint clinical assessments; (d) updates of joint clinical assessments; (e) cooperation with the European Medicines Agency on the preparation and update of joint clinical assessments of medicinal products; (f) cooperation with the notified bodies and expert panels on the preparation and update of joint clinical assessments of medical devices.*

[227] *Member States may carry out a clinical assessment using means other than the rules provided for in Chapter III of this Regulation, on grounds related to the need to protect public health in the Member State concerned and provided the measure is justified, necessary and proportionate as regards achieving that aim.*

4.3 Patients-consumers organizations

Patients and consumers organization have been very active on the proposal, in particular in the post-adoption phase. In fact, after the 31st of January seven on nine organizations published their official statement. Notwithstanding the two remaining organizations such as European Institute of Woman's Health (EIWH) and the International Diabetes Federation European Region (IDF) have not an official opinion, they and full member of European Patients' Forum (EPF) and they share is view on proposal.

4.3.1 Pre-Adoption

Figure 4.6 Word Frequency Query. Patients and Consumers' organization. The pre-adoption.

As being their representatives, it is not a surprise that the main word is "*patient*",. In the public consultation Patient and Consumers organizations welcomed the proposal, underlining that HTA *cooperation* has to be *straight* in order to decrease

disparities between Member States and reach an equitable access to high quality care. This aspect was underline also by the European Cancer Patients Coalition (ECPC) in a bilateral meeting with the European Commission, 24th of April 2017[228]. According to ECPC:

«stronger EU cooperation in HTA could help in reducing inequalities in access to innovative technologies, in particular in cancer treatments.»

To this regard, they confirmed of a 17 collective law suits in Romania won by 165 cancer patients who had to wait a long period of time to get access to a new medicine[229]. Even, the European Public Health Alliance (EPHA) in a bilateral meeting[230] stressed the importance of *strength* the EU cooperation on HTA as a "gatekeepers" in increasing accessibility to medicines whilst ensuring innovation.

In relation to the potential funding mechanism of the future EU cooperation on HTA, patients and consumers associations emphasised that financing of the EU cooperation on HTA should be based on fundamental principles of *transparency*, diversification, good governance and ethical conduct[231]. For this reason, patient and consumers' organizations observe that a mix EU budget and national contribute could provide an HTA stable system. IN line with the Health Providers, Patient and Consumers' organizations believe that in order to guarantee *independence* of the future HTA evaluation, industry should not be required to pay a fee to have their product assessed.

Looking at the governance mechanism, patients and consumers' associations state that in their opinion and based on its working model with the Member States experts, EMA could be entrusted to host the secretariat of the EU cooperation on HTA[232].

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[228] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170424_en_0.pdf

[229] Ibidem

[230] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20160603_sr_en.pdf

[231] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

[232] Ibidem

«Patients' advocates who followed the development of the EMA since 1995 can certainly agree that the EMA has proven its capacity to integrate new domains and legislations, such as orphan drugs or paediatric medicines; developed robust standard and it has proven its capacity to involve stakeholders[233]"

They strongly believe that for the citizens it would be easier to understand a system in which one single agency is responsible for all aspect related to the entry on the market of medicines and the assessment of other health technologies[234]. The Health Action International (HAI) strongly diverge from the general opinion given by patients and consumers' organizations, expressing opposition to integrating HTA activities in *EMA*. HAI also diverges with regard to the *policy* option for the future EU cooperation on HTA. In fact, almost all the organizations in this category confirm their support for the option mandatory participation with mandatory uptake (FIG 4.6), while HAI express as the most preferred option "voluntary participation and voluntary uptake".

Moreover, several associations support the position of Eurordis, who suggest that

«the option mandatory participation with mandatory uptake could also foresee HTA agency joining on a voluntary basis for developing new HTA methodologies to evaluate costs and economic aspect[235]».

They also outline that it is necessary clarify whether the voluntary/mandatory nature applies also to stakeholders. In this regards they suggest introducing a mechanism, for the industry, which provide an obligation to participate to joint assessment for a selection of health technologies. However, at the same time patients' representatives should be consulted during the HTA process.

[233] EURORDIS PC

[234]https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20160603_sr_en.pdf

[235] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

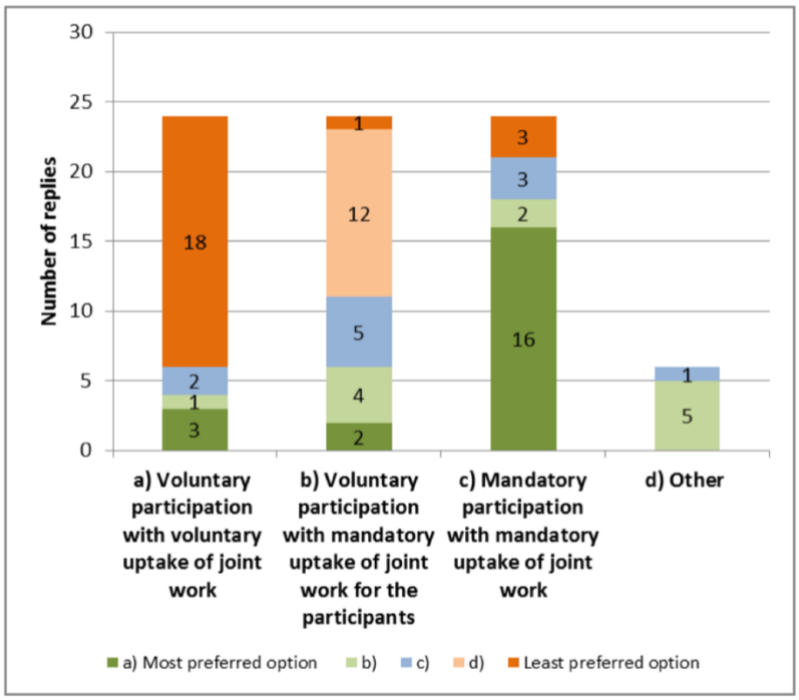

Figure 4.7 Patients and Consumers' organizations. Preferred policy option. Online Public Consultation[236]

4.3.2 Post-Adoption

The seven of nine organization that have been published the statement are: European Cancer Patient Coalition[237] (ECPC), Bureau européen des unions de consommateurs[238] (BEUC), European Federation of Allergy and Airways Disease Patient's Association[239] (EFA), European Patients' Forum[240] (EPF), European Organisation for Rare Disease[241] (EURORDIS), European Public Health

[236]https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

[237] http://www.ecpc.org/ECPC%20Response%20to%20HTA%20-%20Policy%20Paper.pdf

[238]https://www.beuc.eu/publications/beuc-x-2018 027_beuc_comments_to_european_commission_s_proposal_regulation_health_technology_assessment_.pdf

[239]http://www.efanet.org/images/documents/201805EFAs_HTA_Position_Paper-Commission_proposal.pdf

[240] http://www.eu-patient.eu/globalassets/policy/hta/epf-position-statement-on-hta.pdf

[241] http://download2.eurordis.org.s3.amazonaws.com/positionpapers/Statement_final.pdf

Alliance[242] (EPHA) and Health Action International[243] (HAI). These are the documents used for the words' frequency analysis (FIG 4.8 and Annex 4) in the post adoption period.

Figure 4.8 Word Frequency Query. Patients and Consumers' organization. Post-adoption.

From what it is highlighted by the content analysis, patients and consumers' organization *welcome* the publication of the European Commission's legislative proposal, as an important step towards improving *patients'* equitable access to high-quality healthcare. In particular, these organizations strongly support the *mandatory* joint clinical assessment and its inclusion at national level. From a patients' prospective, the fact that HTA bodies in different Member States reach divergent decision on the same medicines leaves that the health technology assessments are conducted in patients' interest. The benefits of the mandatory aspect of the Joint Clinical Assessment were highlighted by EFA, ECPC, EPF and EURODIS.

[242] https://epha.org/wp-content/uploads/2018/07/HTA-recommendations.pdf

[243]http://haiweb.org/wp-content/uploads/2018/02/Statement-European-Commission-Proposal-on-HTA.pdf

« EPF believe mandatory uptake is needed to overcome the current fragmentation and low uptake of joint EU-level work[244]»

«Mandatory uptake of the Joint HTA assessment is the only guarantee that the future cooperation will achieve its goals»

As in the preparatory phase, HAI thought that

«making joint clinical assessment mandatory among EU Member States is a counterproductive step if high evaluation standards are not upheld. [245]»

Notwithstanding, the general supportive attitude to the proposal, several concerns arise. First of all, any organizations of this category were underlined the need to *strength* the role of *Stakeholder* Network, in particular the patients' involvement. As stressed by Healthcare Providers' organizations, the Network should be involved in the HTA process through "regular" meeting instead of "ad hoc" meeting with the Coordination Group (Article 26-Point 3). Moreover, its role should be strength and formalised in order to ensure that stakeholders' views are represented and incorporated into all the reports issued by the Coordination Group (Article 26- Point 4). Additionally, an adequate patient involvement is essential for the Regulation to succeed, as declared by EPF[246]. Thus, the final Regulation should include specific provision formalising meaningful involvement of patient organizations every step of the HTA process, as patients are the ultimate beneficiaries of medical technologies[247], in order to capture their needs and opinions during the entire cycle[248].

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[244] http://www.eu-patient.eu/globalassets/policy/hta/epf-position-statement-on-hta.pdf

[245]http://haiweb.org/wp-content/uploads/2018/02/Statement-European-Commission-Proposal-on-HTA.pdf

[246] http://www.eu-patient.eu/globalassets/policy/hta/epf-position-statement-on-hta.pdf

[247] http://www.ecpc.org/ECPC%20Response%20to%20HTA%20-%20Policy%20Paper.pdf

[248]http://www.efanet.org/images/documents/201805EFAs_HTA_Position_Paper-Commission_proposal.pd

Patients and consumers' organizations call also for more robust transparency provision in the Regulation. The Health Action International and BEUC stated that the new HTA framework should be publicly financed and protected against undue influence and for this reason it is concerned that the system could be financed through industry fees.

«Assessment bodies collect data that is crucial to define drug reimbursement and prices, so they must be independent. If pharmaceutical companies started to fund their work, there would be obvious conflict of interest. Therefore, assessment should stay away industry funding[249]*»*

In this regards EPHA stated that Article 6-Point8[250] should be amended to prevent interreference by the company whose product is being assessed before the publication of the joint assessment[251]. At the same time, EPF suggested that all reports emanating from HTA assessment have to be available in a lay-friendly format; the guidance for the preparation of summary reports should be developed at EU level through an inclusive process. The IT platform should be in principle fully public and the HTA decision-making, must become more transparent for patients and citizens. Comparing with the Health providers' organizations the number of amendments is lower together with its position on the words' frequency list. Notwithstanding, the overall supportive position of patients and consumers'' organizations the position of the words "call "and "amendment" are higher than "welcomes".

[249] http://www.ecpc.org/ECPC%20Response%20to%20HTA%20-%20Policy%20Paper.pdf

[250] "*The assessor shall provide the draft joint clinical assessment report and to the submitting health technology developer and set a time-frame in which the developer may submit comments".*

[251] https://epha.org/wp-content/uploads/2018/07/HTA-recommendations.pdf

4.4 Payers

For the purpose of the new Regulation, payers should be understood as insurance organizations or organizations acting on behalf of a public authority responsible for the payment of healthcare services, namely the International Association of non-profit healthcare payers (AIM) and European Social Insurance Platform (ESIP). In the preparatory period, there were three[252] official bilateral meetings between the European Commission and Payers and they both participated in the Public Consultation as well as the official position paper.

4.4.1 Pre-Adoption

Figure 4.9 Word Frequency Query. Payers' organization. Pre-adoption.

In the Public Consultation as well as in the bilateral meeting payers welcome the proposal, underling that cooperation is needed to continue to maximise the benefits

252 https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20160216_sr_en.pdf; https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20161213_mi_en.pdf; https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170523_mi_en.pdf.

of the tools developed and to work towards a maximum uptake of the *joint* work, which will benefit those countries with limited resources, improve harmonisations and lend support to the sustainability of healthcare system. In particular AIM, in the Public Consultation stated that:

«Although there might be differences between countries and HTA bodies, due to differences in national context, transparency and collaboration can increase the quality and efficiency of the work on HTA at national level. Where possible, joint work should be supported[253]».

In relation to the potential funding mechanism of the future EU cooperation on Health technology Assessment, payers' representatives strongly advocate for ensuring the independence of the system. Thus, the EU cooperation on HTA should remain publicly funded through Member States and EU budget.

«*The introduction of an industry fee for HTA related activities would jeopardize the independence of the HTA bodies[254]*»

«HTA should be an independent process and ant financing system should endure freedom of the process from conflict of interest[255]»

However, in the bilateral meeting with the Commission, they stated that fee from industry were not considered appropriate for joint HTA assessment but might be considered for early dialogue procedures[256].

Looking at the governance mechanism, organizations representing payers are supportive for a coordination mechanism led by a national HTA body on a rotating basis or small group of HTA bodies, and European Commission providing for

[253] AIM, Public Consulation.

[254] AIM, Public Consulation

[255] ESIP, Public Consultation.

[256]https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170523_mi_en.pdf

organizational support[257]. In order to maintain the independency of the HTA process, from both of payers' organization stated that

« in any event it would be important to guarantee the independence of the HTA process from marketing authorization, in this light EMA was not considered the right agency to take to take over the tasks associated with HTA cooperation at European level. »

Both AIM and ESIP stated that the future cooperation should be voluntary with voluntary uptake and for this reason the lowest preferred option is the mandatory participation and uptake (FIG.4.10). From their point of view

«the participation has to be voluntary basis to respect Member States' competence in this field, according to the treaty. »

With regard to the uptake, it should be voluntary in order to encourage greater participation and if the joint work is timely and relevant to a Member States it will use it. However, in the long-term payers' organizations believe that the uptake should be mandatory for those participating in the joint work. In the joint meeting between the European Commission and Payers' organizations[258] it was also highlighted that a more emphasis should be given also at EU level, to re-assessments, a few years after a pricing/reimbursement decision has been taken.

[257] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

[258] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf
https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170523_mi_en.pdf

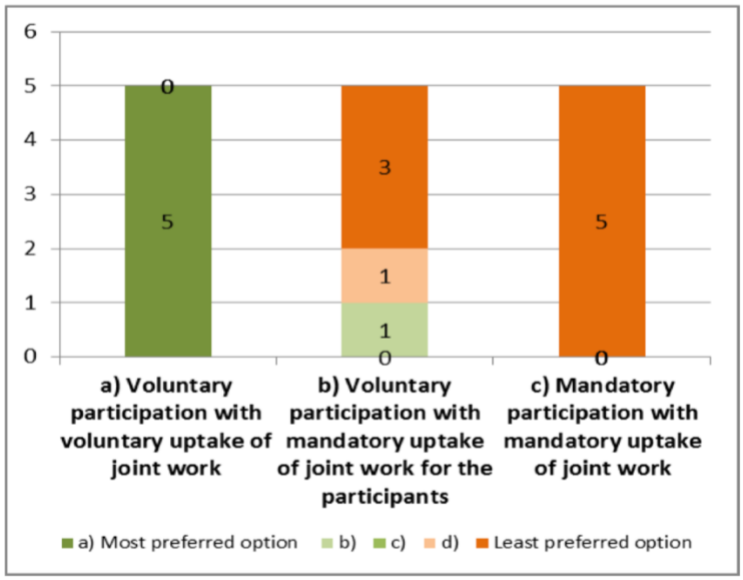

Figure 4.10 Payers preferred policy option. Online Public Consultation[259].

4.4.2 Post adoption

ESIP published three statements on the proposal for a Regulation on Health Technology Assessment. The first official statement was published the 23th of April 2018[260], the second was more a comment on the amendments proposed by the European Parliament's ENVI (8 June 2018[261])and the third the 6th of July 2018[262]. On the other hand, AIM published just one position paper[263] in which it provided a general reflection on the European Commission's proposal for a regulation on health technology assessment (HTA). Differently from the other

[259] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

[260] https://esip.eu/publications-intranet?idf=137&preview=332

[261] Regulation on Health Technology Assessment Draft Report of the European Parliament's ENVI committee Rappourteur: MEP Soledad Cabezòn Ruìz" 8 June 2018.

[262] "Statement supporting the inclusion of a broad scope of medical devices in the proposaed Regulation" 6 July 2018. https://esip.eu/publications-intranet?idf=137&preview=332

[263] https://www.aim-mutual.org/wp-content/uploads/2018/02/AIM-on-HTA.pdf

categories, payers' sample is composed only by two organizations which diverge in number of official statements published.

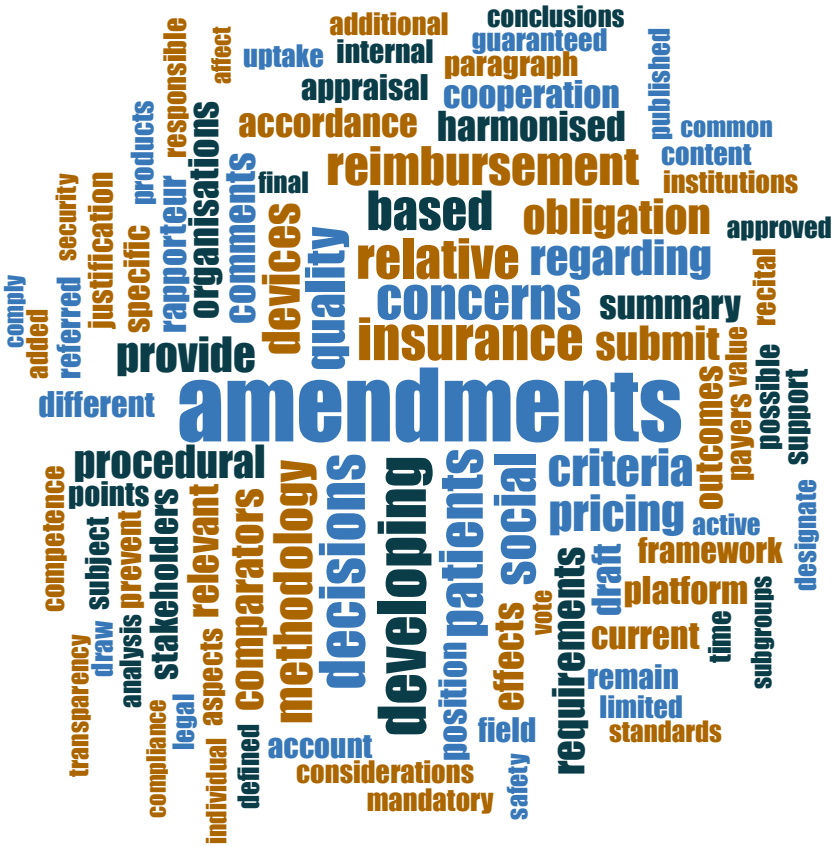

Figure 4.11 Figure 4.9 Word Frequency Query. Payers' organization. Post-adoption.

They both welcomes the initiative of the European Commission:

«to provide for a sustainable framework for cooperation on HTA at EU level[264]*»*

«to improve the quality and timeliness of health technology assessment, and to ensure through Union-wide collaboration that the assessor has timely access to relevant high-quality data to carry out meaningful comparison between the asses' products and the most appropriate comparators[265]*.»*

[264] ttps://esip.eu/publications-intranet?idf=137&preview=332

[265] https://www.aim-mutual.org/wp-content/uploads/2018/02/AIM-on-HTA.pdf

However, s it is possible seen in cloud of words (FIG 4.11) and in the Annex 5 of the words' frequency analysis the key points are the *amendments*. In fact, the number of payers' queries are high.

The proposal should be more orientated on the improvement of *quality* of the healthcare system and this, for payers' point of view, is strictly related to the *mandatory* participation and uptake.

«There would be more pressure to reduce this clinical assessment as quickly as possible, to the potential detriment of quality and safety of care[266]*. »*

«We are convinced that if the joint assessment has the required quality and are produced in a timely manner the uptake of the uptake of those assessment is not going to be an issue[267]*»*

HTA is an essential tool for Member States in order to make evidence-based decisions on *pricing* and *reimbursement* of health technologies. Harmonising clinical assessment of health technologies would inevitably have an impact on *pricing* and *reimbursement* decision at national level. Notwithstanding the scope of the compulsory joint assessment shall be limited to the joint clinical assessment

« *the clinical domains of HTA are not completely void of context-specific criteria reflecting specificities of national health system*[268]*»*

« Non-clinical assessments remain difficult to make for individual Member States and inscrutable for the general public. It is important that countries are being supported in the strengthening of this part of the HTA process. Member States should give priority to collaboration in this field, in strengthening methodologies for (relative) cost-effectiveness studies and transparency of the pricing and reimbursement decision[269]*.»*

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[266] https://www.aim-mutual.org/wp-content/uploads/2018/02/AIM-on-HTA.pdf

[267] ttps://esip.eu/publications-intranet?idf=137&preview=332

[268] Ibidem

[269] https://www.aim-mutual.org/wp-content/uploads/2018/02/AIM-on-HTA.pdf

Moreover, the currently proposal

«does not include any provisions on the content of the harmonised methodological framework».

There should be more detail in the framework, due to the *mandatory* element, in particular on *methodology*, data requirement and the role of the Commission. In that it would be useful a mandatory publication of data from the industry. The European Commission, as stressed by ESIP, according with the Article 7, decides if a joint clinical assessment complies with the "substantive and procedural requirements" and if an assessment is going to be published in the "List of Assessed Health Technologies. The independence of the process would be jeopardised by the European Commission that has the final decision on the validity of the scientific assessment as well as the financing system through industry fees.

4.5 Industry

The industries are directly affected by the future initiative of EU cooperation on HTA. In the online public consultation there were a distinction between pharmaceutical industry (non-SME) and Medical technologies' industry (non-SME), while in this analysis there is just one category named "industry" which included both of them.

4.5.1 Pre-Adoption

In the preparatory period they have been deeply involved by DG SANTE at each level, from the preparation of the Impact Assessment to the public consolation. In total, it is possible to call ten meeting between industries and the European Commission[270].

Figure 4.12 Word Frequency Query. Industry' organization. Pre-adoption.

[270] https://ec.europa.eu/health/technology_assessment/events_en#anchor2

All the representatives of industries and their trade association welcome the proposal, underlining that

«EU cooperation on HTA is necessary to create a sustainable policy. »

This *cooperation* would be an opportunity for the Member States which can benefit from pooled resources and exchange expertise as well as for the industry, and for this reason it is a key word in their meeting with the European Commission. In fact, the difference between HTA procedures among Member States is a constant challenge for the industry, in particular for small to mid-sized companies. This is also evident in the technology sectors focus on Orphan Medical Products, which has a variety of challenges

«In certain markets patients with a certain rare disease are limited, and the cost of an HTA dossier might exceed the actual market value. Moreover, collection of data can be burdensome where patient cohorts may be limited in individual Member States[271]*»*

Nevertheless, they underline also that the diverging requirement of clinical economic data for HTA between Member States as well as the unclear and non-consistent guideline on data requirements

«lead to significant delays in patient access to technologies, even when technology is well established and used in other parts of the world[272]*»*

Industry' representatives considered that funding should be largely based on the EU budget, with some contributions from Member States as well as *voluntary* fee-for-service contributions from industry[273]. In this respect, medical technologies' industry highlights their readiness to contribute only under specific condition while the pharmaceutical industries stated that openness to continue the current

[271] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20161122_mi_en_0.pdf

[272] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20160408_frep_en.pdf

[273] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

practice of paying a fee to receive scientific advice[274]. The same thought was expressed in the online public consultation

« members are open to continue the current practice of paying a fee to receive scientific advice, providing the system to be set up is fit for purpose and responds to industry need[275] »

«members are also open to continue the current practice of paying a fee to receive scientific advice, provided the system to be set up is fit for purpose and responds to industry needs[276]»

Looking at the governance mechanism several representatives observed that at this early stage it is important to clarify the main principle rather than determining the location of this support. Others observes that an existing structure of the European Commission was seen as potential solution for providing support from a secretarial and organisational point of view. However, all the industry' representatives stress that any coordination mechanism should be based on highest scientific standards and should receive appropriate resources[277].

As regards to the *policy* option both pharmaceutical industry and medical technologies' industry have put "other" as the most preferred option. However, for the least preferred option they have divergent opinions. Pharmaceutical industry companies have chosen the voluntary participation with voluntary uptake of the joint work while medical technologies' industry the mandatory participation with mandatory uptake of joint work.

«does not consider that a fully mandatory system can be put in a place at this stage. In order to minimize disruptions (..) the process needs to start on a voluntary basis for both Member States and industry[278].»

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[274]https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

[275] EuropaBio Public Consulation

[276] EFPIA Public Consulatition

[277] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

[278] EFPIA Public Consulatition

«the preferred option is a voluntary participation by pharmaceutical companies and a mandatory uptake of joint work by the participating HTA bodies once the process has proven itself[279].»

Indeed, medicinal technologies' industry have different approaches than pharmaceuticals with timing and selection of technologies to be assessed by HTA bodies and not centrally at EU level[280]. This was stated also in a bilateral meeting between MedTech and the European Commission[281] in which it was underlined that the *differences* between the *pharmaceutical* and *medical technology* sector, in terms of market access path, and the country specific role of HTA in aiming to inform decision making as well as specificities in effectiveness evidence generation. For this reason, MedTech proposed a voluntary, non-legislative collaboration of Member States driven by decision maker's demands on what to collaborate on. Moreover, the coordination and funding should be provided by the EU primarily. On the other hand, EUCOPE Orphan Medical Products working group[282], stated their preference to policy options 3 and 4, emphasising that they see a clear benefit for increased cooperation. In certain markets patients with a certain rare disease are limited. Therefore, the cost of Health Technology Assessment dossier might exceed the actual market value[283].

EFPIA also underlines that a big concern for industry are the different procedures and methodologies applied by national HTA agencies[284]. Multiple requests of evidence were also a reason causing delays in patients' access, as well as increasing costs. For this reason, EFPIA strongly believes that the cooperation on REA should be strengthened at European level, harmonising the clinical parts of the assessment.

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[279] AESGP Public Consulation

[280] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170217_mi_en.pdf

[281] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170217_mi_en.pdf

[282] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20161122_mi_en_0.pdf

[283]Ibidem

[284]https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20161117_mi_en.pdf

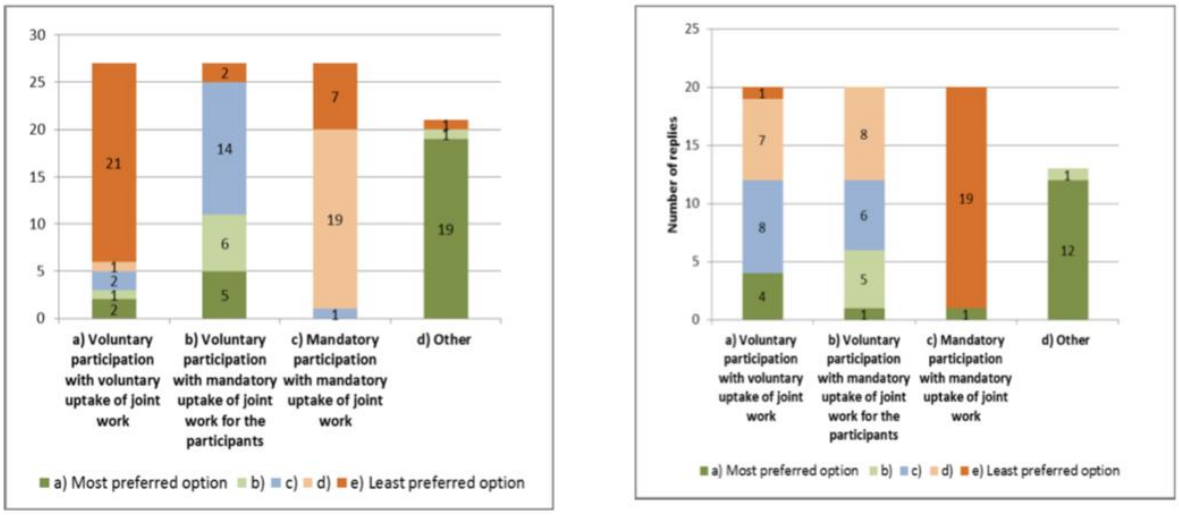

Figure 4.13 Pharmaceutical industry and medical technologies' industry policy option. Online Public Consultation[285].

4.5.2 Post-adoption

After that the Commission has put forward a proposal to boost cooperation among EU Members States for assessing health technology industry, the pharmaceutical industry made a joint statement[286]. The pharmaceutical industry was represented by AESGP, EFPIA, EUCOPE, EuropaBio, Medicine for Europe and PPTA. However, EFPIA published, in May 2018, its own position paper on proposals for a Regulation in which it outlines EFPIA's views on the four pillars of EU HTA cooperation[287]. As regards medical technology industry, just COCIR published its position paper[288].

[285] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20161117_mi_en.pdf

[286]https://www.europabio.org/sites/default/files/FOR%20PUBLICATION_June_FINAL_Joint%20industry%20statement%20HTA.pdf

[287]https://www.efpia.eu/media/361850/efpia-position-paper-on-the-commission-proposal-for-a-regulation-on-hta.pdf

[288]https://www.cocir.org/fileadmin/Position_Papers_2018/COCIR_Position_Paper_on_EC_proposal_on_HTA_-_30_Mar._2018_final.pdf

Figure 4.14 Word Frequency Query. Industry' organization. Post-adoption.

Industry generally welcome the proposal on HTA cooperation in the European Union. In fact, in the joint pharmaceutical industry statement it was declared that this *cooperation* would be *«a unique opportunity for greater alignment on clinical evidence generation requirements, ensuring consistency, transparency and synergies in clinical assessment by Member States as well as evidence that is relevant for Europe*[289]*.»*

Notwithstanding, they believe that there is a need to clarify that *methodologies* that will support JCA will build on existing EUnetHTA methods, be up to date with scientific development and be regularly reviewed[290]. Methodology as well as evidence need to be sufficiently flexible in order to ensure a level playing field for different types of medicine. This is particularly true for the orphan drugs that have

[289]https://www.europabio.org/sites/default/files/FOR%20PUBLICATION_June_FINAL_Joint%20industry%20statement%20HTA.pdf

[290]https://www.europabio.org/sites/default/files/FOR%20PUBLICATION_June_FINAL_Joint%20industry%20statement%20HTA.pdf

limitations resulting in unavoidable evidential uncertainty[291]. All the positive aspects of the proposal were underlined as well by EFPIA through its position paper. It is also stated that the supports of the *mandatory* uptake and the scope of the Commission proposal, limited to a joint clinical assessment at European level for medical products subject to the centralised marketing authorization procedure[292]. However, from EFPIA point of view an appeal mechanism for companies is missing in the proposal. The *joint clinical assessment* is the basis of subsequent national decision making and an opportunity should be given for an independent review of the assessment. In particular, if significant, discrepancies exist in the interpretation. EFPIA also disagree with the inclusion of voluntary cooperation on non-clinical assessment for medicines in the proposed HTA Regulation.

As regard Medical technologies' industry, COCIR was the only one who published an official position paper on the European Commission proposal for a Regulation. COCIR *welcomes* that «*the Commission considered the majority of the concerns highlighted in their contribution to the European Commission public consultation*[293]. »

In particular COCIR is delight the it recognized in the proposal a different approach for *pharmaceutical products* on the one hand, and the medical technologies on the other hand, for health technology assessments[294]. Moreover, taking into account that nowadays the proposal is under consideration by the European Parliament and the Council, COCIR would like to highlight which are their fundamental points elaborated from process and governance prospective. Firstly, COCIR underlined it is important that multi-application technologies

[291] Ivi, pp 116.

[292]https://www.efpia.eu/media/361850/efpia-position-paper-on-the-commission-proposal-for-a-regulation-on-hta.pdf

[293]https://www.cocir.org/fileadmin/Position_Papers_2018/COCIR_Position_Paper_on_EC_proposal_on_HTA_-_0_Mar._2018_fina

[294]Ibidem

remain out of the scope of the proposed legislation. There is also the need to define and develop appropriate *methodologies*, data requirements and outcomes measures. In addition, it was stressed that *« a clear and transparent guideline on the stakeholders' involvement to ensure that a multi-stakeholder' prospective is brought to activities developed by the EU Member States*[295]*.» should be provided*

Looking at the list of words in the appendix 6, it is possible notice how in the first hundred words such as "amendment" or "concerns" does not appear. On the other hand, it is possible find at 10th place the word "support" following by "benefit" "agreed" and "welcome".

4.6 Main evidences of the analysis

The health providers, in the public consultation as well as in the bilateral meeting with the European Commission, have explicitly requested an EU HTA cooperation based on transparency and independence. In order to achieve these two main principles, they strongly believe that, first of all, the system should not be financed through industry fees, and that the stakeholders network, in particular Health Providers' organizations have to be actively involved in the process. However, looking at the official statements published after the adoption of the legislative proposal by the European Commission on 31 January 2018, it is possible notice that their main concerns are pretty aligned with their opinion in the pre-adoption. From the above analysis, it is possible see that the degree of the stakeholders' involvement in the preparatory phase is directly proportionated with the number of concerns expressed on the legal text. In fact, industry was more involved than the others in the preparatory phase and in the post adoption they were very supportive. On the other hand, healthcare providers, which were the

[295]https://www.cocir.org/fileadmin/Position_Papers_2018/COCIR_Position_Paper_on_EC_proposal_on_HTA_-_0_Mar._2018_fina

least involved in preparatory phase expressed in their statement the several concerns, with the annex amendments.

Patients and consumers' organizations have a high number of concerns. However, they diverge from the other categories because the majority of their queries are focus on stakeholder involvement. While payers, in particular ESIP has proposed an elevate number of amendments on more Regulation's argument.

Transparency followed by independency is another word which often appears in the statements. In order to generate and maintain trust in the system there should be more provision on transparency in the Regulation. All of them are also against the industry fees as a financed mechanism, as it would lead to conflicts of interest. Except for the patients and consumers' organization, the other categories are not in favour of the mandatory participation and uptake of the joint clinical assessment.

Almost every involved part, in particular patients and healthcare providers, calls for a greater involvement of stakeholders in the future EU cooperation on HTA. Article 26 should be clearer in its provision, making sure that each category of stakeholder would be constantly involved, not only with *«ad hoc meeting»* but with *«regular meeting»*. From their point of view this is fundamental in order to guarantee a transparent process and assessment. All the four categories converge in a specific concern, they ask for more clarification and provision in the Regulation rather than in implementing or delegated act.

Trying to make a classification based on the number of concerns expressed after the publication of the proposal for a Regulation on EU HTA cooperation, it has to do distinction between pharmaceutical and medical technology industries and between ESIP and AIM, within payers, due to their divergent opinion. Staring from the left[296], there are the pharmaceuticals industry which are very supportive to the proposal and at the same time further active in providing input in both of the phases. It is followed by the medical technologies industry which are as well

[296] Very supportive.

supportive but less active. The third and the fourth position is occupied by payers' category, in which ESIP comes after AIM for the higher number of amendments suggested. On the extreme right there are patients and healthcare providers. The latter in the pre-adoption were not so involved in the process, while after the published of the legal proposal they state a very critical position toward the proposal.

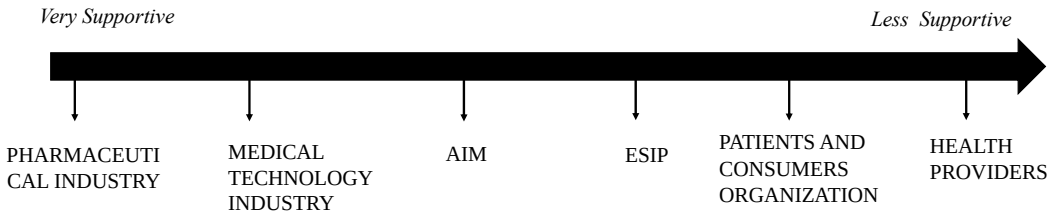

Figure 4.15 Stakeholders'' position.

CONCLUSION

The aim of this thesis is to give an overview of the current European Commission proposal for a Regulation on Health Technology Assessment, with a specific focus on the Stakeholders' Network through a qualitative analysis.

Until some decades ago the term "Health Technology Assessment" was not well-known. However, the aging population, the expanding use and the number of new and expensive technologies have contributed to burgeoning health care cost. Consequently, several counties have implemented health technology assessment as a means of informing the decision process basic on clinical and economic evidence[297].

HTA is considered a valuable tool for ensuring the sustainability of health systems and stimulating innovation at EU level. Nevertheless, a series of shortcoming have prevented the full potential of HTA being reached for Member States and economic operators with subsequent negative consequences also for EU patients and healthcare professional[298]. The European Commission identified three main problems: 1) Impeded and distorted market access; 2) Duplication of work for national HTA bodies; 3) Unsustainability of the current HTA voluntary cooperation.

[297] Kanavos, P., Nicod, E., Van Den Aardweg, S., & Pomedli, S. (2010). The impact of health technology assessments: an international comparison.

[298]https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_exefinal_en.pdf

Thus, the European Commission, in 2016, started work on strengthening EU cooperation on Health Technology Assessment in response to calls from EU countries, the European Parliament, and interested parties to ensure its sustainability beyond 2020[299]. The Commission's proposal was adopted on 31st of January 2018 and has been sent to the Council and the European Parliament for their consideration under the ordinary legislative procedure. The proposal considers the EU-level cooperation which has taken place until now on HTA, the results of the impact assessment process and the views expressed by Member States and stakeholders in the public consultation and various bilateral and multilateral meeting over the course of the last two years. Moreover, the proposal for a new Regulation on HTA would introduce a *common European assessment methods, shared data and expertise* and harmonising the health technology assessment procedures across EU. According to the legal framework the area of cooperation would be four: 1) joint clinical assessment; 2) scientific consultation on the development of new products; 3) mapping of emerging health technologies; 4) voluntary cooperation on other areas. Since, the European assessment, jointly done by Member States, will be on *clinical domains* while national assessment will be focus on *non-clinical domains*, such as pricing and reimbursement. The proposal provides for a Member States-driven approach to the cooperation through the Coordination Group and technical experts made up of MS'HTA bodies

The majority of stakeholders' stresses that EU cooperation beyond 2020 needs to ensure a constant change of information and knowledge between HTA institutions in Europe, with the aim of increasing synergy between Member States, streamlining HTA mythologies, improving transparency and evidence-based decision-making, as well as ensuring business predictability. However, after the publication of the proposal for a new Regulation on HTA, though official statement and bilateral meetings stakeholders expressed several concerns.

[299] https://ec.europa.eu/health/technology_assessment/eu_cooperation_en

Most of this dissatisfaction comes from their marginal role in the future HTA cooperation. Since, they call for more constant involvement of the stakeholders within the process. This was deeply underlined by patients and healthcare providers. They call for a clear link between stakeholder network and the Coordination Group activities, in order to ensure a proactive contribution to the work.

The second main point of the analysis is the mandatory participation and uptake of the joint clinical work. The majority of stakeholder are concerned that quality and safety might be impeded ad a result of having a harmonised clinical assessment causing more stressful conditions. Among the four stakeholders' category the analysis shows that only patients and consumers'' organization are favour of mandatory uptake and involvement.

Additionally, it is a common regret that essential aspects are not sufficiently outlined in the proposed regulation but left to implementing and delegated act. In particular, stakeholders stated that the proposed Regulation fails to adequately address transparency and independence as well as methodology. *Transparency* principle should be applied at each steps of the process through clearer rules, provision and stakeholder involvement. *Independency* is further connected to the governance and financing system of the HTA process. in particular, it was often underline that the system should not be financed by industry's fees on reason of conflict of interest.

The 9th of July 2018, the European Commission, Health and Food Safety Directorate General, organized a conference to take stock of and listen to the view of stakeholders on HTA proposal. In particular, the focus was on the health providers and patients' representatives' involvement in the future EU HTA cooperation due to their several concerns. The Commissioner Vytenis Andriukaitis in his speech stated that:

«*The input from patients, health professionals and industry in the HTA discussion is essential. We now have an opportunity to establish a mechanism*

that ensures that HTA is used to its maximum potential throughout the EU. I believe that joint assessments would not only help patients to have access to the most effective health technologies but would also contribute to the sustainability of health systems. The broad involvement of stakeholders also ensures quality and predictability. Moreover, I believe that our proposal would bring more transparency in the HTA processes in the EU[300].»

Currently, Member States are in the process of analysing the proposal with a view to formulating their official positions while the European Parliament has appointed its Rapporteur (Soledad Cabezon Ruiz S&D). However, given that European Parliament elections will be held in May 2019, the time period for negotiating and finding an agreement on the proposal in Council and between the Council, Parliament and Commission is limited.

[300] The way forward for HAT cooperation- the views of stakeholders. 09-07-2018. https://webcast.ec.europa.eu/the-way-forward-for-hta-cooperation-the-views-of-stakeholders

APPENDIX 1

Art.144 of TFEU.

1. Save where otherwise provided in the Treaties, the following provisions shall apply for the achievement of the objectives set out in Article 26. The European Parliament and the Council shall, acting in accordance with the ordinary legislative procedure and after consulting the Economic and Social Committee, adopt the measures for the approximation of the provisions laid down by law, regulation or administrative action in Member States which have as their object the establishment and functioning of the internal market.

2. Paragraph 1 shall not apply to fiscal provisions, to those relating to the free movement of persons nor to those relating to the rights and interests of employed persons.

3. The Commission, in its proposals envisaged in paragraph 1 concerning health, safety, environmental protection and consumer protection, will take as a base a high level of protection, taking account in particular of any new development based on scientific facts. Within their respective powers, the European Parliament and the Council will also seek to achieve this objective.

4. If, after the adoption of a harmonisation measure by the European Parliament and the Council, by the Council or by the Commission, a Member State deems it necessary to maintain national provisions on grounds of major needs referred to in Article 36 or relating to the protection of the environment or the working environment, it shall notify the Commission of these provisions as well as the grounds for maintaining them.

5. Moreover, without prejudice to paragraph 4, if, after the adoption of a harmonisation measure by the European Parliament and the Council, by the Council or by the Commission, a Member State deems it necessary to introduce national provisions based on new scientific evidence relating to the protection of the environment or the working environment on grounds of a

problem specific to that Member State arising after the adoption of the harmonisation measure, it shall notify the Commission of the envisaged provisions as well as the grounds for introducing them.

6. The Commission shall, within six months of the notifications as referred to in paragraphs 4 and 5, approve or reject the national provisions involved after having verified whether or not they are a means of arbitrary discrimination or a disguised restriction on trade between Member States and whether or not they shall constitute an obstacle to the functioning of the internal market.

In the absence of a decision by the Commission within this period the national provisions referred to in paragraphs 4 and 5 shall be deemed to have been approved.

When justified by the complexity of the matter and in the absence of danger for human health, the Commission may notify the Member State concerned that the period referred to in this paragraph may be extended for a further period of up to six months.

7. When, pursuant to paragraph 6, a Member State is authorised to maintain or introduce national provisions derogating from a harmonisation measure, the Commission shall immediately examine whether to propose an adaptation to that measure.

8. When a Member State raises a specific problem on public health in a field which has been the subject of prior harmonisation measures, it shall bring it to the attention of the Commission which shall immediately examine whether to propose appropriate measures to the Council.

9. By way of derogation from the procedure laid down in Articles 258 and 259, the Commission and any Member State may bring the matter directly before the Court of Justice of the European Union if it considers that another Member State is making improper use of the powers provided for in this Article.

10. The harmonisation measures referred to above shall, in appropriate cases, include a safeguard clause authorising the Member States to take, for one or more of the non-economic reasons referred to in Article 36, provisional measures subject to a Union control procedure.

APPENDIX 2

HEALTH PROVIDERS

Council of European Dentist	CED	It is a non profit organization which represent over 340.000 dentist across Europe
European Association of Hospital Pharmacists	EAHP	EAHP represents more than 21.000 hospital pharmacists in 35 European countries and it is the only association of national organizations representing hosptial pharmacist at EU and international level
European Forum for Primary Care	EFPC	The European Forum for Primary Care was initiated in early 2005 by a group of interested parties from several countries. The aim of the Forum is to improve the health of the population by promoting strong Primary Care.
European Hospital and healthcare Federation	HOPE	It is a European NGO, representing national public and private hospital and healthcare associations and hospital, health and social care service owner
European Public Health Association	EUPHA	It is an umbrella organisations of public healòth associations and institues in Europe.
European Society of Cardiology	ESC	ESC is a non-profit medical society led by expert volunteers.
European Union of General Practitioner/Familiy Physicians	UEMO	It is is the organisation for General Practitioners and Specialists in Family Medicine in Europe. The aims areto promote the highest standard of training, practice and patient care within the field of general practice throughout Europe as well as to defend the role of general practitioners in the healthcare systems.
Pharmaceutical Group of the European Union	PGEU	PGEU represents the community pharmacy prespective in relation to legislative and policy initiatives at EU level which affect profession and public health.
Standing Committee of european Doctors	CPME	It is an international, not for profit association under Belgian Law composed of the National Medical Associations of the European Union

PATIENTS -CONSUMERS

Bureau européen des unions de consommateurs	BUEC	BEUC investigates EU decisions and developments likely to affect consumers, with a special focus on five areas identified as priorities by our members: Financial Services, Food, Digital Rights, Consumer Rights & Enforcement and Sustainability.
European Cancer Patient Coalition	ECPC	The European Cancer Patient Coalition (ECPC) is the voice of cancer patients in Europe. ECPC represents patients affected by all types of cancers, from the rarest to the most common.
European Federation of Allergy and Airways Diseases Patients' Association	EFA	EFA is an independent non-profit organisation, it is a European alliance of over 30 allergy, asthma and chronic obstructive pulmonary disease (COPD) patients' associations representing 30% of European citizens currently living with these diseases.
European Institute of Womens Health	EIWH	EIWH is a non-governmental organisation that promotes gender equity in public health, research and social policies across Europe.
European Patients' Forum	EFP	EPF is an umbrella organisation that works with patients' groups in public health and health advocacy across Europe.
European Public Health Alliance	EPHA	EPHA is a leading non-profit alliance advocating for better health.
European Organisation for Rare Diseases	EURORDIS	EURORDIS- Rare Disease Europe is a unique, non-profit alliance of over 700 rare disease patient organizations from more than 60 countries that work together to improve the lives of 30 million people living with rare disease in Europe.
Health Action International	HAI	HAI is a non-profit organization that conducts resources and advocacy to advance policies in the enable access to medicines and rational medicine use for all people around the world.
International Diabetes Federation European Region	IDF	IDF is an umbrella organization representing 71 national diabetes organisations in 46 countries across Europe.

PAYERS

Association Internationale de la Mutualité	AIM	AIM is an internation association of non-profit healthcare payers. Its members provide healthcare coverage to around 200 million people within Europe. Sustainable access high quality medicines for all is an important objective of the associatio and its members.
European Social Insurance Platform	ESIP	ESIP exists under Belgian law and it is a strategic platform gathers over 50 national sociual security irganizations insuring 240 milion citiziens in 15 Member State sans Switzerland.

INDUSTRY

Association of the European Self-Medication Industry	AESGP	It is aon-profit organization which represents the manufactures of non-prescription medicines. Food supplements and self-care medical device in Europe.
European Association for Bioindustries	EuropaBio	It promotes an innovative and dynamic European biotechnology industry. It is commetted to the socially responsible use of biotechnology to improve quality of life, to prevent, diagnose, treat and cure diseases, to improve the quality and quantity of food and feedstuffs and to move towards a biobased and zero-waste economy.
European Confederation of Pharmaceutical Entrepreneurs	EUCOPE	The European Confederation of Pharmaceutical Entrepreneurs (EUCOPE) is Europe's principal trade body for small-to-medium sized innovative companies working in the field of pharmaceuticals and medical devices.
European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry	COCIR	COCIR is the European Trade Association representing the medical imaging, radiotherapy, health ICT and electromedical industries.
European Federation of Pharmaceutical Industries and Associations	EFPIA	EFPIA represents the pharmaceutical industry operating in Europe. It is the voice on the EU scene of 1,900 companies committed to researching, developing and bringing to patients new medicines that will improve health and the quality of life around the world.
Medicine for Europe		Medicine for Europe goal was representing the emerging generic industy and later growing to include bisimilar medicines to its portfolio. As the pharmaceutical industy an the healthcare envirioment within each it operates have envolved.
MedPharma Europe		MedPharma Group provide Logistics and Warehousing Services for Medical and Pharmaceutical companies who need immediate turnaround on delivery of their products across Europe.
Medtech Europe		It is a NGO organisation based in Brussels, that works for the interests of the European medical technology industry. It is an alliance of two European medical technologyassociations, EDMA and Eucomed, representing the European IVD and medical device industries, respectively.
Plasma Protein Therapeutics Associations Europe	PPT	PPTA Europe is actively engaged in setting advocacy and priority initiatives for improving access to care to plasma protein therapies at both the European Union level and within member states..

APPENDIX 3

Health Providers, word frequencies query. Post and Pre-adoption. NVivo12.

Word-Post Adoption.	Length	Count	Weighted Percentage	Similar Words
1. article	7	79	1,73%	article, articles
2. stakeholder	11	57	1,25%	stakeholder, stakeholders, stakeholders'
3. amendment	9	46	1,01%	amend, amended, amending, amendment, amendments
4. participation	13	45	0,99%	participants, participate, participated, participating, participation, participations
5. national	8	41	0,90%	national
6. update	6	40	0,88%	update, updated, updates, updating
7. regulation	10	40	0,88%	regulate, regulation
8. cooperation	11	39	0,86%	cooperate, cooperation
9. interest	8	37	0,81%	interest, interested, interests
10. procedural	10	36	0,79%	procedural, procedure, procedures
11. products	8	36	0,79%	product, production, products
12. developers	10	35	0,77%	develop, developed, developer, developers, development
13. final	5	33	0,72%	final
14. network	7	33	0,72%	network, networks

15. process	7	33	0,72%	process, processes, processing
16. medical	7	32	0,70%	medical
17. referred	8	31	0,68%	referred
18. provided	8	31	0,68%	provide, provided, provides, providing
19. organisation	12	31	0,68%	organisation, organisational, organisations, organise
20. requirements	12	29	0,64%	require, required, requirement, requirements, requires
21. represents	10	27	0,59%	represent, representative, representatives, represents
22. implementation	14	24	0,53%	implementation, implemented, implementing
23. accordance	10	24	0,53%	accordance, according
24. additional	10	24	0,53%	addition, additional, additionally
25. consultation	12	24	0,53%	consultation, consultations, consulted
26. involvement	11	23	0,50%	involved, involvement
27. request	7	23	0,50%	request, requested, requests
28. evidence	8	23	0,50%	evidence
29. present	7	22	0,48%	present, presentation, presented
30. prepared	8	22	0,48%	preparation, prepare, prepared

31. available	9	21	0,46%	availability, available
32. access	6	21	0,46%	access, accessible
33. decision	8	21	0,46%	decision, decisions
34. platform	8	21	0,46%	platform, platforms
35. scientific	10	21	0,46%	scientific, scientifically
36. appointment	11	21	0,46%	appoint, appointed, appointment
37. independence	12	21	0,46%	independence, independent
38. established	11	20	0,44%	establish, established, establishes, establishing, establishment
39. support	7	20	0,44%	support, supporting, supports
40. safety	6	20	0,44%	safety
41. experts	7	20	0,44%	expert, experts
42. innovation	10	20	0,44%	innovation, innovative
43. transparency	12	20	0,44%	transparency, transparent, transparently
44. designated	10	19	0,42%	designate, designated, designating
45. authorisation	13	19	0,42%	authorisation, authorised
46. board	5	18	0,39%	board
47. time	4	18	0,39%	time, timely, timing
48. professionals'	14	17	0,37%	professional, professionals,

				professionals', professionals’
49. justification	13	17	0,37%	justification, justifications
50. applicable	10	16	0,35%	applicable, application, applications
51. explained	9	15	0,33%	explained
52. summary	7	15	0,33%	summary
53. documents	9	15	0,33%	document, documentation, documented, documents
54. countries	9	14	0,31%	countries, country
55. concerns	8	14	0,31%	concern, concerned, concerning, concerns
56. adoption	8	14	0,31%	adopt, adopted, adopting, adoption
57. authorities	11	14	0,31%	authorities, authority, authorization
58. patients	8	14	0,31%	patient, patients, patients', patients’
59. activities	10	14	0,31%	active, actively, activities, activity
60. devices	7	14	0,31%	device, devices
61. possible	8	14	0,31%	possibility, possible, possibly
62. timeline	8	14	0,31%	timeline, timelines
63. policy	6	13	0,29%	policies, policy
64. advises	7	13	0,29%	advised, advises
65. annual	6	13	0,29%	annual
66. quality	7	13	0,29%	quality
67. responsible	11	13	0,29%	response, responsibilities,

				responsibility, responsible
68. voluntary	9	13	0,29%	voluntary
69. bodies	6	13	0,29%	bodies, body
70. methodology	11	13	0,29%	methodological, methodologies, methodology
71. association	11	12	0,26%	association, associations
72. expertise	9	12	0,26%	expertise
73. pharmacists	11	12	0,26%	pharmacists
74. discussion	10	12	0,26%	discuss, discussion, discussions
75. marketing	9	12	0,26%	market, marketing
76. welcomes	8	12	0,26%	welcome, welcomes
77. position	8	11	0,24%	position, positions
78. publish	7	11	0,24%	publish, published
79. section	7	11	0,24%	section, sections
80. legislation	11	11	0,24%	legislation, legislative, legislators
81. notified	8	11	0,24%	notified, notify
82. specified	9	11	0,24%	specified, specify
83. divergent	9	11	0,24%	divergent, diverging
84. limited	7	11	0,24%	limit, limited
85. detailed	8	11	0,24%	detail, detailed, details
86. financial	9	11	0,24%	financial
87. statement	9	11	0,24%	statement
88. respect	7	10	0,22%	respect, respective
89. appropriate	11	10	0,22%	appropriate

90. directorate	11	10	0,22%	directorate
91. dispense	8	10	0,22%	dispense
92. falsified	9	10	0,22%	falsified
93. features	8	10	0,22%	features
94. framework	9	10	0,22%	framework
95. membership	10	10	0,22%	membership
96. overall	7	10	0,22%	overall
97. people	6	10	0,22%	people
98. selection	9	10	0,22%	selected, selecting, selection, selects
99. submit	6	10	0,22%	submit, submitted, submitting
100.term	4	10	0,22%	term, terms

Word_Pre adoption	**Length**	**Count**	**Weighted Percentage**	**Similar Words**
1. participants	12	9	2,87%	participants, participate, participating, participation
2. involvement	11	9	2,87%	involved, involvement
3. medical	7	7	2,23%	medical
4. safety	6	6	1,91%	safety
5. products	8	5	1,59%	products
6. organisation	12	5	1,59%	organisation, organisations
7. innovation	10	5	1,59%	innovation, innovative
8. directorate	11	5	1,59%	directorate
9. processes	9	4	1,27%	process, processes
10. interest	8	4	1,27%	interest, interesting

11. doctors	7	4	1,27%	doctors, doctors', doctors’
12. discuss	7	4	1,27%	discuss, discussion
13. cooperation	11	4	1,27%	cooperation
14. quality	7	3	0,96%	quality
15. provided	8	3	0,96%	provide, provided
16. policy	6	3	0,96%	policy
17. explained	9	3	0,96%	explained
18. contact	7	3	0,96%	contact
19. transparency	12	2	0,64%	transparency, transparent
20. sustainable	11	2	0,64%	sustainable
21. strengthening	13	2	0,64%	strengthening
22. question	8	2	0,64%	question
23. purpose	7	2	0,64%	purpose
24. professionals'	14	2	0,64%	professionals'
25. preferences	11	2	0,64%	preferences, preferred
26. possible	8	2	0,64%	possible
27. people	6	2	0,64%	people
28. membership	10	2	0,64%	membership
29. location	8	2	0,64%	location
30. introduction	12	2	0,64%	introduction
31. independence	12	2	0,64%	independence, independency
32. framework	9	2	0,64%	framework
33. follow	6	2	0,64%	follow, following
34. fee	3	2	0,64%	fee, fees
35. features	8	2	0,64%	features
36. falsified	9	2	0,64%	falsified

37. expressed	9	2	0,64%	expressed, expression
38. effectiveness	13	2	0,64%	effectiveness
39. dispense	8	2	0,64%	dispense
40. budget	6	2	0,64%	budget
41. aspects	7	2	0,64%	aspects
42. action	6	2	0,64%	action
43. local	5	1	0,32%	local
44. lisi	4	1	0,32%	lisi
45. legal	5	1	0,32%	legal
46. left	4	1	0,32%	left
47. later	5	1	0,32%	later
48. lasting	7	1	0,32%	lasting
49. key	3	1	0,32%	key
50. keen	4	1	0,32%	keen
51. karolina	8	1	0,32%	karolina
52. join	4	1	0,32%	join
53. italy	5	1	0,32%	italy
54. issue	5	1	0,32%	issue
55. invited	7	1	0,32%	invited
56. industry	8	1	0,32%	industry
57. indicate	8	1	0,32%	indicate
58. increase	8	1	0,32%	increase
59. incorporating	13	1	0,32%	incorporating
60. implementation	14	1	0,32%	implementation
61. ideally	7	1	0,32%	ideally
62. governance	10	1	0,32%	governance
63. gathering	9	1	0,32%	gathering
64. firstly	7	1	0,32%	firstly

65. finding	7	1	0,32%	finding
66. felt	4	1	0,32%	felt
67. federation	10	1	0,32%	federation
68. extent	6	1	0,32%	extent
69. extensive	9	1	0,32%	extensive
70. explored	8	1	0,32%	explored
71. expertise	9	1	0,32%	expertise
72. europe	6	1	0,32%	europe
73. ethical	7	1	0,32%	ethical
74. entitled	8	1	0,32%	entitled
75. enrol	5	1	0,32%	enrol
76. engage	6	1	0,32%	engage
77. disconnecting	13	1	0,32%	disconnecting
78. different	9	1	0,32%	different
79. dialogue	8	1	0,32%	dialogue
80. depends	7	1	0,32%	depends
81. decommissioned	14	1	0,32%	decommissioned
82. declared	8	1	0,32%	declared
83. crucial	7	1	0,32%	crucial
84. covering	8	1	0,32%	covering
85. country	7	1	0,32%	country
86. contribute	10	1	0,32%	contribute
87. continue	8	1	0,32%	continue
88. considerations	14	1	0,32%	considerations
89. consequently	12	1	0,32%	consequently
90. confirmed	9	1	0,32%	confirmed
91. concern	7	1	0,32%	concern
92. clarified	9	1	0,32%	clarified
93. association	11	1	0,32%	association

94. allowed	7	1	0,32%	allowed
95. agreed	6	1	0,32%	agreed
96. agenda	6	1	0,32%	agenda
97. agency	6	1	0,32%	agency
98. adequate	8	1	0,32%	adequate
99. addition	8	1	0,32%	addition
100. added	5	1	0,32%	added

APPENDIX 4

Patients and Consumers' organization word frequency query. pre-adoption. NVivo12.

Word _ Post Adoption	Length	Count	Weighted Percentage	Similar Words
1. interest	8	23	2,56%	interest, interested, interesting
2. involvement	11	20	2,23%	involve, involved, involvement, involving
3. network	7	18	2,00%	network
4. patients	8	17	1,89%	patient, patients, patients'
5. organisations	13	15	1,67%	organisation, organisations
6. particular	10	14	1,56%	particular, particularly
7. european	8	13	1,45%	european
8. stakeholders	12	12	1,34%	stakeholder, stakeholders, stakeholders'
9. consultation	12	12	1,34%	consult, consultation
10. discussion	10	11	1,22%	discuss, discussion, discussions
11. follow	6	10	1,11%	follow, following
12. work	4	10	1,11%	work
13. processes	9	9	1,00%	process, processes
14. innovation	10	9	1,00%	innovation, innovative
15. medical	7	9	1,00%	medical
16. possible	8	9	1,00%	possible
17. public	6	9	1,00%	public
18. cooperation	11	8	0,89%	cooperation
19. policy	6	8	0,89%	policy

20. products	8	8	0,89%	product, products
21. expression	10	8	0,89%	expressed, expression
22. initiative	10	8	0,89%	initiative, initiatives
23. participants	12	7	0,78%	participants, participating, participation
24. representative	14	7	0,78%	represent, representative
25. technology	10	7	0,78%	technologies, technology
26. topic	5	7	0,78%	topic, topics
27. directorate	11	7	0,78%	directorate
28. launched	8	6	0,67%	launch, launched
29. access	6	6	0,67%	access, accessibility
30. action	6	6	0,67%	action
31. joint	5	6	0,67%	joint
32. national	8	6	0,67%	national
33. planned	7	6	0,67%	planned
34. safety	6	6	0,67%	safety
35. workshop	8	6	0,67%	workshop
36. provided	8	5	0,56%	provide, provided, providers, providing
37. views	5	5	0,56%	view, views
38. basis	5	5	0,56%	basis
39. important	9	5	0,56%	important
40. next	4	5	0,56%	next
41. packages	8	5	0,56%	package, packages
42. position	8	5	0,56%	position
43. purpose	7	5	0,56%	purpose

44. report	6	5	0,56%	report, reports
45. strengthening	13	5	0,56%	strengthening
46. sustainable	11	5	0,56%	sustainability, sustainable
47. agenda	6	4	0,45%	agenda
48. confirmed	9	4	0,45%	confirmed
49. considers	9	4	0,45%	considered, considering, considers
50. consumers	9	4	0,45%	consumers
51. doctors	7	4	0,45%	doctors, doctors', doctors’
52. experts	7	4	0,45%	experts
53. explained	9	4	0,45%	explained
54. foresee	7	4	0,45%	foresee, foresees
55. foreseen	8	4	0,45%	foreseen
56. general	7	4	0,45%	general
57. included	8	4	0,45%	include, included, including
58. industry	8	4	0,45%	industry
59. medicine	8	4	0,45%	medicine, medicines
60. natsis	6	4	0,45%	natsis
61. perspective	11	4	0,45%	perspective
62. independence	12	4	0,45%	independence, independency
63. last	4	4	0,45%	last, lasting
64. activities	10	3	0,33%	activities, activity
65. budgets	7	3	0,33%	budget, budgets
66. dialogue	8	3	0,33%	dialogue, dialogues
67. making	6	3	0,33%	make, making
68. market	6	3	0,33%	market, marketing

69. potentially	11	3	0,33%	potential, potentially
70. specifically	12	3	0,33%	specific, specifically
71. structure	9	3	0,33%	structure, structures
72. sunsparency	12	3	0,33%	transparency, transparent
73. contribute	10	3	0,33%	contribute
74. depth	5	3	0,33%	depth
75. different	9	3	0,33%	different
76. location	8	3	0,33%	location
77. nevertheless	12	3	0,33%	nevertheless
78. office	6	3	0,33%	office
79. paper	5	3	0,33%	paper
80. play	4	3	0,33%	play
81. quality	7	3	0,33%	quality
82. question	8	3	0,33%	question
83. single	6	3	0,33%	single
84. stressed	8	3	0,33%	stressed
85. thanked	7	3	0,33%	thanked
86. unit	4	3	0,33%	unit
87. uptake	6	3	0,33%	uptake
88. adequate	8	2	0,22%	adequate
89. advice	6	2	0,22%	advice
90. affordability	13	2	0,22%	affordability, affordable
91. agreement	9	2	0,22%	agreement
92. aspects	7	2	0,22%	aspects
93. bodies	6	2	0,22%	bodies
94. brief	5	2	0,22%	brief

95. campaign	8	2	0,22%	campaign, campaigns
96. capacity	8	2	0,22%	capacity
97. chosen	6	2	0,22%	chosen
98. communication	13	2	0,22%	communication
99. concluded	9	2	0,22%	concluded
100. conclusion	10	2	0,22%	conclusion, conclusions

APPENDIX 5

Payers, word frequency query. Pre and post-adoption. NVivo12.

Word _ Pre Adoption	Length	Count	Weighted Percentage	Similar Words
cooperation	11	105	1,82%	cooperation
joint	5	83	1,44%	joint, jointly
european	8	74	1,28%	european, european’
technologies	12	68	1,18%	technologies, technologies', technologies’, technology
participation	13	57	0,99%	participants, participate, participated, participating, participation, participation’
representatives	15	56	0,97%	represent, representative, representatives, represented, representing, represents
medical	7	56	0,97%	medical, medication
industry	8	54	0,94%	industries, industry
companies	9	50	0,87%	companies, company
stakeholders	12	48	0,83%	stakeholder, stakeholders, stakeholders', stakeholders’
products	8	47	0,82%	product, production, products
options	7	44	0,76%	option, options
discussion	10	43	0,75%	discuss, discussed, discussing, discussion, discussions
process	7	40	0,69%	process, processes
patient	7	39	0,68%	patient, patients, patients', patients’
support	7	36	0,63%	support, supporting, supports

study	5	35	0,61%	studies, study
europe	6	33	0,57%	europe, europe’
collaborative	13	33	0,57%	collaborate, collaborating, collaboration, collaborations, collaborative
national	8	32	0,56%	national, national’
voluntary	9	32	0,56%	voluntary
action	6	31	0,54%	action, actions
network	7	31	0,54%	network, networks
medicines	9	30	0,52%	medicinal, medicines
access	6	29	0,50%	access, accessible
interest	8	29	0,50%	interest, interested
contribute	10	27	0,47%	contribute, contributes, contributing, contribution, contributions
decision	8	27	0,47%	decision, decisions
follow	6	26	0,45%	follow, followed, following
strengthening	13	26	0,45%	strengthen, strengthened, strengthening
pharmaceutical	14	25	0,43%	pharmaceutical, pharmaceuticals
consulted	9	24	0,42%	consult, consultation, consultations, consulted
provide	7	24	0,42%	provide, provided, providers, provides
initiative	10	24	0,42%	initiative, initiatives
current	7	23	0,40%	current, currently
innovation	10	23	0,40%	innovation, innovations, innovative
making	6	22	0,38%	make, making
activities	10	22	0,38%	active, actively, activities, activity
coordinator	11	22	0,38%	coordinate, coordinated, coordinating,

				coordination, coordinator
times	5	22	0,38%	time, timely, times, timing
issues	6	22	0,38%	issue, issues
mte	3	22	0,38%	mte
presented	9	21	0,36%	present, presentation, presentations, presented
organisation	12	21	0,36%	organisation, organisational, organised, organising
continuity	10	21	0,36%	continuation, continue, continued, continuing, continuity, continuous
public	6	21	0,36%	public, publications
medtech	7	21	0,36%	medtech
specific	8	20	0,35%	specific, specifically, specificities, specificity
policy	6	20	0,35%	policies, policy
safety	6	20	0,35%	safety
considers	9	19	0,33%	consider, considered, considering, considers
different	9	19	0,33%	differences, different
requires	8	19	0,33%	require, requirements, requires
appropriate	11	19	0,33%	appropriate
dialogue	8	19	0,33%	dialogue, dialogues
important	9	19	0,33%	importance, important
ppta	4	19	0,33%	ppta
development	11	18	0,31%	develop, developed, development, developments

duplicative	11	17	0,30%	duplicate, duplication, duplicative
based	5	17	0,30%	based
secretarial	11	17	0,30%	secretarial
uptake	6	17	0,30%	uptake
expression	10	17	0,30%	express, expressed, expressing, expression
general	7	16	0,28%	general, generally
results	7	16	0,28%	result, results
however	7	16	0,28%	however
two	3	16	0,28%	two
manufacturers	13	15	0,26%	manufacturers, manufacturers', manufacturing
effectiveness	13	15	0,26%	effective, effectively, effectiveness
value	5	15	0,26%	value, value'
common	6	15	0,26%	common
early	5	15	0,26%	early
future	6	15	0,26%	future
europabio	9	14	0,24%	europabio
mandatory	9	14	0,24%	mandatory
launch	6	14	0,24%	launch, launched, launching
bodies	6	14	0,24%	bodies, body
funding	7	14	0,24%	funded, funding, funds
including	9	14	0,24%	include, includes, including
model	5	14	0,24%	model, models
directorate	11	13	0,23%	director, directorate
explained	9	13	0,23%	explain, explained
resources	9	13	0,23%	resource, resources
clinical	8	13	0,23%	clinical
evidence	8	13	0,23%	evidence
permanent	9	13	0,23%	permanent
rea	3	13	0,23%	rea

responses	9	13	0,23%	response, responses, responsibility, responsible
involvement	11	13	0,23%	involved, involvement, involving
benefit	7	13	0,23%	benefit, benefits
sustainable	11	13	0,23%	sustainability, sustainable
location	8	13	0,23%	located, location
case	4	12	0,21%	case
clarified	9	12	0,21%	clarified
eucope	6	12	0,21%	eucope
quality	7	12	0,21%	quality
increase	8	12	0,21%	increase, increased, increases, increasingly
relative	8	12	0,21%	related, relation, relative
report	6	12	0,21%	report, reported, reports
selection	9	12	0,21%	select, selected, selection

Word_ Post-adoption	**Length**	**Count**	**Weighted Percentage**	**Similar Words**
1. option	6	19	2,03%	option, options
2. joint	5	18	1,92%	joint
3. cooperation	11	14	1,49%	cooperation
4. participants	12	13	1,39%	participants, participate, participating, participation
5. regarding	9	10	1,07%	regard, regarding, regards
6. discussion	10	10	1,07%	discuss, discussed, discussion, discussions
7. action	6	10	1,07%	action
8. involvement	11	10	1,07%	involved, involvement
9. process	7	9	0,96%	process, processes
10. payers	6	9	0,96%	payer, payers,

				payers'
11. voluntary	9	9	0,96%	voluntary
12. activities	10	8	0,85%	active, actively, activities, activity
13. european	8	8	0,85%	european
14. market	6	8	0,85%	market, marketing
15. technologies	12	8	0,85%	technologies, technology
16. products	8	8	0,85%	product, production, products
17. interest	8	8	0,85%	interest, interested
18. consultation	12	8	0,85%	consultation, consultations
19. possible	8	8	0,85%	possible, possibly
20. inception	9	7	0,75%	inception
21. medical	7	7	0,75%	medical
22. public	6	7	0,75%	public
23. presentation	12	6	0,64%	present, presentation, presentations
24. decision	8	6	0,64%	decision, decisions
25. insurance	9	6	0,64%	insurance
26. initiative	10	5	0,53%	initial, initiating, initiative
27. might	5	5	0,53%	might
28. national	8	5	0,53%	national
29. pointed	7	5	0,53%	point, pointed
30. policy	6	5	0,53%	policy
31. time	4	5	0,53%	time, timing
32. area	4	4	0,43%	area, areas
33. associated	10	4	0,43%	associated, association
34. coming	6	4	0,43%	coming
35. directorate	11	4	0,43%	directorate
36. expressed	9	4	0,43%	express, expressed, expression
37. innovation	10	4	0,43%	innovation
38. legal	5	4	0,43%	legal
39. organisations	13	4	0,43%	organisations
40. purpose	7	4	0,43%	purpose

41. represent	9	4	0,43%	represent, representative, representatives, represented
42. role	4	4	0,43%	role
43. safety	6	4	0,43%	safety
44. sustainability	14	4	0,43%	sustainability
45. term	4	4	0,43%	term, terms
46. agreed	6	4	0,43%	agree, agreed
47. authorisation	13	4	0,43%	authorisation, authorisations
48. considered	10	4	0,43%	considered, considering
49. current	7	4	0,43%	current, currently
50. effectiveness	13	4	0,43%	effective, effectiveness
51. particular	10	4	0,43%	particular, particularly
52. views	5	4	0,43%	view, views
53. aspects	7	3	0,32%	aspect, aspects
54. differ	6	3	0,32%	differ, different
55. explained	9	3	0,32%	explained, explaining
56. including	9	3	0,32%	included, including
57. launch	6	3	0,32%	launch, launched, launches
58. obligation	10	3	0,32%	obligation, obligations, obliges
59. operational	11	3	0,32%	operational, operative
60. preferred	9	3	0,32%	preference, preferred
61. provide	7	3	0,32%	provide, provided, providing
62. question	8	3	0,32%	question, questionable
63. reports	7	3	0,32%	report, reports
64. respective	10	3	0,32%	respecting, respective
65. stakeholders	12	3	0,32%	stakeholder, stakeholders
66. support	7	3	0,32%	support, supporting

67. available	9	3	0,32%	available
68. clinical	8	3	0,32%	clinical
69. committee	9	3	0,32%	committee
70. corresponds	11	3	0,32%	corresponds
71. cost	4	3	0,32%	cost
72. criteria	8	3	0,32%	criteria
73. document	8	3	0,32%	document
74. early	5	3	0,32%	early
75. ema	3	3	0,32%	ema
76. follow	6	3	0,32%	follow
77. general	7	3	0,32%	general
78. light	5	3	0,32%	light
79. location	8	3	0,32%	location
80. mandatory	9	3	0,32%	mandatory
81. mentioned	9	3	0,32%	mentioned
82. pharmaceuticals	15	3	0,32%	pharmaceuticals
83. post	4	3	0,32%	post
84. prioritisation	14	3	0,32%	prioritisation
85. procedures	10	3	0,32%	procedures
86. social	6	3	0,32%	social
87. stressed	8	3	0,32%	stressed
88. taken	5	3	0,32%	taken
89. thanked	7	3	0,32%	thanked
90. agencies	8	2	0,21%	agencies, agency
91. agreement	9	2	0,21%	agreement, agreements
92. asked	5	2	0,21%	asked
93. authorities	11	2	0,21%	authorities, authorization
94. aware	5	2	0,21%	aware
95. boehm	5	2	0,21%	boehm
96. budget	6	2	0,21%	budget
97. built	5	2	0,21%	built
98. called	6	2	0,21%	called
99. carry	5	2	0,21%	carry
100. certain	7	2	0,21%	certain

APPENDIX 6

Industry, word frequency query. Pre and post adoption. NVivo 1.2.

Word_PRE-ADOPTION	Length	Count	Weighted Percentage	Similar Words
1. cooperation	11	71	1,92%	cooperation
2. participation	13	42	1,14%	participants, participate, participated, participating, participation, participation’
3. options	7	42	1,14%	option, options
4. companies	9	37	1,00%	companies, company
5. products	8	37	1,00%	product, production, products
6. representatives	15	35	0,95%	represent, representative, representatives, represented, representing
7. patient	7	33	0,89%	patient, patients, patients', patients’
8. discussion	10	31	0,84%	discuss, discussed, discussing, discussion, discussions
9. stakeholders	12	29	0,79%	stakeholder, stakeholders, stakeholders', stakeholders’
10. support	7	28	0,76%	support, supporting, supports
11. voluntary	9	26	0,70%	voluntary
12. access	6	25	0,68%	access, accessible
13. contribute	10	22	0,60%	contribute, contributes, contributing, contribution, contributions

14. action	6	22	0,60%	action, actions
15. pharmaceutical	14	21	0,57%	pharmaceutical, pharmaceuticals
16. current	7	19	0,52%	current, currently
17. decision	8	19	0,52%	decision, decisions
18. considers	9	19	0,52%	consider, considered, considering, considers
19. dialogue	8	19	0,52%	dialogue, dialogues
20. activities	10	18	0,49%	active, actively, activities, activity
21. presented	9	18	0,49%	present, presentation, presentations, presented
22. organisation	12	18	0,49%	organisation, organisational, organised, organising
23. duplicative	11	17	0,46%	duplicate, duplication, duplicative
24. innovation	10	17	0,46%	innovation, innovations, innovative
25. timely	6	17	0,46%	time, timely, timing
26. appropriate	11	17	0,46%	appropriate
27. continuity	10	17	0,46%	continuation, continue, continued, continuing, continuity, continuous
28. secretarial	11	17	0,46%	secretarial
29. uptake	6	17	0,46%	uptake
30. network	7	17	0,46%	network, networks
31. policy	6	16	0,43%	policies, policy

32. important	9	16	0,43%	importance, important
33. provide	7	16	0,43%	provide, provided, providers, provides
34. requires	8	16	0,43%	require, requirements, requires
35. development	11	15	0,41%	develop, developed, development, developments
36. interest	8	15	0,41%	interest, interested
37. based	5	14	0,38%	based
38. europabio	9	14	0,38%	europabio
39. mandatory	9	14	0,38%	mandatory
40. manufacturers	13	13	0,35%	manufacturers, manufacturers’
41. value	5	13	0,35%	value, value’
42. permanent	9	13	0,35%	permanent
43. rea	3	13	0,35%	rea
44. safety	6	13	0,35%	safety
45. eucope	6	12	0,33%	eucope
46. fee	3	12	0,33%	fee, fees
47. increase	8	12	0,33%	increase, increased, increases, increasingly
48. involved	8	12	0,33%	involved, involvement, involving
49. model	5	12	0,33%	model, models
50. relative	8	12	0,33%	related, relation, relative
51. contractor	10	12	0,33%	contractor, contractors

52. effective	9	11	0,30%	effective, effectively, effectiveness
53. resources	9	11	0,30%	resource, resources
54. strengthening	13	11	0,30%	strengthen, strengthened, strengthening
55. benefit	7	11	0,30%	benefit, benefits
56. common	6	11	0,30%	common
57. different	9	11	0,30%	differences, different
58. ema	3	11	0,30%	ema
59. future	6	11	0,30%	future
60. medtech	7	11	0,30%	medtech
61. specific	8	11	0,30%	specific, specifically, specificity
62. structure	9	10	0,27%	structure, structures
63. certain	7	10	0,27%	certain
64. choose	6	10	0,27%	choose, chooses
65. organization	12	10	0,27%	organization, organizations, organize, organized
66. procedures	10	10	0,27%	procedure, procedures
67. see	3	10	0,27%	see
68. market	6	10	0,27%	market, marketing, markets
69. advice	6	10	0,27%	advice, advices
70. location	8	10	0,27%	located, location
71. survey	6	10	0,27%	survey, surveys
72. tools	5	9	0,24%	tool, tools

73. addition	8	9	0,24%	addition, additional, additionally
74. function	8	9	0,24%	function, functioning, functions
75. address	7	9	0,24%	address, addressed, addressing
76. diseases	8	9	0,24%	disease, diseases
77. experience	10	9	0,24%	experience, experiences
78. methodologies	13	9	0,24%	methodological, methodologies, methodology
79. responsibility	14	9	0,24%	response, responses, responsibility, responsible
80. sustainability	14	9	0,24%	sustainability, sustainable
81. limited	7	9	0,24%	limitations, limited
82. project	7	9	0,24%	project, projects
83. agency	6	8	0,22%	agencies, agency
84. directly	8	8	0,22%	direct, directly
85. economic	8	8	0,22%	economic, economically, economics
86. financing	9	8	0,22%	financed, financing
87. treatment	9	8	0,22%	treatment, treatments
88. approach	8	8	0,22%	approach, approaches
89. commitment	10	8	0,22%	commitment, commitments
90. expressed	9	8	0,22%	expressed, expressing, expression

91. implemented	11	8	0,22%	implement, implementation, implemented
92. plans	5	8	0,22%	plan, planned, planning, plans
93. published	9	8	0,22%	publish, published
94. regards	7	8	0,22%	regard, regarding, regards
95. added	5	8	0,22%	added
96. agenda	6	8	0,22%	agenda
97. believe	7	8	0,22%	believe, believes
98. budget	6	8	0,22%	budget
99. clarified	9	8	0,22%	clarified
100.criteria	8	8	0,22%	criteria

Word_POST-Adoption	**Length**	**Count**	**Weighted Percentage**	**Similar Words**
1. cooperation	11	14	1,06%	cooperation
2. requirements	12	14	1,06%	required, requirement, requirements
3. patients	8	13	0,98%	patient, patients, patients’
4. market	6	12	0,90%	market, marketing
5. products	8	11	0,83%	products
6. development	11	11	0,83%	developed, developer, developers, developing, development

7. position	8	11	0,83%	position, positive
8. timely	6	11	0,83%	time, timely
9. stakeholders	12	10	0,75%	stakeholders, stakeholders'
10. specific	8	10	0,75%	specific, specifically, specificities
11. supports	8	10	0,75%	support, supported, supporting, supportive, supports
12. pharmaceutical	14	10	0,75%	pharmaceutical, pharmaceuticals
13. believes	8	9	0,68%	believe, believes
14. delays	6	9	0,68%	delay, delayed, delaying, delays
15. application	11	9	0,68%	application, applications
16. methodology	11	9	0,68%	methodological, methodologies, methodology
17. access	6	9	0,68%	access
18. decision	8	8	0,60%	decision, decisions
19. vaccines	8	8	0,60%	vaccination, vaccines
20. paper	5	8	0,60%	paper, papers
21. legislation	11	8	0,60%	legislation

22. regulatory	10	8	0,60%	regulatory
23. building	8	8	0,60%	build, building, builds
24. generation	10	7	0,53%	generate, generation
25. criteria	8	7	0,53%	criteria
26. relevant	8	7	0,53%	relevant
27. considered	10	7	0,53%	considered, considering, considers
28. activities	10	7	0,53%	active, activities, activity
29. appropriate	11	7	0,53%	appropriate, appropriately, appropriateness
30. addition	8	6	0,45%	addition, additional
31. association	11	6	0,45%	association, associations
32. companies	9	6	0,45%	companies
33. mandatory	9	6	0,45%	mandatory
34. timeline	8	6	0,45%	timeline, timelines
35. voluntary	9	6	0,45%	voluntary
36. benefit	7	6	0,45%	benefit, benefits
37. defined	7	6	0,45%	define, defined

38. involve	7	6	0,45%	involve, involved, involvement, involving
39. transparent	11	6	0,45%	transparency, transparent
40. consultations	13	6	0,45%	consultations, consulted
41. framework	9	6	0,45%	framework, frameworks
42. important	9	6	0,45%	importance, important
43. approval	8	5	0,38%	approval, approved
44. considerations	14	5	0,38%	consideration, considerations
45. evaluation	10	5	0,38%	evaluation, evaluations
46. innovative	10	5	0,38%	innovation, innovative
47. providers	9	5	0,38%	provide, providers
48. duplication	11	5	0,38%	duplication, duplicative
49. participate	11	5	0,38%	participate, participating, participation
50. perform	7	5	0,38%	perform, performance, performed, performing

51. procedures	10	5	0,38%	procedural, procedure, procedures
52. represented	11	5	0,38%	represent, representatives, represented, represents
53. selection	9	5	0,38%	selected, selection
54. based	5	5	0,38%	based
55. different	9	5	0,38%	different
56. opportunity	11	5	0,38%	opportunity
57. agreed	6	4	0,30%	agree, agreed
58. centrally	9	4	0,30%	centralized, centrally
59. contribute	10	4	0,30%	contribute, contribution
60. existing	8	4	0,30%	exist, existing
61. governance	10	4	0,30%	governance, governments
62. objective	9	4	0,30%	objective, objectives
63. practices	9	4	0,30%	practical, practices
64. principles	10	4	0,30%	principle, principles
65. priority	8	4	0,30%	priorities, priority
66. achieve	7	4	0,30%	achieve, achieved, achieves

67. alignment	9	4	0,30%	alignment
68. author	6	4	0,30%	author, authorization, authorized
69. authorisation	13	4	0,30%	authorisation
70. availability	12	4	0,30%	availability
71. belgium	7	4	0,30%	belgium
72. common	6	4	0,30%	common
73. continues	9	4	0,30%	continue, continues, continuing
74. critical	8	4	0,30%	critical
75. devices	7	4	0,30%	devices
76. dialogue	8	4	0,30%	dialogue
77. directive	9	4	0,30%	directive
78. emerging	8	4	0,30%	emerging
79. final	5	4	0,30%	final
80. focus	5	4	0,30%	focus
81. key	3	4	0,30%	key
82. leads	5	4	0,30%	lead, leading, leads
83. leopold	7	4	0,30%	leopold
84. october	7	4	0,30%	october
85. office	6	4	0,30%	office
86. pricing	7	4	0,30%	pricing

87. primary	7	4	0,30%	primary
88. recommendations	15	4	0,30%	recommendations, recommends
89. reimbursement	13	4	0,30%	reimbursement
90. related	7	4	0,30%	related, relative
91. transition	10	4	0,30%	transition, transitional
92. trône	5	4	0,30%	trône
93. undergo	7	4	0,30%	undergo
94. value	5	4	0,30%	value
95. welcomes	8	4	0,30%	welcomes
96. approach	8	3	0,23%	approach
97. burden	6	3	0,23%	burden
98. council	7	3	0,23%	council
99. greater	7	3	0,23%	greater
100.horizon	7	3	0,23%	horizon

BIBLIOGRAPHY

Banta HD, Oortwijn W. "*Health Technology assessment in the European Union."* Int J Technol Asseess Health Care. 16:626-635. (2000).

Banta HD. "Introduction to the EUR-ASSESS report." *Int J Technol Asseess Health Care*. 13:133-143. (1997).

Banta, D. "*The development of health technology assessment*". Health policy 63.2.121-132. (2003).

Banta, D., Finn Børlum K., and Egon J... *"A History of Health Technology Assessment at the European Level."* International Journal of Technology Assessment in Health Care 25. S1. 68–73. (2009)

Briganti, P., Ferrara, M., Salvatore D.."*Temi emergenti negli studi di organizzazione sanitaria",* G. Giappichelli, cap. VIII. (2011)

Cicchetti, A. and M. Marchetti. "*Manuale di Health Technology Assessment*." Il Pensiero Scientifico Editore (2010).

Cochrane, A. L. Archie Cochrane in his own words: Selections arranged from his 1972 introduction to "*effectiveness and efficiency: Random reflections on the health services".* Controlled clinical trials, 10(4), 428-433. (1989).

Cranovsky, R., Matillon, Y., & Banta, "*D.EUR-ASSESS Project Subgroup Report on Coverage*." International Journal of Technology Assessment in Health Care, *13*(2), 287-332. (1997).

Duncan B. *"Health policy in the European Union: how it's made and how to influence it."* BMJ : British Medical Journal. 1027-1030. (2002)

Etzkowitz, H., & Leydesdorff, L. *"The dynamics of innovation: from National Systems and "Mode 2" to a Triple Helix of university–industry–government relations*". Research policy, 29(2), 109-123. (2000).

Fattore, G., Nikos M., Lorenzo G., and Boriani. L. *"Health technology assessment: what is it? Current status and perspectives in the field of electrophysiology." Europace* 13, no. suppl_2 (2011).

Favaretti, C., Cicchetti, A., Guarrera, G., Marchetti, M., & Ricciardi, W. "*Health technology assessment in Italy*." International Journal of Technology Assessment in Health Care, 25(S1), 127-133. (2009)

Finn Børlum K.,. "*European network for Health Technology Assessment, EUnetHTA: Planning, development, and implementation of a sustainable European network for Health Technology Assessment."* International journal of technology assessment in health care 25.S2 (2009).

Fricke, F. U., & Dauben, H. P. *"Health technology assessment: a perspective from Germany."* Value in Health, *12*, S20-S27.(2009)

Goodman, C. *"HTA 101: Introduction to health technology assessment."* US National Library of Medicine, National Institutes of Health, National Information Centre on Health Services Research and Health Care Technology (NICHSR). (2004).

Goodman, C. *"Technology assessment: A tool for technology management and improved patient outcomes."* USA: The Lewin Group, 1998.

Gray J. *"Evidence Based Health Care."* New York: Churchill Livingston; 1997.

Jonsson E, Banta HD, Henshall C, Sampietro-Colom L. "E*uro- pean collaboration for health technology assessment: Develop- ing an assessment network*". Int J Technol Assess Health Care.;18:213-455. (2002)

Kanavos, P., Nicod, E., Van Den Aardweg, S., & Pomedli, S. "*The impact of health technology assessments: an international comparison."* (2010).

Lorusso S., "*Health Technology Assessment come strumento di supporto al managment: aspetti cognitivi e metodologici".* Mecosan, Vol. 53. (2005)

Mikhail, O., Swint, J. M., Brinker, M. R., Moye, L. A., & Sabino, M. *"Technology evolution: the technology spectrum and its application to orthopaedic technologies."* International journal of technology assessment in health care.15(1), 254-263. (1999).

Nolte, E., & Knai, C. "*Managing chronic conditions: experience in eight countries"* (No. 15). WHO Regional Office Europe. (2008).

Scaletti, A. "*Evaluating Investments in Health Care Systems: Health Technology Assessment*." Springer. (2014).

WEBLIOGRAPHY

http://www.who.int/en/

http://www.euro.who.int/__data/assets/pdf_file/0008/259955/Everything-you-always-wanted-to-know-about-European-Union-health-policies-but-were-afraid-to-ask.pdf

http://ec.europa.eu/health/ph_overview/Documents/key01_mobility_en.pdf

http://www.who.int/medical_devices/Sat_am_HTA_3_CERBO.pdf

https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:088:0045:0065:en:PDF

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2014_strategy_eucooperation_hta_en.pdf

https://www.eunethta.eu/wp-content/uploads/2018/01/Overview-of-the-EUnetHTA-Project-Results-2006-2008_0.pdf

http://www.eunethta.eu/Stakeholder_Forum/ Activities_for_Stakeholders/

http://www.eunethta.net/Stakeholder_ Forum/Home/

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20091215_co01_en.pdf

https://www.eunethta.eu/ja1-archive/

https://www.eunethta.eu/wp-content/uploads/2018/01/EUnetHTA-JA-Stakeholder-Involvement-Policy.pdf

https://www.eunethta.eu/ja2-archive/

https://webgate.ec.europa.eu/chafea_pdb/health/projects/724130/summary

https://www.eunethta.eu/ja3-archive/

http://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2014_strategy_eucooperation_hta_en.pdf.

http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1473406227181&uri=CELEX:52015XG1217%2801%29

http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1473409810047&uri=CELEX:52016XG0723(03)

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf

http://www.salute.gov.it/portale/temi/p2_6.jsp?id=1202&area=dispositivi-medici&menu=tecnologie

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

https://www.eca.europa.eu/Lists/ECADocuments/SR16_28/SR_HEALTH_EN.pdf

https://ec.europa.eu/health/technology_assessment/eu_cooperation_en

https://ec.europa.eu/health/technology_assessment/events_en#anchor3

https://eupha.org/repository/advocacy/EUPH_Statement_on_EU_Commission_Legislative_Proposal_on_HTA.pdf

http://www.eahp.eu/press-room/eahp-response-proposal-regulation-hta

http://www.euprimarycare.org/news/efpc-invited-eu-commissioner-health-food-safety-dr-andriukaitis-editorial-diederik-aarendonk

http://www.hope.be/wp-content/uploads/2018/07/HOPE-Position-Paper-on-Health-Technolgy-Assessment.pdf

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170424_en.pdf

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20160603_sr_en.pdf

http://www.ecpc.org/ECPC%20Response%20to%20HTA%20-%20Policy%20Paper.pdf

https://www.beuc.eu/publications/beuc-x-2018 027_beuc_comments_to_european_commission_s_proposal_regulation_health_technology_assessment_.pdf

http://www.efanet.org/images/documents/201805EFAs_HTA_Position_Paper-Commission_proposal.pdf

http://www.eu-patient.eu/globalassets/policy/hta/epf-position-statement-on-hta.pdf

http://download2.eurordis.org.s3.amazonaws.com/positionpapers/Statement_final.pdf

https://epha.org/wp-content/uploads/2018/07/HTA-recommendations.pdf

http://haiweb.org/wp-content/uploads/2018/02/Statement-European-Commission-Proposal-on-HTA.pdf

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20160216_sr_en.pdf; https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20161213_mi_en.pdf; https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170523_mi_en.pdf.

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

https://esip.eu/publications-intranet?idf=137&preview=332

https://esip.eu/publications-intranet?idf=137&preview=332

https://www.aim-mutual.org/wp-content/uploads/2018/02/AIM-on-HTA.pdf

https://ec.europa.eu/health/technology_assessment/events_en#anchor2

https://www.europabio.org/sites/default/files/FOR%20PUBLICATION_June_FINAL_Joint%20industry%20statement%20HTA.pdf

https://www.efpia.eu/media/361850/efpia-position-paper-on-the-commission-proposal-for-a-regulation-on-hta.pdf

https://www.cocir.org/fileadmin/Position_Papers_2018/COCIR_Position_Paper_on_EC_proposal_on_HTA_-_30_Mar._2018_final.pdf

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/20161020_frep_en.pdf

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20170217_mi_en.pdf

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20161122_mi_en_0.pdf

https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/ev_20161117_mi_en.pdf

https://webcast.ec.europa.eu/the-way-forward-for-hta-cooperation-the-views-of-stakeholders

SUMMARY

In the last five decades, technology innovation has yielded truly remarkable advance in the health care. Technological innovation has taken a strategic role in transforming the economy of industrialized countries from manufacturing economy into service economy. Its introduction in the health sector will lead to a higher operating cost. However, rather than costs, it should be a strategic investment to an overall improvement of the system, in medium and long run. This focus on technology innovation is present in the healthcare service sector, as the implementation of new technologies can offer a better level of diagnosis, treatment and of better effectiveness[301]. Moreover, the development, adoption, and diffusion of technology has been, and continues to be, influenced by an expanding group of health sector policymakers and stakeholders. Increasingly, Health Technology Assessment (HTA) is being utilised, primarily to provide input into decision making. Over the years, there have been several definitions of Health Technology Assessment and all emphasize its role, as tool supporting decision making at different level of the healthcare system, its multidisciplinary nature, and its strong reliance on transparent scientific rigours methods. However, for this thesis the official definition of Health Technology Assessment is the one, given by EUnetHTA

[301] Effectiveness in this context means the success of the medical service and consequently complete satisfaction and well-being of the patient. It is important make a difference between efficacy, that is, the ability to achieve the desired results, and effectiveness the ability to achieve the excepted results under real conditions in the given time.

«*a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective health policies that are patient focused and seek to achieve best value*»[302]».

HTA dates back to around 1975 (when the Office of Technology Assessment in the US established its health program) and, in its early years of development, aimed at synthesising available evidence dealing with efficacy and cost-effectiveness of health care interventions in order to be helpful to health policy-makers. Since the early 1980s, HTA has sought more effective links with these policy-makers, particularly in Europe, where at present the main scope has been to influence administrators and clinicians with more effective dissemination and implementation of activity and results[303]. The first national HTA agency was founded in Sweden in 1987 establishing the Swedish HTA Council (SBU) due to the high expenditure for health care, the visibility of new technologies, and the necessity to begin to rationalise health care technology[304]. Since that moment the number of institutions involved in the assessment of health technologies has multiples within the member states. Some of them have also been institutionalized within the country's health system. During the years the European Union and the European Commission have gradually become more active in health care. For the first time, in 1992 with the Maastricht Treaty, the public health was included as a task of the European Commission, including a special section to regulate the public health (TITLE X). According to the treaty, the EU has a mandate of "encouraging cooperation between member states" and "if necessary, leading support to their actions" in public health (article 129(1))[305]. Moreover, the EU was given the power

[302] EUnetHTA Joint Action definition.

[303] http://www.astrid-online.it/static/upload/7787/7787e169a7f0afc63221153a6636c63f.pdf

[304]Banta, D. "*The development of health technology assessment*". Health policy 63.2.121-132. (2003).

[305]The Conmunity shall contribute towards ensuring a high level of human health protection by encouraging cooperation between the Mernber States and, if necessary, lending support to their action.

to spend money on European level health projects but forbidden to pass laws harmonising health measures in the member states (article 129 (4))[306]. At international level, during the 1970s and 1980s, it starts to think about international cooperation on Health Technology Assessment. This thought became reality in 1985 with the first meeting of the International Society for Technology Assessment in Health Care (ISTAHC) in Copenhagen, followed by the International Network of Agency for Health Technology Assessment (INAHTA), created in 1993. As a result, in Europe a group of agency heads began others, including Egon Jonsson (Sweden), David Banta (the Netherlands), Michael Peckham and Chris Henshall (UK), Yves Matillon (France), Alicia Granados (Catalonia), and Richard Cranovsky (Switzerland) began to talk about the need for coordination of HTA activities in Europe[307]. In this purpose, in1993 a proposal was submitted to the funding of the project EUR-ASSES, the first European cooperation on HTA. EUR-ASSESS project was followed by a European Commission-sponsored activity named HTA-Europe, from 1997 to 1998. The aim of this new project was to develop paper on HTA and health system of all members of the European Union. In 2000, the European Commission strongly supported a third major project in the field named *The European Collaboration for Assessment of Health Intervention and Technology* (ECHTA/ECAHI) and led by Egon

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Community action shall be directed towards the prevention of diseases, in particular the major health scourges, including drug dependence, by promoting research into their causes and their transmission, as well as health information and education. Health protection requirements shall form a constituent part of the Community's other policies.

[306] In order to contribute to the achievement of the objectives referred to in this Article, the Council:
- acting in accordance with the procedure refenced to in Article 189b, after consulting the Economic and Social Committee and the Committee of the Regions, shall adopt incentive measures, excluding any harmonization of the laws and regulations of the Member States;
- setting by a qualified majority on a proposal from the Commission, shall adopt recommendations.

[307] Cranovsky, R., Matillon, Y., & Banta, D. *"EUR-ASSESS Project Subgroup Report on Coverage".* International Journal of Technology Assessment in Health Care, *13*(2), 287-332. (1997)

Jonsson[308]. In 2004 the European Commission established a High-Level Group on Health Service and Medical Care (HLG) consisting of high-level officials from Member State ministries of health to endorse and implement the recommendations issued from the patient mobility reflection process[309]. the HLG work resulted in a report that identifies an urgent need to establish a sustainable network for HTA and proposed several steps, starting with a three years project supported by the EU Public Health Program. This was approved by the Council of Ministers and follows by a call for proposal in SANCO's work program for 2005 aiming at projects to establish a European network for HTA (EUnetHTA)[310].

In the same period, the Commission call was answered by a group of 35 organizations throughout Europe, and the activities of the EUnetHTA Project were led by the Danish Centre for HTA (DACEHTA) in Copenhagen. The consequent activities oh European network of Health Technology Assessment were organised throughout the establishment of the EUnetHTA Collaboration 2009, the EUnetHTA Joint Action 2010-2012. EUnetHTA Joint Action 2 2012-2015 and EUnetHTA Joint Action 3 2016-2020. Whereas EUnetHTA is a voluntary association of organisations involved in HTA with a clear focus on scientific aspect of HTA, the so called Cross Border Directive the Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 provides the legal bases for a European HTA network with an overall mandate concerning HTA cooperation in Europe[311].

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[308]Banta HD, Oortwijn W. "*Health Technology assessment in the European Union."* Int J Technol Asseess Health Care. 16:626-635. (2000).

[309] Finn Børlum K.,. "*European network for Health Technology Assessment, EUnetHTA: Planning, development, and implementation of a sustainable European network for Health Technology Assessment."* International journal of technology assessment in health care 25.S2 (2009).

[310] Finn Børlum K.,. "*European network for Health Technology Assessment, EUnetHTA: Planning, development, and implementation of a sustainable European network for Health Technology Assessment."* International journal of technology assessment in health care 25.S2 (2009).

[311]https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2014_strategy_eucooperation_hta_en.pdf

The Article 15 (1) "Cooperation on health technology assessment" of the latter stated that

> *«The Union shall support and facilitate cooperation and the exchange of scientific information among Member States within a voluntary network connecting national authorities or bodies responsible for health technology assessment designated by the Member States. The Member States shall communicate their names and contact details to the Commission. The members of such a health technology assessment network shall participate in, and contribute to, the network's activities in accordance with the legislation of the Member State where they are established. That network shall be based on the principle of good governance including transparency, objectivity, independence of expertise, fairness of procedure and appropriate stakeholder consultations.*[312]*»*

However, after 20 years of voluntary cooperation, the European Commission made great efforts and investment to support the cooperation between HTA bodies. The first two Joint Action were followed by a number of projects, and the third Joint Action was launched in June 2016 and runs until 2020, with a total budget of EUR 20 million. The participation in the Joint Action has been very high, including participation from all EU Member States. In addition, following the Directive CBHC, the HTA Network was established in 2013 to provide strategic and political guidance to the scientific and technical cooperation at Union-level. Notwithstanding the achievements of the current EU cooperation, a number of shortcoming have been identified, which cannot be sufficiently addressed by continued project-based voluntary cooperation on HTA. The main problems identify by the European Commission and analysed in the Impact Assessment, published the 31st of January of 2018, are three: 1) Impeded and distorted market access; 2) Duplication of work for national HTA bodies; 3) Unsustainability of HTA cooperation. Without an EU initiative, it is unlikely that long-term

[312] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:088:0045:0065:en:PDF

cooperation on HTA between Member States would be strengthened, with a potential risk of losing the results achieved until now. By carrying joint clinical assessments, economies of scale, greater business predictability, increased quality and consistency and improved transparency for patients would be achieved in the long run[313]. In conformity with the identifies shortcoming, experiences with the current cooperation and stakeholders' consultation were identify five policy option in the *Impact Assessment.* Moreover, "option 5" was discussed in the GOG-LSE study, in which raised concern as regards its proportionality, Member States' responsibility under the above-mentioned Art 168(7) TFEU and its feasibility. However, after an in deep analysis of each policy options described above, the impact assessment reports present the preferred policy option, which has provided the basis for the contest of the proposal. The preferred policy option is option 4.2 "Permanent cooperation on common tools, procedures, early dialogues and joint REA" with some adjustment of policy option 2 and 4.1.

The proposal for a regulation of the European Parliament and of the Council on health technology assessment and amending Directive 2011/24/EU was presented by the European Commission the 31st of January 2018. It aims, as declared by the Commissioner Andriukaitis

«*is to ensure patients will have a timely access to innovative health technologies and to improve the sustainability of health system in the EU.* »

The proposal takes the form of a new Regulation. As explained in the explanatory memorandum of the proposal, this type of instrument is considered to be most suitable considering that a key element of the proposal is the establishment of procedures and structures for the cooperation on joint work at Union-level[314].

To sum up the key elements of the proposal it is important to underline that the system envisage by the Commission's proposal will be a Member States driven. Member States HTA organizations will coordinate the work and jointly develop

[313] Ibidem

[314] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/com2018_51final_en.pdf

outputs while the Commission will play a supportive role. Transparency plays an important role in the proposal, for this reason the Commission shall develop and maintain an IT platform to facilitate information sharing. It will be publishing on the IT platform, which would also include tools for HTA bodies to share early information on their planned and on-going assessment, the lists of both completed joint clinical assessment and assessed health technologies. However, transparency[315] is also about involvement of stakeholders and this should happen at technical level, during the presentation of the Joint Clinical Assessment and Joint Scientific Consultations reports, and at strategic level, when horizontal documents and reports such as the work programme, guidance documents. The proposal is divided in five chapters consisting a total of 36 articles. In chapter I is outline the subject matter of the proposal and defines the key terms used in the Regulation[316]. The joint work is outline in the chapter II (Art.5-Art.17), which establishes the four pillars of the of the future cooperation between Member States at Union level, in other words, joint clinical assessment, joint scientific consultation, emerging health technologies and voluntary cooperation on HTA. The third chapter lays down common rules for carrying out clinical assessments at Member States level which will then be developed in detail in tertiary legislation[317], with the aim of harmonize the clinical assessment approach across Member States. Chapter IV, on the other hand, designs the support framework which will support the joint work at EU-level. It is also established a stakeholder network (Article 26). Following the entry into force, it is proposed a period of three-years in order to allow the development of all tertiary legislation provided for in the proposal for the joint work.

In order to understand the main differences and concerns on the proposal among the interested parties, a content analysis has been made. The permission to conduct the study was obtained from the European Commission, DG SANTE, Unit B4,

[315] Article 7 and Article 22 provide the legal basis of transparency and independence

[316] https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/com2018_51final_en.pdf

[317] Ibidem

HTA team. During my internship in the HTA team[318] I had the opportunity to interact with the HTA stakeholder's pool (ANNEX 1) and collect data. The literature used to describe the stakeholder's position before the implementation of the proposal included the public consultation[319] and several bi-lateral meetings[320] held from October 2016 and January 2018. On the other hand, to analyse the stakeholder position on the proposal after the 31st of January, it was used the official statement or official position that nearly every stakeholder published.

Before moving to the analysis of data result, a definition of content analysis should be provided. A content analysis is defined (Berelson, 1952) as

"A research technique for the objective systematic and quantitative description of the manifest content of communication[321]".

This type of analysis assumes that groups of words reveal underlying themes, and that for instance, co-occurrences of key words can be interpreted as reflecting association between the underlying concepts[322]. The software program named NVivo12. was used in order to conduct this qualitative examination and find out the main groups of words. Based on the above-described division of documents, it was used the "Word Frequency Criteria", of the 100 most frequent words, in order to find out the key words for any categories in each phase. The main groups of words, highlight by NVivo12 programme, would have been the starting point to

[318] From February 2018 to May 2018

[319] The Public Consultation was launched on 21 October 2016. The consultation, which run until 13 January 2017, gathered opinion on the future of EU cooperation on HTA. https://ec.europa.eu/health/technology_assessment/eu_cooperation_en

[320] https://ec.europa.eu/health/technology_assessment/events_en#anchor3

[321] Berelson, B."*Content analysis in communication research."* (1952).

[322] Duriau, V. J., Reger, R. K., & Pfarrer, M. D. "*A content analysis of the content analysis literature in organization studies: Research themes, data sources, and methodological refinements."* Organizational Research Methods, 10(1), 5-34. (2007).

explain their calls of the preparatory period and the main concern of the post-adoption.

The health providers, in the public consultation as well as in the bilateral meeting with the European Commission, have explicitly requested an EU HTA cooperation based on transparency and independence. In order to achieve these two main principles, they strongly believe that, first of all, the system should not be financed through industry fees, and that the stakeholders network, in particular Health Providers' organizations have to be actively involved in the process. However, looking at the official statements published after the adoption of the legislative proposal by the European Commission on 31 January 2018, it is possible notice that their main concerns are pretty aligned with their opinion in the pre-adoption. From the above analysis, it is possible see that the degree of the stakeholders' involvement in the preparatory phase is directly proportionated with the number of concerns expressed on the legal text. In fact, industry was more involved than the others in the preparatory phase and in the post adoption they were very supportive. On the other hand, healthcare providers, which were the least involved in preparatory phase expressed in their statement the several concerns, with the annex amendments.

Patients and consumers' organizations have a high number of concerns. However, they diverge from the other categories because the majority of their queries are focus on stakeholder involvement. While payers, in particular ESIP has proposed an elevate number of amendments on more Regulation's argument.

Transparency followed by independency is another word which often appears statements. In order to generate and maintain trust in the system there should be more provision on transparency in the Regulation. All of them are also against the industry fees as a financed mechanism, as it would lead to conflicts of interest. Except for the patients and consumers' organization, the other categories are not in favour of the mandatory participation and uptake of the joint clinical assessment.

Almost every involved part, in particular patients and healthcare providers, calls for a greater involvement of stakeholders in the future EU cooperation on HTA. Article 26 should be clearer in its provision, making sure that each category of stakeholder would be constantly involved, not only with *«ad hoc meeting»* but with *«regular meeting»*. From their point of view this is fundamental in order to guarantee a transparent process and assessment. All the four categories converge in a specific concern, they ask for more clarification and provision in the Regulation rather than in implementing or delegated act.

Trying to make a classification based on the number of concerns expressed after the publication of the proposal for a Regulation on EU HTA cooperation, it has to do distinction between pharmaceutical and medical technology industries and between ESIP and AIM, within payers, due to their divergent opinion. Staring from the left[323], there are the pharmaceuticals industry which are very supportive to the proposal and at the same time further active in providing input in both of the phases. It is followed by the medical technologies industry which are as well supportive but less active. The third and the fourth position is occupied by payers' category, in which ESIP comes after AIM for the higher number of amendments suggested. On the extreme right there are patients and healthcare providers. The latter in the pre-adoption were not so involved in the process, while after the published of the legal proposal they state a very critical position toward the proposal.

The 9th of July 2018, the European Commission, Health and Food Safety Directorate General, organized a conference to take stock of and listen to the view of stakeholders on HTA proposal. In particular, the focus was on the health providers and patients' representatives' involvement in the future EU HTA cooperation due to their several concerns. The Commissioner Vytenis Andriukaitis in his speech stated that:

[323] Very supportive.

«*The input from patients, health professionals and industry in the HTA discussion is essential. We now have an opportunity to establish a mechanism that ensures that HTA is used to its maximum potential throughout the EU. I believe that joint assessments would not only help patients to have access to the most effective health technologies but would also contribute to the sustainability of health systems. The broad involvement of stakeholders also ensures quality and predictability. Moreover, I believe that our proposal would bring more transparency in the HTA processes in the EU*[324].»

Currently, Member States are in the process of analysing the proposal with a view to formulating their official positions while the European Parliament has appointed its Rapporteur (Soledad Cabezon Ruiz S&D). However, given that European Parliament elections will be held in May 2019, the time period for negotiating and finding an agreement on the proposal in Council and between the Council, Parliament and Commission is limited.

[324] The way forward for HAT cooperation- the views of stakeholders. 09-07-2018. https://webcast.ec.europa.eu/the-way-forward-for-hta-cooperation-the-views-of-stakeholders