POSITION PAPER
ON "STRENGTHENING OF THE EU COOPERATION ON HEALTH TECHNOLOGY ASSESSMENT"

I. INTRODUCTION

The Commission's health unit (DG SANTE) published on September 16 an initiative entitled „Strengthening of the EU cooperation on Health Technology Assessment" (hereinafter called "initiative")[1]. In this autumn it will be launched a public consultation to the stakeholders on this document.

The main goal of the initiative is establishing of a new approach/framework for HTA in the EU, specially based on the Joint Action EUnetHTA experience[2].
The Joint Action EUnetHTA is co-funded through the EU Health Programme. Its scope is scientific and technical: EUnetHTA develops common methodologies, pilot joint early dialogues, Joint REA and Full HTA reports. It develops and maintains common IT tools. EUnetHTA is a voluntary, time-limited initiative with a defined work plan[3].

The general objectives[4] of the initiative are:
1. Enable Member States to strengthen their cooperation on HTA in a sustainable manner,
2. Ensure a better functioning of the internal market of health technologies,
3. Contribute to a high level of human health protection, as stated in Article 168 TFEU and Article 35 of the Charter of Fundamental Rights.

The specific objectives[5] of the initiative are:
1. Reduce duplication of efforts for HTA bodies and industry;
2. Promote convergence in HTA procedures and methodologies;
3. Improve the uptake of joint work in Member States;
4. Ensure the long-term sustainability of EU HTA cooperation.

II. HTA TERMINOLOGY

As terminology, the initiative uses so called HTA Core Model®[6]. According to this, health technology assessment (HTA) is defined as "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".

HTA covers different aspects ("domains"), but does not include pricing and reimbursement decisions, which is a national level prerogative.

[1] See http://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf
[2] EUnetHTA 1 ran from 2010-2012 (budget EUR 6 million), EUnetHTA 2 ran from 2012-2015 (budget EUR 9.5 million). A third Joint Action – EUnetHTA 3, running from 2016 until 2020 – has been launched (budget EUR 20 million) on the 1st June 2016.
[3] See footnote 26 of the initiative.
[4] See p. 13 of of the initiative.
[5] See p. 13 of of the initiative.
[6] http://www.eunethta.eu/hta-core-model

Two types of assessments can be identified:
1. Rapid Relative Effectiveness Assessment (REA) covers the clinical domains and measures the medical/therapeutic added value of a technology:
- Health problem and current use of technology;
- Description and technical characteristics;
- Safety;
- Clinical effectiveness.

2. Full HTA Assessment, along with the REA domains shown above, also includes other non-medical domains:
- Cost and economic evaluation;
- Ethical analysis;
- Organisational aspects;
- Patient and social aspects;
- Legal aspects.

III. PROPOSALS. SHORT DESCRIPTION

The Initiative takes into considerations 5 options, as follows:

1. The status quo – Voluntary Joint Action until 2020
HTA is regulated and organised at national/regional level. In parallel, the Commission and the Member States have set up a voluntary cooperation mechanism through the Joint Actions and the HTA Network.
The third EUnetHTA Joint Action (2016-2020) will include 75 partners from 27 Member States (i.e. national and regional bodies active in HTA) and Norway. Luxembourg will also participate as collaborating party.

2. Long-term voluntary cooperation (financed by the EU beyond 2020)
This option foresees the continuation of the current cooperation model, but on a longer-term basis. The main difference to option 1 is that the short-term financing of Joint Actions will be replaced by a long-term mechanism so the sustainability of the cooperation is ensured/improved.

3. Cooperation on collection, sharing and use of common tools and data
This option foresees the introduction of a legal framework for HTA cooperation, enabling the efforts by national bodies to be compatible, shared and used. This will facilitate cooperation of Member States, and ultimately allow for the production of joint REA reports on a voluntary basis. The legal framework would set out how data is collected, shared and used. It would also create common tools/IT platforms, building on the solutions already developed within the current cooperation model.

Key elements of this option are:
(1) a notification to other HTA bodies about planned and ongoing assessments (e.g. via an IT platform);
(2) collaboration between HTA bodies on the prioritisation of technologies to be assessed;
(3) the use of common tools (e.g. use of submission templates) and possibly methodologies (e.g. the HTA Core Model developed by EUnetHTA);
(4) a mechanism to share results of national HTAs reports;
(5) cooperation on early dialogues and
(6) cooperation on the generation of post marketing data to streamline clinical evidence requirements
(7) possibility for preparing joint HTA reports on a voluntary bases.

4. Cooperation on production of joint REA reports and their uptake (cooperation on clinical/medical matters)
This option foresees that Member States jointly produce REAs (i.e. reports on the relative effectiveness in terms of clinical/medical benefits of the technology), available to all through a shared repository, with measures for the uptake of the joint work at national level. The cooperation – and therefore the uptake – is limited to REA reports; the assessment of non-clinical domains would remain under the responsibility of Member States.

Two sub-options of option 4 can be envisaged:
a) participation by Member States in the preparation of joint REA reports is voluntary, but Member States that opted in are bound by the results of the joint work and commit not to replicate it. In other words, the duplication at national level of assessments for the same technologies under the same conditions (i.e. same comparator, same targeted population) would not be allowed, or
b) both participation in the joint clinical/medical assessments and their subsequent uptake are mandatory for all Member States.

5. Cooperation on production of joint Full HTA reports and their uptake (cooperation on cost-effectiveness).
This option foresees the joint production of Full HTA reports, thus comprising not only the assessment of clinical/medical domains (as already provided in the REA reports, see option 4), but also the assessment of economic, ethical, legal and organisational domains. This means that the joint work will also include a substantial amount of context-specific information and parameters.

Again, two sub-options can be envisaged:
a) participation by Member States in the preparation of joint Full HTA reports is voluntary, but their subsequent uptake is mandatory, as described in option 4a, or
b) both participation in the joint full assessments and their uptake are mandatory for all Member States, as described in option 4b.

IV. REGULATORY/LEGAL ASPECTS

The options 1 and 2 are based on Article 15[7] of the Directive 2011/24/EU *on the application of patients' rights in cross-border healthcare*[8]. It would however be necessary to solve the budgetary issue in order to ensure long term financing of the cooperation. Therefore, these options are non-regulatory solutions.
The options 3, 4 and 5 can be achieved only through a legislative proposal (Directive or Regulation). According to the initiative, the key legal basis for a legislative proposal is Article 114 TFEU. A legislative proposal on HTA contributes to the objectives set out in Article 114 (1) TFEU aiming at improving the functioning of the internal market, whilst ensuring a high level of public health. Essentially it would address the current fragmentation of the national HTA systems (divergences of procedures and methodologies, which impact on market access). The legal basis could be supplemented by means of Article 168 (4) (c) TFEU.
Any legal proposal would need to respect Article 168 (7) TFEU which stipulates that the Union shall respect the responsibilities of Member States for the definition of their health policies and for the organisation and delivery of health services and medical care. This includes decisions on pricing and reimbursement levels, which are not within the scope of this initiative.

V. THE ECPC POSITION

1. Preamble

[7] Article 15 is about cooperation on health technology assessment.
[8] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011L0024&from=EN

Generally, the options 1 and 2 maintain broadly the current state of fact. From this point of view, the shortcomings identified so far is maintained[9]; therefore the ECPC considers that the options 1 and 2 do not cause any noticeable improvements.
In these conditions, the options 3, 4 and 5 should be taken in consideration. We notice that these options ensure a gradual integration of HTA national systems, as follows:
- common tools and data (option 3);
- joint REA (option 4);
- full HTA (option 5).

As we shown, for the options 3, 4 and 5, it is necessary to have a legal basis and the initiative is based on Article 114 TFEU, specially paragraph (1) which provide: "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."
We can see that the approach of the initiative is based on the approximation of the national legislations regarding to "internal market". The same article was used in case of the Directive 2011/24/EU *on the application of patients' rights in cross-border healthcare*[10].

2. Referring to the use of Article 114 TFEU as legal basis for initiative

The "Public Health" is regulated by art. 168 of the Treaty on the Functioning of the European Union. The "Public Health" area is part of the category of competence areas shared between the Member States and the Union. Therefore, the principles of subsidiarity and proportionality are applicable, regulated by art. 5 of the Treaty on the Functioning of the European Union and the Protocol 2 to the Treaty on the Functioning of the European Union.

Pursuant to the subsidiarity principle, in the areas which are not under its exclusive competence, the Union intervenes solely and inasmuch as the objectives of the foreseen action cannot be satisfactorily achieved by the Member States neither at central, nor at regional or local level, however due to the proportions and effects of the action thus expected, these can be better attained at the Union level.

Pursuant to the proportionality principle, the Union action does not exceed, in terms of content and form, what is necessary to achieve the objectives of the treaties.

The Union action complements the national policies in the "Public Health" area (shared competence). The objectives/ purposes of the Union action are as follows:
- improving public health,
- preventing physical and mental illness, and the sources of danger to physical and mental health,
- fighting against major health epidemics, by promoting research into their causes, their transmission and their prevention,
- health information and education,
- monitoring serious cross-border threats to health, alerting and combating such threats.

The Member States of the Union shall be responsible for the:
- definition of their health policies,
- organization and delivery of health services and medical care.

[9] Commission Report on the operation of Directive 2011/24/EU on the application of patients' rights in cross- border healthcare, COM (2015) 421 final.
[10] See recital (2) of the Directive.

The responsibilities of the Member States include the:

- management of health services and medical care,
- allocation of the resources assigned to them.

The medicine pricing and reimbursement mechanisms are results of multiple factors: technical, financial and political. For that reason, the Union leaves the decision in this area to the discretion of the Member States.

In a reference book[11] it was questioned whether Article 114 TFEU can be used as legal bases in the the field of health:

> "If the answer to this question is yes, then the interference of European Union in the field of health and education is great, first of all because of the qualified majority procedure that permits some Member States' interests to be set aside and secondly because the economic aspects targeted by Article 114 TFEU (ex Article 95 EC) would be put on a hierarchical scale above other objectives.
> Since the removal of the obstacles to trade and the elimination of distortions of competition are the main targets of Article 114 TFEU (ex Article 95 EC), and since the internal market has a strong impact on other policies (including education and health) it is interesting to see if and how, while harmonising, internal market aspects can be separated from other policies. What happens if the laws that are supposed to be harmonised are of direct concern to health or education? Can Article 114 TFEU (ex Article 95 EC) still be used as a legal basis for issuing harmonising laws when we know that legislation in the health and education sector prohibits this? Do Member States have any safeguards that would protect their national policies from European Union's intrusion?"

Further, the author analyzes the Court of Justice of the European Union's judgements issued in several cases that were challenged in front of the Court on grounds that Article 114 TFEU is an illegal basis chosen for the adoption of several Directives whose objective was primarily the protection of public health. One of them was the Directive 98/43/EC *on the approximation of the laws, regulations and administrative provisions of the Member States relating to the advertising and sponsorship of tobacco products*[12], which was annulled by the Court.

Another author[13], related to this case, identifies three conditions which must be met for justifying the use of Article 114 TFEU:

1. A real need to harmonise,
2. A favourable internal market purpose,
3. A favourable internal market effect.

Once these conditions have been fulfilled, then the measure that used as legal basis Article 114 TFEU (ex Article 95 EC) is legal, no matter if other aspects (in our case health aspects) were included among the objectives of that measure. Article 114(3) TFEU (ex Article 95(3) EC) lays down an obligation for the Commission to take as a base a high level of protection in its proposals envisaged in Article 114(1) TFEU (Article 95(1) EC) concerning health, safety, environmental and consumer protection. This should be corroborated with what the Court stated in para 78 that the exclusion of the possibility for the harmonisation of measures in the field of health in Article 148 TFEU (ex Article 129 EEC) does not mean that harmonising measures adopted on the basis of other provisions of the Treaty cannot have any impact on the protection of human health.

The ECPC suggests that the authors of the initiative to consider the relevant jurisprudence of Court of Justice of the European Union on using of Article 114 TFEU as legal bases in the field of health. For this purpose, it should be checked if there are met for justifying the use of Article 114 TFEU, the following three conditions as they are described in the literature:

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[11] Nistor L. *Public Services and the European Union. Healthcare, Health Insurance and Education Services,* Ed. Springer, 2011, p. 317-326.

[12] Case C-376/98 Federal Republic of Germany v. European Parliament and Council of the European Union [2000] ECR 8419; See also 'Better competence monitoring', (2005) 30 EL Rev. 23, 27; Dashwood, 'The Relationship between the Member States and the European Union/ European Community' (2004) 41 CML Rev., 355 to Dashwood (2004).

[13] Crosby S *The new tobacco control directive: an illiberal and illegal disdain for law*. 2002, ELRev 27(2):177–193.

- A real need to harmonise,
- A favourable internal market purpose,
- A favourable internal market effect.

3. Referring to the options 4 and 5

With regard to the option 3, the ECPC agrees with the authors` initiative position, namely "there is no guarantee that the uptake of joint work will increase significantly, or that the duplication efforts will be adequately reduced, while a greater financial support is required". Thus, we are focusing on the options 4 and 5 and we will analyse if these options are feasible and complied with the EU legal framework.

As we shown above, according to Article 148 TFEU, the medicine pricing and reimbursement mechanisms are under the Member States competence. The initiative underlines that "pricing and reimbursement is a national competence and will not be affected by the current initiative"; the initiative will cover just the Health Assessment Technology area: joint REA (option 4) and joint Full HTA (option 5).
The real problem is whether HTA influences the pricing and reimbursement mechanisms of medicines:

a) Option 4 (joint REA)
As we noticed, according with the HTA Core Model®, Rapid Relative Effectiveness Assessment (REA) covers the clinical domains and measures the medical/therapeutic added value of a technology. In principle, targeting only the medical/therapeutic aspects, the assessment has no influence on pricing and reimbursement. From the information at our disposal and review of specific literature, there is not identified any link between the clinical domains as is described in REA and pricing and reimbursement.

a) Option 5 (joint Full HTA)
As we noticed, according with the HTA Core Model®, along with the REA domains shown above, Full HTA also includes other non-medical domains:

- Cost and economic evaluation;
- Ethical analysis;
- Organisational aspects;
- Patient and social aspects;
- Legal aspects.

Among these non-medical areas we will further analyse "the cost and economic evaluation".
HTA Core Model® distinguishes 5 main types of „economic evaluation" which can contribute to HTA[14]:

- cost-effectiveness analysis (CEA),
- cost-utility analysis (CUA),
- cost-consequences analysis (CCA),
- cost-benefit analysis (CBA), and
- cost-minimisation analysis (CMA).

Choosing of an „economic evaluation" type is related to "budget impact" which is limited, inter alia, by „national differences in the structure and funding of healthcare systems, resource utilisation and

[14] HTA Core Model®, p. 209-210 (see http://eunethta.eu/sites/5026.fedimbo.belgium.be/files/HTACoreModel3.0.pdf)

costs"[15]. In other words, EUnetHTA recognizes that there is a "link" between „economic evaluation", as part of HTA, and pricing and reimbursement which is under the national competence of the Member States.

This fact mentioned in HTA Core Model® is confirmed by the literature, also. We will evoke just two relevant studies:

i) A study entitled "The Role of Health Technology Assessment in Medicine Pricing and Reimbursement"[16] reviews *inter alia* the literature to identify and describe the available evidence on the impact of HTA on pricing and access to medicines. To meet the objectives of this review a systematic literature search has been conducted.
There are some conclusions of this study:

> - A 1999 study of pharmacoeconomic research in 13 European countries[17] found that HTA was used most frequently for reimbursement decisions and the least common use was for price negotiations. Other uses included formulary decisions, development of clinical practice guidelines, and communication with prescribers.
> - A consistent theme throughout the literature is that information on cost-effectiveness, and HTA more generally, has an important and influential role in reimbursement decision making[18].
> - Further evidence of the influence of HTA information is provided from a review of HTA activity in Poland - now a high income country (24). A positive HTA pharmaceutical review by the Agency for Health Technology Assessment in Poland (AHTAPol) is very often linked to a decision for reimbursement. The review revealed 30 medicines with positive HTA recommendations were included on the reimbursement list and four with negative HTA recommendations.[19]

ii) An other comprehensive study[20] analyses the arguments for a national approach of HTA and economic evaluation:

> - One reason that can limit the transferability of economic evaluations is that an economic evaluation conducted in one setting may use methods that are deemed inappropriate for use in another setting. This might be caused by variations between analysts in terms of what makes an acceptable evaluation. It may also reflect lack of standardization of methods; lack of compliance with accepted methods of economic evaluation; and methodological creep over time…..A good example of this can be drawn from the comparison of the way economic evaluation is used to inform decisions in England and in Germany. In England, the National Institute for Health and Clinical Excellence (NICE) has tended to focus on the incremental cost per quality-adjusted life-year (QALY) gained. It has adopted an explicit threshold of £20,000 per QALY and recommends that a common approach be taken to measure costs and benefits across therapeutic areas [7]. In contrast, in Germany the Institut Für Qualität und Wirtschaftkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care, IQWiG) has focused on the efficiency of resource use within a specific therapeutic area and has advocated the use of an efficiency frontier to inform decisions [8].
> Methodological criticisms can be advanced for both approaches. The use of a threshold value for a cost per QALY does not inform a decision-maker about where the resources required to implement a more effective intervention will come from. It also requires a method of eliciting QALYs that can

[15] Ibidem p. 210.
[16] This study was provided by the Pricing Policy Working Group under the World Health Organization (WHO) and Health Action International (HAI) (see http://haiweb.org/wp-content/uploads/2015/08/HTA-final-Aug2013a1.pdf)
[17] Drummond, M et al. Current trends in the use of pharmacoeconomic and outcomes research in Europe. Value in Health, 1999, 2(5):323-332.
[18] Ngorsuraches S, Meng W, Kim BY, Kulsomboon V. Drug reimbursement decision-making in Thailand, China, and South Korea. Value in Health, 2012, 15(suppl. 1): S120-S125.
Bending MW, Hutton J, McGrath C, Glanville J. What influences pharmaceutical reimbursement decisions? A systematic review of factors reported to influence decisions in OECD countries. Value in Health, 2011, 14(3):A22.
Bentkover JD, Corey R. Effective utilization of pharmacoeconomics for decision makers. Disease Management and Health Outcomes, 2002, 10(2):75-80.
[19] Kolasa K, Schubert S, Manca A, Hermanowski T. A review of Health Technology Assessment (HTA) recommendations for drug therapies issued between 2007 and 2009 and their impact on policymaking processes in Poland. Health Policy, 2011, 102(2-3):145-151.
[20]Luke Vale, Health Technology Assesment and Economic Evaluation: Arguments for a National Approach (see http://www.valueinhealthjournal.com/article/S1098-3015(11)71814-9/pdf)

capture the benefits of all relevant health-care interventions. The use of an efficiency frontier can be criticized because what interventions lie on the efficiency frontier will depend upon the method used to measure benefits. Therefore, choosing a different measure of benefit may change the shape of the efficiency frontier in a given therapeutic area. Furthermore, without a common method of measuring benefits, it is difficult to draw judgements about efficient allocation of resources across therapeutic areas.

The merits or otherwise of the approaches adopted within individual jurisdictions can be debated and over time, if necessary, refined. Nevertheless, at any given point in time, those analysts conducting economic evaluation for national decision- makers such as NICE or IQWiG are expected to conduct them using methods deemed relevant to that organization.

- An example of the effects of context can be seen by considering the hypothetical example of an economic evaluation comparing two different methods of surgical treatment for angle closure glaucoma (a common cause of blindness). If the economic evaluation were to be conducted for both the UK and Singapore, then it is likely that the care pathways that patients would follow in each country will differ. Specifically, care after successful and unsuccessful initial treatment might differ because the beliefs of practitioners about the value (and hence availability) of subsequent treatments might differ. Furthermore, differences in the method of financing health care may alter patients' behavior. For example, differences in out-of-pocket expenses may alter the use of services after surgery, and hence alter both longer-term effectiveness as well as costs. The implication of this is that the structure of a model in terms of the sequence of therapies may vary between countries.

Therefore, ECPC understands the existing methodological barriers to the implementation of scenario 5b. However, calls on the European Commission and national HTA bodies to identify possible methodological solutions, on the basis of the identified obstacles.

4. Limits of option 4

The option 4 assumes that the Member States jointly produce REAs (i.e. reports on the relative effectiveness in terms of clinical/medical benefits of the technology), available to all through a shared repository, with measures for the uptake of the joint work at national level.

i) The problem is that in the UE there are disparities among the HTA systems of the Member States: some of them are very powerful (NICE from UK, SMC from Scotland, IQWIG from Germany), while others are less developed; it is hard to imagine how the HTA authorities will produce together REA reports.

The ECPC considers the HTA systems should be compatible and that is expected to require permanent/continuous financial support from the EU and from the Member States.

ii) From other perspective, some countries will jointly produce REA reports and others just will use them.

In this case, the ECPC proposes setting out a financial mechanism for covering of REA reports costs.