

High prices, poor access: What is Big Pharma fighting for in Brussels?

Chapter 5. EU HTA proposal: the need to safeguard against industry influence

A gatekeeper against high-priced drugs

A Health Technology Assessment (HTA) is the scientific analysis of the added therapeutic value of a new treatment. Put simply, HTA looks at whether a new drug or treatment is better, the same as, or worse than existing alternatives. Drug companies promote the use of new drugs that are covered by patent protection, over old ones that aren't, even if the new product is no better than existing ones. HTAs therefore help to indicate whether a new drug justifies the (often very high) price being asked for it.

With constraints on public spending and growing concerns over the sustainability of public healthcare systems, HTAs play a crucial role. They feed into national health systems' decisions about what price they are willing to pay for a new medicine being promoted by a pharmaceutical firm, and about which medicines should be reimbursed (and therefore made available to patients) under their national health systems. As more medicines without added therapeutic value (ie 'new' but not meaningful improvements on existing treatments, yet expensive thanks to being under patent) enter the market, HTA has grown in importance as a gatekeeper to protect public-interest public spending. It is a crucial part of the access to medicines debate in Europe.

Pricing and reimbursement decisions (including negotiations with companies over price) are taken by member states, and are a fiercely defended national competence. Yet the secrecy around them, and often the lack of good evidence available to health ministries (and other payers such as social healthcare insurers) about the benefits – or lack thereof – of a new drug, gives Big Pharma companies a lot of leverage. It becomes all too easy to rip governments off. However, with strong assessments of a new treatment's effectiveness relative to those already available – in other words, robust and independent HTA – governments are in a stronger position to negotiate. This can help curb Big Pharma's excessive power to secure sky-high and often unjustified prices.

Cooperation to ensure robust and independent assessments

Up till now, HTA has been conducted at national (or regional) level, but in January 2018 the Commission made a very open-ended legislative proposal for an EU-wide regulation on HTA.¹ Prior to

this the EU had supported voluntary cooperation on HTA, for well over a decade (the EUNetHTA Joint Action²). Low uptake of joint assessments at national level however meant the network's effectiveness remained limited. In addition, even after years of voluntary cooperation, differences in HTA capacity amongst Member States remained stark. The Commission's proposal, despite short-comings, was intended to respond to this situation.³ As the European Public Health Alliance notes, EU collaboration on HTA, if well-designed, could be a "powerful weapon to reduce inequalities and improve access". But if joint-EU HTA were too friendly to industry-interests – as is the case with the European Medicines Agency (see Box 3) – there is also a risk that rather than improve capacity it could actually lead to "convergence towards the lowest common denominator in clinical assessments".⁴ Looking at the corporate lobbying towards the Commission around this file, we see that industry infiltration of the HTA process – with more control over what goes in and what comes out – has been central to the Big Pharma lobby's wish-list. But all is not lost: despite considerable success with the Commission, the pharma lobby had a tougher time with the European Parliament, which strengthened the public interest aspects of the proposal.

Currently the proposal remains tied up in the Council. As member states debate thorny issues, a common position that it can take to negotiations with Commission and Parliament seems far off, leaving the fate of the HTA proposal uncertain, including whether and in what form it will survive with a new Parliament and Commission. Given the important role that EU collaboration on HTA could play in helping member states safeguard their public health systems from unjustified high-price medicines, we encourage the EU institutions to continue to work towards agreement. We need European cooperation that helps ensure robust and independent HTAs, that improves on the Commission's proposal, and that resists industry pressure for undue influence over the process.

Box 3. The European Medicines Agency: Lessons for EU HTA

HTA has increasingly been seen as a way to deal with problems caused by an inadequately functioning and industry-friendly European Medicines Agency (EMA). More and more drugs are being approved by the EMA with low or uncertain value, as documented by *Prescrire*,⁵ based on premature data or a weak evidence base. For example, between 2009 and 2013 the EMA authorised new cancer drugs in most cases without clear evidence that they improved patients' quality of life and their life expectancy.⁶ HTA can help respond to this "weak evidence-high prices conundrum" believes EPHA, but only if "HTA itself does not become subordinated to the EMA".⁷ Subordinated to, or modelled on, since the EMA is a regulatory agency with a too-close relationship with the industry it is supposed to regulate. This is due to the revolving door between regulator and regulated, dependence on industry funding, and an institutional culture that sees the pharma industry as its partner or even client. This isn't helped by the weak interpretation of conflict of interest rules, which the EMA renamed "competing interests" in 2017, replacing "terminology such as conflict, risks, etc" with "more neutral language", in order to "address the perception issue".⁸

Revolving door: The EMA has a well-established revolving door with Big Pharma.⁹ For example, the EMA's Head of Legal Affairs Stefano Marino joined after two decades in the pharma industry. EMA's former Legal Head Vincenzo Salvatore joined the 'European life sciences regulatory practice' of law firm Sidley Austin LLP. After leaving his job overseeing medicines' safety and efficacy at EMA, Xavier Luria became a consultant for the pharmaceutical sector. EMA's ex-Director Thomas Lönnngren went on to set up Pharma Executive Consulting Ltd.¹⁰ These appointments reflect lack of stringency in EMA conflicts of interest rules and risk blurring the interests of regulator and regulated, which are fundamentally different: the industry being regulated seeks to maximise its profits, but the job of the regulator is to safeguard public health, by ensuring strict safety and efficacy conditions are met before a drug can be sold in the EU.

Reliance on industry experts, funding and data: As of December 2017 nearly one thousand of EMA's European experts have direct or indirect interests in the pharmaceutical industry.¹¹ Direct interests include financial interests or employment with, consultancy to, or a strategic advisory role for a company. And even indirect interests – which include being an Investigator or Principal investigator (in an industry instigated/ sponsored clinical trial), or organisational grants or funding from the pharma industry – are rather direct!¹² EMA is also reliant on the pharmaceutical industry for its funding (for example, through fees for giving scientific advice), and reliant on clinical trials data provided by the industry, which it doesn't have the means to verify. All these things contribute towards a power imbalance in favour of Big Pharma. The EMA at times has been too willing to serve or capitulate to the industry's interests. When the EMA made moves towards greater clinical trials data transparency, for example, the then-president of EFPIA (and Chief Executive of Sanofi) warned this would discourage critical investment in crisis-hit Europe, and threatened that Sanofi's "next euro of investment would go to the United States or to emerging markets."¹³ Following this, and other industry pressure (including a lawsuit by AbbVie, ending in a deal over access to clinical study reports about their drug Humira)¹⁴, the EMA backtracked, shifting to a more restrictive transparency approach that raised concerns with the European Ombudsman, payers, and civil society.¹⁵ Although there have subsequently been some welcome developments in this area (with, for example, the EMA starting to publish clinical reports for new medicines, the first regulator to routinely do so), there is still much to improve.¹⁶

Corporate influence: Industry often appears to be overwhelmingly represented at EMA's events. In October 2018 EMA held a 'multi-stakeholder workshop' to launch a consultation on regulatory science:¹⁷ EFPIA sat on five out of six panel sessions. The dominance of industry (or industry-funded) groups (including EFPIA, EBE, VaccinesEurope, EuropaBio, EUCOPE, and MedTechEurope) was combined with the absence of consumer or public health groups.¹⁸ The organising committee for this workshop included EMA's Head of Human Medicines R&D Support, who came to EMA from a long career at Merck-Serono (whose Chief Executive is President of EFPIA),¹⁹ while EMA's 'Industry Stakeholders' Liaison was formerly a Senior Regulatory Affairs executive at Pfizer.²⁰ sits within EMA's 'Stakeholders and Communication Division' In recent years, the EMA has held annual meetings with industry groups like EFPIA and EuropaBio, covering topics such as HTA and early-stage "multi-stakeholder engagement".²¹ It also produces annual reports on EMA's interaction with industry, which, ironically, are "not intended to provide a

comprehensive overview of all contacts”.²² One such reveals that 51 per cent of all EMA stakeholder events in 2017 were industry only, and of the 39% multi-stakeholder events, industry participated in 83%.²³

Ombudsman’s concerns over industry influence: In July 2017 the European Ombudsman opened a strategic inquiry into EMA’s pre-submission activities. The utter lack of transparency around the EMA’s early dialogues with, and scientific advice given to, industry led the Ombudsman to conclude that “there is a risk that the eventual decisions by EMA on the authorisation of medicines may be influenced – or be reasonably perceived to be influenced – by what has been discussed during the meetings with medicine developers prior to receiving their formal submission”.²⁴ The inquiry is ongoing, with results expected in 2019.

All in all, the EMA’s industry-friendly ecosystem offers warnings for what the proposed joint EU HTA must avoid. It shows why clear, enforceable rules on independence, conflict of interests, transparency, and public funding are vital from the outset. Yet the pharmaceutical industry has been eager to promote the EMA as a model for EU HTA. EFPIA told the Commission the EMA is “a good model for a successful and scientifically based secretarial/organization support”.²⁵ EUCOPE lobbied to grant “a more prominent role to the EMA” to ensure “joint HTA work is well-integrated with the existing regulatory framework”.²⁶ This is hardly surprising, given the “ever-closer partnership” Big Pharma has with EMA, but as EPHA notes, allowing EU HTA to “become a subdivision of the EMA” would lead to “an excessive concentration of power” and undercut HTA’s potential to mitigate problems caused by the EMA’s approvals.²⁷ Thankfully, there is little appetite in the Council for this. As for the EMA itself, “a mindset shift is necessary – one that treats pharmaceutical companies as a business sector in need of regulation and not as clients or partners, as they are currently viewed.”²⁸ And this is a lesson that joint EU HTA must learn, in order to be a successful gatekeeper against high-priced medicines of questionable therapeutic value.

Industry singled out for special input

Big Pharma had a big presence in the Commission’s preparatory phase for the HTA regulation. Individual companies like Sanofi and Lilly lobbied DG Sante,²⁹ whilst a Commission focus group with pharma companies including Johnson & Johnson, Pfizer, and Lilly, makes it clear that Big Pharma anticipates EU HTA could mean lower standards of evidence than those they are currently required to provide in some member states.³⁰

This lends credence to fears that a mandatory EU HTA system – if overly-influenced by industry-interests – could actually weaken the gatekeeper role played by the most robust national HTA bodies. Given this, it was worrying that Commission invitations to HTA stakeholder meetings placed more emphasis on industry’s input than on that of patients/consumers. Only letters to industry stakeholders contained this addition (in bold):

It is my utmost priority to meet all stakeholders organised at EU level, to hear your views on the matter and discuss this proposal with each of you, **in particular issues regarding the**

production of joint clinical assessments (process and outcomes) and the governance, including the involvement of stakeholders.³¹

It is of great concern that the Commission appears to have wanted to speak only to the pharma/med tech industry about the “involvement of stakeholders” in the governance of European HTA!

Industry infiltration of HTA process

EFPIA also lobbied the Commission over its HTA proposal, with indications of a close and cooperative relationship: for example, an email from EFPIA shared the “first batch of compromises” from the Parliament’s ENVI committee with the Commission.³² In addition there was an invitation to DG Sante to join an EFPIA board meeting and “engage at the level of senior leaders of our industry, in particular regarding next steps in the legislative process and the role industry should play moving forward”, which was welcomed by DG Sante as “a very good idea”.³³ Once the Commission’s proposal was out, EFPIA lobbied for assessments to be based on a “submission dossier” from the industry, warning that without this, “HTA bodies would compile the evidence and assess it without any input from the companies”. In other words, they want a greater role for companies on what they are assessed over, giving industry more control.³⁴ And whilst EFPIA welcomed the Commission’s proposal, it also pushed for the “inclusion of a scoping meeting,” for companies to “carry out a 'fact checking' of the final report”, and for stakeholder involvement to include industry.³⁵ This is all about giving industry more control over what goes in to and what comes out of the HTA process.

Attempt to extract the teeth from the proposal

In a meeting with DG Sante, “EFPIA expressed serious concern about the terminology ‘Relative effectiveness assessment’”. The pharma lobby group’s argument was that HTAs ‘mainly’ use evidence from clinical trials, which relate to a medicine’s efficacy (ie whether a drug produces the results expected in a lab setting), not its effectiveness (ie the degree of benefit a drug has in more normal clinical settings).³⁶ This might sound technical, but a lot is at stake with this argument. The rationale of HTAs is to assess whether a treatment is more or less effective than other available treatments. It is precisely the *relative* effectiveness – this aspect of *comparative* evaluation – which is the whole point of HTA, in order to help governments decide what is worth paying for. So in contrast to EFPIA’s argument, it is not enough to only have data on a drug’s efficacy compared to, for example, a placebo it was tested against in a lab (ie in a non-comparative clinical trial).

EFPIA’s explicit demands echoed by US business lobby

EFPIA also sent the Commission a “technical” position paper setting out its article-by-article demands,³⁷ which is longer and more explicit than its publicly available HTA position paper.³⁸ This paper pushes for important details of how the EU HTA would function not to be written into the law, but rather to be left until afterwards to be developed, in EFPIA’s words, “between all stakeholders”, essentially leaving the door open for the industry to influence the details. It talks of “the necessity of a scoping meeting”, of protecting all “confidential data”, and for industry to be responsible for “managing

the exchange” between joint HTA and the EMA. Unlike its public paper, which says only there should be “clear rules” for determining stakeholders, EFPIA’s non-public paper says they should “explicitly” include “the health technology developers of the medicinal products” in the preparation of assessments.³⁹ Many of EFPIA’s messages were mirrored by AmCham EU, whose members include many Big Pharma companies.⁴⁰ The Commission promised to read AmCham EU’s position paper “with great interest”.⁴¹ It also asked for “formalised stakeholder input” with “health technology developers”, emphasised the importance of confidentiality, pushed for a “scoping meeting”, and for an “appeal mechanism” to challenge decisions. In other words, both EFPIA and AmCham EU want an EU HTA system that is as porous to industry’s influence, and as difficult to audit, as possible,⁴² to prevent it from being an effective gatekeeper against high-priced medicines.

Industry wants less oversight of most expensive medicines

Another demand from industry actors such as EUCOPE, EuropaBio, and US biotech firm Biogen was that orphan drugs for rare diseases get special (more ‘flexible’) treatment in HTA.⁴³ The misuse of the orphan drugs regulation (which gives faster market access with less stringent evidence requirements at the EMA) is of major concern (see Box 1). Demands from industry that may be intended to weaken the assessment of orphan drugs’ effectiveness relative to other treatments are, therefore, also a concern for access to affordable and effective medicines. And it seems likely the lobbying did not stop at the Commission, given that the Parliament added amendments which focused on orphan drug specificities. This caused *Prescrire* to flag concerns that it must not risk paving the way for orphan drug HTAs to be dealt with by the more industry-friendly EMA (see Box 3).⁴⁴

Revolving door-lobby firm running ‘stakeholder’ roundtables

Notably, DG Sante presented its HTA proposal at an event organised by lobby firm Fipra.⁴⁵ This was followed-up with two more Fipra ‘stakeholder roundtables’ in June 2018, also attended by Sante officials. The first was sponsored by EFPIA, Pfizer, Amgen, and Roche,⁴⁶ and the second by EFPIA, EUCOPE, EuropaBio (and several of their corporate members).⁴⁷ The latter focused on HTA of treatments for rare diseases, and noted that the Commission had been lobbied “to consider methodological flexibility for rare conditions in HTA”.⁴⁸ It is astonishing that these ‘stakeholder’ roundtables (which don’t appear to include any consumer or public health groups) on these subjects have been *de facto* privatised into Big Pharma’s hands via a consultancy firm. And not just any consultancy firm; Fipra’s clients include EFPIA, EuropaBio, Pfizer, Amgen, Novartis, and many other pharma companies.⁴⁹ Fipra’s Chair, Robert Madelin, meanwhile, came through the revolving door after 12 years in “senior leadership” positions at the Commission, including as Director General for Health and Consumer Policy.⁵⁰

MedTech lobby keen to avoid stricter oversight

The medical technology industry has been one of the most vociferous in lobbying the Commission,⁵¹ in particular EU trade association MedTech Europe.⁵² The International Consortium of Investigative

Journalists (ICIF) has exposed how inadequately tested medical devices, thanks to insufficient regulatory oversight, have caused harm - , including injuries and deaths - to patients across the globe.⁵³ ICIJ warns that the industry is pushing for speedier regulatory approvals, which go hand in hand with demands for lower evidence thresholds.

In line with this, the med tech industry has lobbied for medical technology to be treated differently in EU HTA (either by not being included, being voluntary, or facing different assessment conditions) and for 'stakeholder' ie industry involvement in the details of how the regulation will be implemented. MedTechEurope sent DG Sante a confidential article-by-article "Input for consideration to strengthen the proposal".⁵⁴ They also admitted that its fingerprints were recognisable in DG Sante's proposal, which "reflect[s] some of the points made by MedTechEurope", particularly "the differentiation between pharma and medical devices".⁵⁵ COCIR, another med tech lobby,⁵⁶ also said "the majority" of its concerns had been considered in the proposal, and sent further proposed amendments to the Parliament's responsible committees.⁵⁷ Prior to the inter-service consultation between all Commission directorates, the med tech industry also lobbied DG Grow,⁵⁸ warning that DG Sante's plans "might block innovation" and "create additional burden" to industry.⁵⁹ The European Consumer Organisation (BEUC), on the other hand, argued that medical devices need strong HTA, as they have "huge significance for consumers' lives, as well as healthcare budgets".⁶⁰ Patients group EPF also called for their inclusion.⁶¹

Industry gains and loses ground

Industry won a number of its asks from the Commission, whose proposal for a HTA regulation left so many core aspects and important details about the set-up, methods and processes of joint EU HTA to be decided at a later date, that it has been likened to being asked to sign a contract blindfolded. By leaving the details to be sorted out in implementing acts (which enable the Commission to clarify how the regulation shall be implemented), the door is left wide open for industry to influence the details to reflect their interests (this is why this was one of their key demands). In contrast, BEUC argued that "[p]rocedural rules for ensuring the independence and transparency of HTA processes should be included in the Regulation and not be relegated to implementing acts."⁶² Other issues with the proposal (or wins for the industry) included not stringent enough requirements to provide all evidence (ie all data from all trials) and the absence of explicit conflicts of interest rules. The association of non-profit healthcare payers, AIM, also expressed their concern at the Commission's proposal for HTA funding to come in part from industry fees, as it could "lead to conflicts of interest".⁶³

Fortunately MEPs strengthened the Commission's proposal, adding improvements in transparency, independence, governance, and standards.⁶⁴ As *Prescrire* notes, the Parliament called for EU HTA to require comparative trials, public (not industry) funding, and guarantee the highest quality standards (rather than the lowest common denominator).⁶⁵ Health Action International also welcomed the transparency requirement that scientific consultation reports on health technologies that have

undergone joint clinical assessments should be made public (which relates to the Ombudsman's investigation of the EMA – see Box 3).⁶⁶

It wasn't only public health groups who were pleased with MEPs' improvements: the European Social Insurance Platform (ESIP), which represents public health care payers, also welcomed provisions for broader public access to information, as well as for a mechanism to require companies to provide information in cases of non-compliance.⁶⁷ To EFPIA's disappointment, MEPs did not pick up its proposal for "scoping meetings" with companies, which it lamented as "a lost opportunity for the health technology developer to... jointly define the scope of the assessment and the evidence to be submitted".⁶⁸ In other words, a lost opportunity for companies to have more sway over the assessment. Not everything was rosy however, as MEPs also added in more protections for "commercially sensitive data", and capitulated to industry wishes for a "less rigorous approach for medicines which treat rare diseases", even though these, as BEUC points out, "are precisely the drugs which can be the most expensive and which need the most investigation".⁶⁹

Tricky talks in Council leave EU HTA with uncertain fate

The picture is more complicated in the Council, where member states' health ministers must negotiate and agree a compromise. Some – particularly those with stronger national HTA systems – are concerned an EU HTA might erode their standards. Mandatory participation and uptake of EU HTA therefore crosses their red lines. Many are unwilling to see the freedom over reimbursement choices of their health ministries and payers limited in any way (by a weak *or* by a strong EU HTA – as not all member states are keen to have strong, independent HTA). Big Pharma meanwhile, as EPHA notes, is already "used to doing business with the current fragmented European HTA landscape",⁷⁰ and is not unhappy with the status quo (though it is clear from its lobbying that it would be delighted to get an industry-porous EU HTA, similar to the EMA). Discussions are still with the Council but agreement is not expected any time soon.⁷¹ And with both a new Parliament and a new Commission arriving in 2019, the fate of Joint EU HTA – whether as an independent and strong gatekeeper against Big Pharma's high prices, or as a one-stop-shop for Big Pharma's influence, or even as a proposal that gets buried by new political dynamics – is uncertain.⁷²

EU cooperation on robust and independent HTA could help member states curb high prices

One thing is clear: member states have serious and legitimate concerns about extremely high-priced medicines. Whilst it is true that a 'bad' EU-wide HTA – based on poor methodology/lack of comparative data, and that too easily gives a positive assessment – could hamstring decision-makers in pricing and reimbursement decisions, putting further pressure on public spending, it is also true that 'good' EU HTA – strong, independent assessments based on good, comparative data and all relevant evidence – can empower national authorities to make sound pricing and reimbursement decisions. This would help to improve access to better and more affordable medicines, and provide doctors and patients with the evidence they need to discuss which therapy would be better for which patient. The devil may all be in the details. But the details add up to fundamentally different choices. And rather than letting EU

collaboration on HTA fizzle out, the new Parliament and Commission, as well as the ministers negotiating in the Council, should recognise the important role of EU-level cooperation on HTA in enabling member states to curb high prices, providing it reflects the choice for robust, independent, and transparent joint assessments.

1 EC, Proposal for a Regulation on HTA, 2018
2 EC, EUNetHTA Joint Actions, https://ec.europa.eu/health/technology_assessment/joint_actions_en
3 EC, Impact Assessment Strengthening of the EU Cooperation on HTA, 2018, https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_ia_final_en.pdf
4 EPHA, The top 5 issues...2018, *ibid*.
5 Articles published in *Prescrire International* between 2004 and 2017; see also, *Prescrire* (2016) New drugs, new indications in 2015, *ibid*.
6 BEUC, HTA Factsheet *ibid*.
7 EPHA, The proposed European Commission Regulation on HTA: a golden opportunity for patients and health budgets, by Yannis Natsis, July 2018, <https://epha.org/proposed-ec-regulation-on-hta-golden-opportunity-for-patients-and-health-budgets/>
8 EMA, 2016 and 2017 EMA Annual Reports on Independence, https://www.ema.europa.eu/documents/report/2016-2017-annual-report-independence_en.pdf
9 CEO, EMA's revolving door with Big Pharma, 2014, <http://corporateeurope.org/revolving-doors/2014/06/emas-revolving-door-big-pharma-alive-and-well>
10 CEO, Revolving Door Watch, <https://corporateeurope.org/revolvingdoorwatch/>
11 962 of 4010 European experts have declared direct (537) or indirect (425) interests in the pharmaceutical industry, according to their Declarations of Interest, ie 24% or approx. one quarter. EMA, European Experts, http://www.ema.europa.eu/ema/index.jsp?curl=pages%2FAbout_us%2Fanding%2Fexperts.jsp&url=&mid=WC0b01ac058043244a&searchTab=&authorityId=&alreadyLoaded=true&isNewQuery=true&startLetter=View+all&selectedCountry=, as of 8/12/17. Source: ALTER-EU, Corporate Capture in Europe, *ibid*.
12 EMA policy on the handling of competing interests of scientific committees' members and experts, 2016, www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500216190; According to the type of 'competing' interest, and a person's role - ie scientific expert, staff or Management Board - varying levels of restrictions, exclusion or cooling-off periods apply; <https://www.ema.europa.eu/en/about-us/how-we-work/handling-competing-interests>
13 Reuters, EU's drug data stance threatens investment - Sanofi CEO, 24/06/13, <https://www.reuters.com/article/europe-drugs-transparency/eus-drug-data-stance-threatens-investment-sanofi-ceo-idUSL5N0F022G20130624>
14 See, eg, EMA policy on transparency is "strikingly" similar to deal struck with drug company, say experts, <https://www.bmj.com/content/348/bmj.g3852>
15 AIM, MeIEF, ISDB et al., Backpedalling on EMA's "proactive publication of clinical data" draft policy, May 2014, http://english.prescrire.org/Docu/DOCSEUROPE/20140520_EMATransparencyPolicy.pdf; EU Clinical Trials Regulation: EMA steers away from transparency by misinterpreting exception provisions, February 2015, <http://english.prescrire.org/en/79/207/46302/4103/4089/SubReportDetails.aspx>; European Ombudsman, Ombudsman concerned about change of policy at Medicines Agency as regards clinical trial data transparency, May 2014, http://europa.eu/rapid/press-release_EO-14-13_en.htm; <https://blogs.plos.org/speakingofmedicine/2014/05/20/ema-poised-make-major-u-turn-transparency-initiative/>
16 HAI and Transparimed, Clinical Trials in the European Union: A Roadmap to Greater Transparency, 2019, haiweb.org/wp-content/uploads/2019/02/Clinical-Trials-in-the-EU-A-Roadmap-to-Greater-Transparency.pdf
17 EMA, Multistakeholder workshop to launch consultation on EMA human regulatory science to 2025, 24/10/2018, <https://www.ema.europa.eu/en/events/multistakeholder-workshop-launch-consultation-european-medicines-agency-ema-human-regulatory-science>
18 Agenda, EMA - Regulatory Science to 2025 Launch of Human Stakeholder Consultation, https://www.ema.europa.eu/documents/agenda/agenda-multistakeholder-workshop-launch-consultation-european-medicines-agency-ema-human-regulatory_en.pdf
19 EMA, Enrica Alteri Declaration of interests (dated Feb 26 2018)http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500129303; PMLive, Merck Serono's Enrica Alteri appointed head of safety and efficacy at EMA, http://www.pmlive.com/pharma_news/merck_serono_enrica_alteri_appointed_head_safety_efficacy_ema_410688, EFPIA Appoints New President and Vice Presidents, 20.06.17, <https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/20-june-2017-efpia-appoints-new-president-and-vice-presidents/>
20 Linked-in, Marie-Helene Pinheiro, <https://www.linkedin.com/in/marie-helene-pinheiro-77a7a610/> (accessed 25/10/18)
21 Second EMA-EFPIA annual bilateral meeting, 10/07/2017, <https://www.ema.europa.eu/events/second-ema-efpia-annual-bilateral-meeting>; First European Medicines Agency-EuropaBio annual bilateral meeting, 09/06/2017, <https://www.ema.europa.eu/events/first-european-medicines-agency-EuropaBio-annual-bilateral-meeting>
22 EMA's interaction with industry stakeholders Annual report 2016 http://www.ema.europa.eu/docs/en_GB/document_library/Report/2017/06/WC500229508.pdf
23 EMA's interaction with industry stakeholders Annual report 2017, https://www.ema.europa.eu/documents/report/european-medicines-agencys-interaction-industry-stakeholders-annual-report-2017_en.pdf Figures 1 and 2.
24 Report on the meeting with the European Medicines Agency in the European Ombudsman inquiry into pre-submission activities organised by the Agency (OI/7/2017/KR), Opened on 17 July 2017, <https://www.ombudsman.europa.eu/en/correspondence/en/87563>
25 EFPIA response to HTA consultation, <https://www.efpia.eu/media/25703/efpia-response-the-european-commission-hta-consultation-january-2017.pdf>
26 Sante docs, EUCOPE, RE: Speaker invitation: EUCOPE Members Meeting, 27 June 2018, Brussels
27 EPHA, The top 5 issues...2019, *ibid*; The proposed European Commission Regulation on HTA, *ibid*.
28 EPHA, The top 5 issues...2019, *ibid*.
29 Sante docs, part 1 doc 24 Sanofi, part 2 doc 16 Lilly.
30 "[I]t is perceived likely that a framework for an EU HTA may provide a compromise between data needs" vis-a-vis those markets requiring the "highest level of evidence" to those with "lower standard[s]", and "Harmonisation of data requirements" will "not necessarily result in overall cost reduction as the data needs at EU level will likely not end up at the level of the lowest denominator". Source: Sante docs, meeting minutes with Pharmaceuticals focus group 02-05-2017
31 Sante docs, Letters from Commissioner Andriukaitis to COCIR, EFPIA, EUCOPE, EuropaBio, Medicines for Europe, MedTech Europe, MedPharmPlast Europe, Association of the European Self-Medication Industry, and Plasma Protein Therapeutics Association Europe; and Letters from Commissioner Andriukaitis to BEUC, European Cancer Patient Coalition (ECP), European Federation of Allergy and Airways Diseases Patients' Association, European Institute of Women's Health, European Patients' Forum, EURORDIS-Rare Diseases Europe, EPHA, HAI, International Diabetes Federation European Region.
32 Sante docs, EFPIA Fwd: ENVI | CABEZÓN Report on HTA: first batch of compromises
33 Sante docs, DG Sante RE: Invitation to join Board members for discussion on proposed HTA regulation – 30.11.2018
34 Sante docs, meeting summary with EFPIA 16-03-2018
35 Sate docs, meeting summary with INDUSTRY REPRESENTATIVES (including EFPIA), 16-06-2018
36 Sante docs, meeting summary with EFPIA 18-01-2017 DG Sante B4. See also P. O'Donnell, The Real Divides on European HTA, 2017, <http://www.appliedclinicaltrials.com/real-divides-european-hta>
37 Sante HTA docs, EFPIA position on proposed HTA Regulation
38 For example, in its public paper "EFPIA recommends considering the following principles...", but its 'technical' paper uses language like "EFPIA does not agree to...". EFPIA position on proposal for a Regulation on HTA <https://www.efpia.eu/news-events/the-efpia-view/efpia-news/08052018-efpia-position-on-proposal-for-a-regulation-of-the-european-parliament-and-the-council-on-hta-and-amending-directive-201124eu/>
39 Also absent from its public paper is EFPIA's insistence on an "oral" or face-to-face discussion during its preparation as written communication "is not sufficient".
40 Including Abbot, AbbVie, AstraZeneca, Baxter, Celgene, Lilly, Gilead, GSK, Johnson & Johnson, MSD, Pfizer and Shire. AmCham EU, Members, <http://www.amchameu.eu/about-us/members>
41 Sante HTA docs, Strengthening Member State cooperation on HTA - AmCham EU position
42 Sante HTA docs, Re: Strengthening Member State cooperation on HTA - AmCham EU position
43 Sante HTA docs, meeting summary with Biogen 04-04-2018; part 1 doc 14 meeting summary with industry reps, inc. EUCOPE & EuropaBio, 16-06-2018
44 *Prescrire*, The EP's position on HTA improves the Commission proposal to a great extent by outlining evaluation needs and improving transparency and independence, 05/10/18, http://english.prescrire.org/Docu/DOCSEUROPE/20181005_PressRelease_HTA.pdf
45 Sante docs, meeting minutes Fipra, The use of real world evidence 08-03-2018
46 Sante docs, Foresight International Policy and Regulatory Advisers SAVE THE DATE: 23 November 16:45-20:30 Multi-stakeholder roundtable on new approaches for improved patient access to personalised medicine
47 Shire, Sanofi Genzyme, Celgene, BioMarin, Takeda and Actelion.
48 Sante docs, Foresight International Policy and Regulatory Advisers FW: TRUST-4RD: Summary Report and Next Steps
49 Namely, Eli Lilly, Gilead, MSD, Shire, Sanofi, Celgene and Abbot. Also MedTech Europe. Transparency Register, Fipra, <http://ec.europa.eu/transparencyregister/public/consultation/displaylobbyist.do?id=58746194306-23>, last modified: 08/11/2018. Clients 2017.
50 Fipra International, Robert Madelin, <https://fipra.com/our-people/robert-madelin/>; CEO, Revolving Door Watch, Robert Madelin, <https://corporateeurope.org/revolvingdoorwatch/cases/robert-madelin>
51 Sante HTA docs. Predominantly MedTechEurope (inc. jointly with COCIR and MedPharmPlast), with some lobbying by Siemens, Spitzenverband and Terumo.
52 Members include Terumo, GE Healthcare, Siemens Healthineers, Medtronic, Abbot, Baxter, Johnson & Johnson, NovoNordisk and Roche (the latter three are also members of EFPIA); <https://www.medtecheurope.org/about-us/members/>
53 ICIJ, About the Implant Files investigation, <https://www.icij.org/investigations/implant-files/about-the-implant-files-investigation/>
54 Sante HTA docs, MedTech Europe Confidential: Input for consideration to strengthen the proposal.
55 Sante HTA docs, meeting summary with MedTech Europe 22-02-2018.
56 COCIR's members include Abbot, Bayer, IBM, Medtronic, Philips and Samsung; <https://www.cocir.org/about-cocir/members.html>
57 "...to each member of ENVI, IMCO and ITRE" - ENVI is responsible, the latter two were opinion-giving committees. Sante HTA docs, COCIR Re: 9 July 2018: Save the date! The way forward for HTA cooperation – the views of stakeholders
58 Grow HTA docs 1-8
59 Grow HTA docs, Meeting with Serge Bernasconi, CEO, MedTech Europe, note to the file, 07-11-17
60 BEUC, HTA Factsheet, https://www.beuc.eu/publications/beuc-x-2018-044_health_technology_assessment_-_factsheet_0.pdf

- 61 EPF, HTA: Improvements in Parliament but Still More Work to do, <http://www.eu-patient.eu/News/News/hta-improvements-in-parliament-but-still-more-work-to-do/> NB. EPF, like many patients representatives, receives significant pharma industry funding – see Box 2.
- 62 BEUC Comments To European Commission's Proposal Regulation Health Technology Assessment, https://www.beuc.eu/publications/beuc-x-2018-027_beuc_comments_to_european_commission_s_proposal_regulation_health_technology_assessment_pdf
- 63 First general AIM Response to the European Commission Proposal on HTA, February 2018, <http://www.aim-mutual.org/wp-content/uploads/2018/02/AIM-on-HTA.pdf>
- 64 EP amendments adopted to EC HTA proposal, October 2018, <http://www.europarl.europa.eu/sides/getDoc.do?type=TA&language=EN&reference=P8-TA-2018-0369>
- 65 *Prescrire*, The EP's position on HTA improves the Commission proposal... *ibid*.
- 66 HAI, Statement on ENVI Committee Report on HTA 13/09/18, <http://haiweb.org/publication/statement-on-envi-committee-report-on-health-technology-assessments/>
- 67 ESIP, Statement on ENVI Draft report on HTA regulation, June 2018, <https://esip.eu/publications-intranet?id=137>
- 68 EFPIA statement on European Parliament Plenary on HTA regulation, 03/10/18, <https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/efpia-statement-on-european-parliament-plenary-vote-on-hta-regulation/>
- 69 BEUC, A better system in the making for testing efficiency of medicines and medical devices in the EU, 03/10/2018, https://www.beuc.eu/publications/beuc-web-2018-031_a_better_system_in_the_making_for_testing_efficiency_of_medicines_and_medical_devices_in_the_eu.pdf
- 70 EPHA, The proposed European Commission Regulation on HTA, *ibid*.
- 71 See, eg EP Legislative Train: HTA, <http://www.europarl.europa.eu/legislative-train/theme-deeper-and-fairer-internal-market-with-a-strengthened-industrial-base-products/file-health-technology-assessment>; *Politico*, Brussels gets into drug business: 2018 is make-or-break for push to get countries to join up on prices, 1/8/18, <https://www.politico.eu/article/brussels-to-find-out-how-much-it-can-do-on-drug-pricing/>; Mandatory or voluntary? A sticking point for European HTA, Leela Barham, January 10, 2019, <https://pharmaphorum.com/views-analysis-market-access/mandatory-or-voluntary-a-sticking-point-for-european-hta/>
- 72 EPHA, The top 5 issues...2019, *ibid*.