

Legal Governance in HTA: Environment, Health and Safety Issues / Ethical, Legal and Social Issues (ELSI/ELSI), the Ongoing Debate

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Volume 3, Number 1, 2020

URI: <https://id.erudit.org/iderudit/1070226ar>

DOI: <https://doi.org/10.7202/1070226ar>

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Publisher(s)

Programmes de bioéthique, École de santé publique de l'Université de Montréal

ISSN

2561-4665 (digital)

[Explore this journal](#)

Cite this article

Bernier, L., Legault, G.-A., Daniel, C.-É., K.-Bédard, S., Béland, J.-P., Bellemare, C. A., Dagenais, P., Gagnon, H., Parent, M. & Patenaude, J. (2020). Legal Governance in HTA: Environment, Health and Safety Issues / Ethical, Legal and Social Issues (ELSI/ELSI), the Ongoing Debate. *Canadian Journal of Bioethics / Revue canadienne de bioéthique*, 3(1), 83–92. <https://doi.org/10.7202/1070226ar>

Article abstract

This paper aims to provide a better understanding of the law circumscribing the social role of Health Technology Assessment (HTA) and gain insight into the reasons challenging the inclusion of ethics into HTA. We focused on a debate at the core of the perceived role of regulatory law in health technology development, namely: Environment, Health and Safety Issues (EHSI) vs Ethical, Legal and Social Issues (ELSI) that arose in technology governance. Data collection was based on a literature review and a case study analysis. The former was founded on previous work. Three HTA agencies were selected for the latter using categories ranging from a greater to a lesser level of legal obligatory intensity. Our literature review revealed five different themes relating to the social role of HTA and a distinction between the role/use of “hard law” and “soft law” in regulatory law, thus providing an understanding of how agencies used law for handling ethics in HTA. Both approaches revealed that the debate, first observed in the EHSI/ELSI technology-governance and assessment, is reproduced in HTA. The main trend revealed by the literature review and the case study, is the presence of a pact between science and regulatory law. The social demand for integrating ELSI, and more precisely, ethical evaluation into HTA, is not the main preoccupation of the traditional legal frameworks governing HTA and remains to be considered primarily by alternative, soft law initiatives. The reported difficulties in integrating ethics into HTA demonstrate the need for rethinking legal governance in HTA.



ARTICLE (ÉVALUÉ PAR LES PAIRS / PEER-REVIEWED)

Legal Governance in HTA: Environment, Health and Safety Issues / Ethical, Legal and Social Issues (EHSI/ELSI), the Ongoing Debate

Louise Bernier¹, Georges-Auguste Legault², Charles-Étienne Daniel³, Suzanne K.-Bédard⁴, Jean-Pierre Béland⁵, Christian A. Bellemare⁶, Pierre Dagenais⁷, Hubert Gagnon⁸, Monelle Parent⁹, Johane Patenaude¹⁰

Résumé

Nous voulons mieux comprendre les lois circonscrivant le rôle social de l'Évaluation des technologies en santé (ETS) et les raisons empêchant l'inclusion de l'éthique en ETS. Nous avons ciblé un débat qui est au cœur du rôle perçu du droit réglementaire dans le développement de technologies en santé: l'opposition entre les enjeux environnementaux, sécuritaires et sanitaires (EHSI) et les enjeux éthiques, légaux et sociaux (ELSI), issus de la gouvernance technologique. La collecte de données est basée sur une revue de la littérature issue de travaux antérieurs, et sur une analyse de cas où trois agences d'ETS ont été sélectionnées en utilisant différentes catégories d'obligation légale selon leur degré de force contraignante. La revue de littérature a révélé cinq thèmes relatifs au rôle social de l'ETS et une distinction entre le rôle/utilisation du droit dur et du droit souple dans le droit réglementaire, permettant ainsi de comprendre comment les agences ont utilisé le droit pour intégrer (ou non) l'éthique en ETS. Les deux approches ont démontré que le débat, EHSI/ELSI observé initialement dans la gouvernance et l'évaluation de technologies est reproduit en ETS. La principale tendance confirmée par ces analyses est la présence d'un pacte entre la science et le droit réglementaire. La demande sociale d'intégrer les ELSI, particulièrement l'évaluation éthique en ETS, n'est pas prise en compte par le droit réglementaire traditionnel régissant l'ETS et doit plutôt être considérée par le droit souple. Les difficultés d'intégration de l'éthique en ETS démontrent la nécessité de repenser la gouvernance juridique de l'ETS.

Mots-clés

gouvernance, rôle social, évaluation des technologies en santé, éthique

Abstract

This paper aims to provide a better understanding of the law circumscribing the social role of Health Technology Assessment (HTA) and gain insight into the reasons challenging the inclusion of ethics into HTA. We focused on a debate at the core of the perceived role of regulatory law in health technology development, namely: Environment, Health and Safety Issues (EHSI) vs Ethical, Legal and Social Issues (ELSI) that arose in technology governance. Data collection was based on a literature review and a case study analysis. The former was founded on previous work. Three HTA agencies were selected for the latter using categories ranging from a greater to a lesser level of legal obligatory intensity. Our literature review revealed five different themes relating to the social role of HTA and a distinction between the role/use of "hard law" and "soft law" in regulatory law, thus providing an understanding of how agencies used law for handling ethics in HTA. Both approaches revealed that the debate, first observed in the EHSI/ELSI technology-governance and assessment, is reproduced in HTA. The main trend revealed by the literature review and the case study, is the presence of a pact between science and regulatory law. The social demand for integrating ELSI, and more precisely, ethical evaluation into HTA, is not the main preoccupation of the traditional legal frameworks governing HTA and remains to be considered primarily by alternative, soft law initiatives. The reported difficulties in integrating ethics into HTA demonstrate the need for rethinking legal governance in HTA.

Keywords

governance, social role, health technology assessment, ethics

Introduction

Traditionally, the regulatory system of law has been exclusively concerned with health and safety issues in technological assessment but, over time, environmental issues came to be included in any conventional technology evaluation in what is now referred to as Environmental, Health and Safety Issues (EHSI). With genetic research's impact on modified organisms and gene therapy, the integration of Ethical, Legal and Social Issues (ELSI) have also come to the forefront of the technological assessment field, involving a complex exercise operationalized either by reference to an integrated framework (1) or to a responsible innovation procedure (2). Over the last decade, the EHSI/ELSI debate prevailing in technological assessment has migrated into the Health Technology Assessment (HTA) field. According to the World Health Organisation, "Health technology assessment (HTA) refers to the systematic evaluation of properties, effects, and/or impacts of health technology. It 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. The main purpose of conducting an assessment is to inform a policy decision making" (3). Based on this definition, we can conclude that both EHSI and ELSI analysis are required in HTA and are necessary in order to best inform decision makers. However, in HTA agencies' everyday practice, such dual analysis is not easily achieved, since this directly effects their social role.

In 2003, INHATA published the results of a survey conducted amongst its members, providing them with data on how ethics is being integrated into HTA (4). This initiated a report and recommendations from INAHTA's Working Group in Ethics on how best to handle ethical issues in HTA. Since the publication of this report in 2005, the pros and cons of integrating ethics into HTA have been at the centre of many initiatives and debates in the literature. For instance, EUnetHTA sought to develop its HTA Core model (5), integrating chapters (domains) on Ethical, Legal and Social Issues (ELSI) in order to address this topic. Recent studies, under the leadership of Assasi, have also charted what they term barriers and facilitators for the integration of ethics into HTA (6,7). As shown in Table 3B of Assasi et al's 2015 study (7), 38.5% of respondents insisted on the enhancement of existing guidelines and frameworks to promote more ethics in HTA while 57.7% mentioned that a clear demand from policy makers would be a way to facilitate the integration of ethics into HTA. As noted by some authors (8–10), the different ways in which HTA agencies interpret and fulfill their mandates contributes to limit and restrain a coherent

integration of ethics into HTA. More precisely, demands for scientific assessments by decision makers seem often to preclude a more extensive and complete technology appraisal within the process. What has been referred to as Parliamentary Technology Assessment (PTA), whereby ethical inquiry is left to political forces and enshrined in regulatory or political priorities, is a way to frame what should be the scope and focus of HTA. In this context, the question raised is: should ethical analysis be limited to PTA and thus excluded from agency's concrete HTA or should it also be the task of HTA professionals? (11,12)

This paper aims to clarify how the EHSI/ELSI distinction in regulatory law has migrated into HTA and structures the debate on the integration of ethics in HTA. Since this distinction rests on the scope of the legal constitutive statutes of HTA agencies and their official mandates, analysis of these constitutive laws should show how well ELS issues are considered. However, even if ELS issues are not clearly mentioned in the official mandates of agencies, the integration of ethical considerations in HTA practices have emerged in the field but have not been subjected to clear analysis to this date. A prerequisite step for setting the debate in regulatory law is required to fully understand the migration of the EHSI/ELSI debate in HTA (part 1). An analysis of the HTA literature can then identify what specific issues in the general debate on legal governance are raised (part 2). Finally, a case study of three HTA agencies' constitutive laws (hard law) and practices (soft law) highlights different ways in which HTA agencies integrate ethics (part 3).

EHSI/ELSI debate in legal governance (regulatory law)

Many countries have created agencies to protect their citizens from harm coming from different foods, drugs and dangerous products, as well as protecting the environment from damaging pollutants and biohazards. These agencies have the power to regulate the production and distribution of substances in different ways. Their decisions are supported by laws and regulations and they can impose sanctions upon noncompliant individuals or companies. Regulatory law's concerns are limited to the impacts of these products and processes on EHSI and the agencies' decisions must be legitimized at two levels: the degree of harm that can justify public constraints and the degree of proof that warrants the decision. This is where the hard sciences play a major role in the legitimization of the agencies' decision. How can science accomplish this role if not through its access to truth, thus providing truth to power? (13) The so called "objectivity of science" based on its access to the laws of nature (14) can justify the agencies' focus. If we adopt this view, risk assessment is exclusively science-based (14) and completely independent of risk management. Risk management is another process that takes risk assessment into account and introduces economists' cost-benefit analyses in final decisions with respect to risk hazards.

Many social factors can explain why this conception of regulatory science has been criticized. In our view (1), the governance crisis relating to genetically modified organisms (GMO) that has risen within the European Community, in some nations of the Americas (the United States, Canada, Mexico, Brazil and Argentina) as well as in other countries such as Australia, India and New Zealand, clearly shows the limitation encountered by scientific investigation when it comes to risk management. The difference in perspectives lies in the answer given to two basic questions emerging from the regulatory agencies: the degree of harm that can justify public constraints and the degree of proof that warrants a decision. Risk analysis rests essentially on the framing of what is considered as health, safety or environmental risks. To identify such EHS risks, some concepts and objects such as "fine particulate matter", "maximum tolerated doses" (13) and in particular with GMOs, "substantial equivalence", must be defined. But they cannot be defined by science alone because risk perception rests on other key contextual, psycho-social and cultural dimensions. Furthermore, one may wonder, should only short-term risk or both short-term and long-term risk be considered? Does one examine the toxicity of the agent by itself or should other synergetic aspects also be taken into consideration? Moreover, the debate over the level of evidence needed to warrant a decision depends on: i) how many risk factors an agency is willing to expose its population to, ii) how much scientific evidence is needed for decision-making, and iii) how scientific evidence can draw the line between *ignorance* (not knowing what will occur), *uncertainty* (knowing what will occur without knowledge of the probabilities) and *some degree of certainty* (knowing what will occur and the probability of its occurrence) (15).

Debates in the fields of biotechnology and nanotechnology have highlighted other limitations of the regulatory process, namely that there exist other effects of these technologies which are not accounted for in regulatory law. These include those that affect the way persons live individually and collectively, and more precisely: their quality of life, their privacy, their rights and freedoms, their jobs, and their "living togetherness". These effects are all gathered under the heading of ELSI. In regulatory law, they are not considered as a basis for constraints but are relevant to the social dynamics between producers and consumers. Therefore, these effects should be taken into consideration by technology producers in order to guarantee trust and acceptance of novel technological developments. ELSI are thus left in the hands of stakeholders. Here, different Social Sciences and Humanities studies are mobilized to understand risk perception, risk communication, social engagement practises, etc., in order to help technology developers to respond to the possible barriers of technologies' social acceptance. In other words, regulatory law is concerned exclusively with environmental, health and safety risks, while stakeholders remain responsible for the other ELSI impacts of technological developments. Therefore, when stakeholders define their corporate responsibility in relation to their products and processes and when they publicize written pledges relating to corporate social responsibility in order to reassure citizens, their social engagement is viewed as a form of law referred to as "soft law". According to Trubek, Cottrell and Nance, "soft law is a very general term, and has been used to refer to a variety of processes. The only common feature between these processes is that while all have normative content they are not formally binding" (16). As Snyder puts it, soft law can be defined as "rules of conduct which in principle have no legally binding force but which nevertheless may have practical effects" (17), such as financial, administrative or social consequences. In this context, what

this expression denotes contrasts sharply with “hard law”, which refers to traditional statutory laws and regulations that entail a legal binding force. Hard law “can be characterized as command and control, court based dispute resolution, uniform rules, punitive sanctions, and court challenges for noncompliance” (18).

The EHSI/ELSI debate lies primarily on the scope of legal governance, but it also relies on the power of science to deliver truth to a given authority in order to legitimize its decisions. This debate has highlighted several limitations with respect to truth delivery by science. Its first limitation relates to the means for obtaining truths: epistemology. It gives rise to the following questions: Can science really capture truths in the laws of nature? Are empirical sciences only based on quantifiable data? Can qualitative research also provide valid information for decision-making? The second limitation relates to the fact that the scientific methodologies applied in risk analysis are value-laden. The choice of outcome measures and comparators such as in the concept of “substantial equivalence”, for example, are grounded in values (19). The third limitation refers to the intrinsic validity of scientific research and the way scientific proof, in itself, is enough to legitimize agencies’ decisions, despite what is ignored and what is uncertain (20).

At the governance level, the exclusion of ELSI in regulatory law can be criticized on two grounds. The first is the lack of justification for limiting scientific inquiry to only EHSI, even when it clearly encompasses broader effects on people’s lives and more globally, on society itself. This is why an approach integrating all impacts of scientific innovations (whether positive or negative) on Environmental, Ethical, Economical, Legal and Social issues (E₃LS) was introduced in the contexts of genomic research funding (21), governance in nanotechnologies (22) and regulation of nanomedicine (23) in Canada. The second ground for critique is the democratic deficit resulting from a “post-war social contract” (10) between science and regulatory law, where risk acceptability is wrongfully considered as a scientific fact and not as a value-laden process. Yet, pressure to include citizens’ point of view has made its way through different initiatives (e.g., citizen conferences and public debates), each time, trying, albeit with difficulty, to include ELSI in regulatory law (24).

The EHSI/ELSI debate in legal governance raises different issues. Those supporting this distinction claim that: i) the scope of regulatory law is to protect against important harms; ii) the role of scientific proofs is the fundamental guide to regulatory decisions; and iii) appraisal of scientific proofs and other outcomes should rest in political decision making. In contrast, opponents to this distinction claim that: i) the scope of regulatory law should not only focus on limiting harm; ii) relying on scientific proofs alone is not enough given scientific uncertainty on numerous issues; iii) scientific methods used in decision making processes remain value-laden; and iv) priority given to the scientific community in regulation impairs democracy.

Methodology

Data collection was based on two methodological approaches: a literature review and a case study analysis. The literature review was based on results of our systematic review on the integration of ethics into HTA (25). In this systematic review, an analytical qualitative approach known as the general inductive method (26) was used to select relevant quotes from eligible articles. A subset of quotes referring to the integration of ethics into HTA was then extracted in order to identify similarities between the obstacles inherent to ethical integration into HTA and the EHSI/ELSI dichotomy. Keywords relating to “ethics in” and “ethics of” (HTA) were defined and used in the process.

Since the strategies and procedures of HTA agencies can vary because of their national settings and, more precisely, the legal conventions defining their mandates, we decided to undertake a case study originally focussing on four different HTA agencies in order to help highlight different approaches of the integration of ELSI into HTA. To this end, a conducive selection of agencies based on our geographical and cultural specificities was performed. Since our research project is based on the particular context prevailing in the Province of Québec, Canada, the first agencies chosen were the Institut national d’excellence en santé et services sociaux (INESSS) and the Canadian Agency for Drugs and Technology in Health (CADTH). Moreover, in order to adequately capture the duality of cultures (French and English) on which the Province of Québec takes roots, the French Haute Autorité de Santé (HAS) and the United Kingdom National Institute for Health and Care Excellence (NICE) were also selected for this study.

In order to categorize the normative documents emerging from these agencies, we built upon the 2013 annual study of the French ‘Conseil d’État’ (27). Legal governance was then divided into three categories, each of them ranging from a greater to a lesser level of legal obligatory intensity:

1. Traditional *hard law*: fully obligatory and constraining (i.e., the HTA agencies’ constitutive statutory laws)
2. *Soft law integrated in hard law*: included normative instruments that can either be employed as auxiliary means to complement regulations (used by legislators) or be used to interpret hard law normative documents (used by judges) (e.g., legal recognition of ethical codes)
3. *Soft law*: without being explicitly recognized by traditional hard law, *soft law* includes non-obligatory and non-constraining normative instruments aiming to orient the human conduct and behaviours (e.g., ethical charters, codes of conduct, etc.)

This categorization allowed us to review, in different contexts, whether traditional *hard law* or *soft law integrated in hard law* defines the HTA agencies' mandate and also, whether these agencies based their decisions solely on EHS issues (EHSI) leaving it to *soft law* to address ELS issues (ELSI).

Results

Literature review

Table 1 shows that the EHSI/ELSI distinction (theme a) is a specific indication of the challenge of integrating ELSI in HTA. ELSI is generally an add-on to the HTA process (viewed as a separate chapter of the HTA report or a separate part or process of HTA). Since a typical HTA assessment is evidence-based, findings on clinical effectiveness, health and safety for patients, and cost analysis are central and there is little doubt that the EHSI/ELSI debate is reproduced in the HTA context.

Table 1. The EHSI/ELSI distinction debate in HTA literature converges on five different themes

Distinction	Comment	References
Theme a) <i>EHSI/ELSI</i>	Integrating ELSI in HTA: as an add-on to the real thing.	Ali-Khan et al., 2015 (28); Potter et al., 2008 (29); Potter et al., 2009 (30); Hofmann et al., 2014 (12).
Theme b) <i>Assessment/Appraisal</i>	The aim of HTA variables: assessment / appraisal; synthesize knowledge / make recommendations	Ten Have, 2004 (31); Refolo et al., 2016 (10); Hanvoravongchai, 2008, (32); Lysdahl et al., 2016 (33); Martin et al., 2011 (34); Sandmann et Heintz, 2014 (35); Burls et al., 2011 (36); Hofmann, 2008, (37).
Theme c) <i>Fact/Value dichotomy</i>	Epistemological reasons explaining the resistance of integrating non testable data into HTA.	Refolo et al., 2016 (10); Hofmann al., 2014 (12); Hofmann, 2005 (38); Rawlins, 2014 (39); Assasi et al., 2015 (7); Reuzel et al., 1999, (40).
Theme d) <i>Neutral/Value-laden</i>	The HTA process is neutral as a scientific unbiased process / Value judgments are part of the assessment process.	Grunwald, 2004 (41); Sacchini et al., 2010, (42); Hofmann al., 2014 (12); (Ten Have, 2004 (43); Ashcroft, 1999 (44); Hofmann, 2005 (38); Saarni et al., 2008 (45); Saarni et al., 2011 (46); Duthie & Bond, 2011 (47); Reuzel et al., 2004 (48); Burls et al., 2011 (36); Hofmann et al., 2015 (49); Hofmann, 2008 (37); Oortwijn et al. 2004 (11); Abelson et al., 2007 (50); Autti-Rämö & Mäkelä, 2007 (51).
Theme e) <i>Patient/citizen's involvement</i>	Participation of patients / citizens in acceptability discussions of a technology.	Culyer, 2016 (52); Daniels & Van Der Wilt, 2016 (53); Gagnon et al., 2012 (54); Klerme et al., 2014 (55); Grunwald, 2004 (41); McMillan et al., 2006 (56); Martin et al., 2011 (34); Rawlins, 2014 (39); Abelson et al., 2013 (50); Bombard et al., 2011 (8); Arellano et al., 2011 (57); Assasi et al., 2014 (6); Facey et al., 2017 (58).

The EHSI/ELSI debate on the social role of HTA is reflected in the dichotomy between assessment and appraisal (Table 1, theme b). Even if the difference of national settings is recognized as a cultural factor defining the mandate of HTA agencies, the debate is focussed on the nature of HTA reports. For some agencies, the reports should only be centred on knowledge synthesis, stating that the evidence be based on its findings (31). Other agencies (34) suggest a two phase report: the first being an assessment followed by another consisting in an appraisal. In HTA reports, the assessment basically covers clinical effectiveness and safety. This clinical review of scientific literature on the health technology or intervention assesses the scientific proof related to the clinical effects on health and security. The economic evaluation of the technology, which is also based on a quantitative scientific approach, establishes its cost/effectiveness. Implementing a health technology or intervention has other impacts on the hospital organisation or healthcare services for the population, on the quality of life of patients, and also triggers ethical and legal issues. Analysis of these is conducted in the appraisal phase, where contextual studies are undertaken and explicit recommendations are made in the reports. In other words, assessment covers EHS issues while appraisal covers ELS issues.

The EHSI/ELSI debate takes a notable turn in HTA when the barriers concerning the integration of ethics in this process are considered as a fundamental epistemological distinction between facts and values (Table 1, theme c) (7). Since traditional HTA has been linked to the capability of science to demonstrate according to levels of evidence, ethical considerations could only be integrated in its reports if the results produced were testable or verifiable (10). Emerging from discussions on patients' involvement, the integration of the findings that were not evidence-based also align with the role allocated to qualitative studies included in HTA (58).

The value-ladenness of HTA (Table 1, theme d) raises questions about the role of science in regulatory law, especially the link between risk assessment and risk management. The main question being: is risk assessment value free? When risk assessment is not considered related to the decision-making process, it seems value free. But since the aim of HTA is to guide and ground governmental decisions, there is an essential link between risk assessment and risk management, because risk assessment is part of the decision-making process. The HTA process is therefore considered value laden because it aims to guide the choice of the best alternative which in turn implies a value judgment as to which alternative is best. The value-ladenness of the decision process in HTA, from the initial scoping phase to the final report, has been explicitly addressed (22-24). Furthermore, methodological decisions in effectiveness, safety and cost analysis have also been found to be value-laden (25-26).

The democratic deficit recognized in the EHSI/ELSI debate is imbedded in the value-ladenness of assessments (Table 1, themes d and e). Can the scientific values entrenched in assessments justify the acceptability of risks and benefits for patients and citizens? Citizen's forums, public participation, and national debates have been proposed to cope with such democratic deficit. In HTA, this concern has been addressed through particular involvement of patients and citizens in the HTA processes referred to, in this field, as participatory approaches (58).

Case study

As previously stated, four HTA agencies were originally selected for our case study: Haute Autorité de Santé/HAS (France), National Institute for Health and Care Excellence/NICE (United Kingdom), Canadian Agency for Drugs and Technologies in Health/CADTH (Canada) and Institut national d'excellence en santé et services sociaux/INESSS (Québec, Canada). Since CADTH does not have a constitutive statutory law, it was ultimately excluded from the case study; so only three agencies were compared. In our investigation to identify how ethics is being mobilized in different HTA contexts, we performed an analysis of the legal, administrative and procedural documents relating to the existence and assessment processes of these three agencies. This analysis was conducted by taking into consideration: i) the normative strength of the documents associated with the categories of *hard law* or *soft law*, ii) the definition of the agencies' social role expressed in legal constitutive documents, and iii) the integration of ethics in the agencies' mandates and actions. We also made the distinction between "ethics of" and "ethics in" HTA in our case study analysis. The examination of these formulations brought additional light to how those two expressions are used in the literature (5,38,44,59). Indeed, we found that, throughout our case study, the expression "ethics of" HTA referred to how ethics is being mobilised to govern the process or the agencies' functioning *per se* (e.g., management of conflicts of interests, objectivity standards, transparency, equity requirements, etc.). As for the expression "ethics in" HTA, it refers specifically to the ethical dimension needed for assessment and appraisal activities.

INESSS

The Québec *Institut national d'excellence en santé et services sociaux* (INESSS) was created in 2011 through a binding constitutive law: the *Act respecting the Institut national d'excellence en santé et en services sociaux* (60). Such an act represents traditional hard law and defines the agency's mandate in its Sections 4 and 5. Ethics were first mobilised through hard law in reference to the agencies' values and the unfolding of its mission. Referring to excellence, independence, openness, scientific rigor, transparency, integrity and equity, Section 4 of the INESSS act defines the conduct that should be expected of stakeholders involved in HTA activities. Sections 5 and 10 of the INESSS act (7) refer to the requirement for public involvement in the agency's consultations and scientific activities. Such use of ethics in framing the agencies' practices, deontology and stakeholder conduct is best described as the "ethics of" HTA. It differs from "ethics in" HTA which refers to the social role of HTA and how ELSI have made their way into the actual appraisal of health technologies.

In relation to "ethics in" HTA, the INESSS act not only focusses on the assessment of the health technologies' impact on EHSI but it also explicitly integrates ELSI in its overall mission, through singular and unique effort, using hard law, in order to ensure a definite role for ethics in assessment activities (Section 6, *in fine*, INESSS act). Thus, in addition to the traditional concerns on EHSI, the core regulatory mandate of the Québec agency in charge of HTA has included the integration of ELSI in its assessment activities. To this end, the act explicitly refers to an ethical framework that has to be drafted and published and lay out principles guiding the assessment and appraisal of scientific evaluations, and for stakeholders to explain the reasons behind their recommendations and practice guides. In this sense, for INESSS, hard law seems to play an important role in the integration of ELSI into HTA.

As we look closer, we realise that despite clear constraining obligations emerging from regulatory law, INESSS and its stakeholders have, so far, fallen short on delivering and putting into place the prescribed ethical framework. Indeed, despite Section 6 of the INESSS constitutive act, it appears that no ethical framework has been adopted or published to this date. However, recent work on an ethical framework based on Accountability for Reasonableness (A4R), presented at the HTAi annual meeting in 2018, proposes a multicriteria analysis including ethics and patient involvement. In the soft law initiatives produced by INESSS, we found some reference to ethics but no ethical framework *per se*. In fact, INESSS published two codes of ethics (one for the agencies' leaders and one for external experts) and some rules governing its scientific committee actions on drug evaluation (61-63). In those soft law documents, INESSS refers to values that should be at the heart of the agency's and committees' mission ("ethics of" HTA). It also refers directly to the need for its scientific committee to respect the ethical framework prescribed by hard law (Sections 4 and 7, INESSS act). Moreover, in some of its best-practice documents regarding the consultation of stakeholders and on practice guidelines, the agency recognises, albeit in very general terms, the importance

of the inclusion of ELSI for fulfilling its mandate. For example, referring to ethical issues emerging from HTA practices (64) or by including ethical issues in the scientific and contextual data collected for an HTA (65).

Even if hard law seems to play a central role in the integration of ethics in the general mandate of INESSS, it has not yet been translated in a defined and concrete role for ELSI in HTA. EHSI thus remains the main focus of HTA despite some clear legal intentions to the contrary.

HAS

The French *Haute Autorité de Santé* (HAS) is an independent public scientific authority, created through the French Social Security Code (66), and has two distinct missions: 1) assessment and recommendation, 2) accreditation and certification (articles L161-37- L161-40 & R161-71 to R161-78-18). The constitutive act of HAS, referred herein as its Code (*hard law*), requires that when establishing and publicising recommendations and medico-economic positions on efficient prevention, care or prescription strategies, HAS should take into consideration the respect of ethical principles. The Code, however, places the focus of HTA activities on EHSI, privileging mainly clinical, economic and scientific data for fulfilling the agency's missions. In this sense, *hard law* defines the HAS mandate as based solely on EHSI.

Looking outside the realm of *hard law* into the agency's documents and procedures, an ethics Charter establishes ethical obligations for stakeholders involved in HAS' mission (67). Again, this refers to "ethics of" HTA and does not shed light on the role of "ethics in" HTA. Another HAS document, a methodological guide for the assessment of ethical aspects (68), gives an interesting take on the inclusion of ELSI into HTA through *soft law*. This guide is not prescribed by *hard law* but is offered as a *soft law* initiative coming from HAS itself in order to help public decision-making through better information on ethical issues arising from health interventions targeted towards decision-makers and stakeholders (p. 5 of this guide). This guide uses descriptive ethics and principlism in a very specific way and is intended for specific situations where controversial aspects of the technologies are addressed and where value conflicts are anticipated. It proposes an ethical analysis by which the ethical debate in society is compared to an ethical evaluation that would imply using value judgments in its appraisal. The proposed standardised approach in reference to ethics includes many interesting elements on the social role and mission of HAS aimed at public decision-making. However, in order to help solve value conflicts and facilitate complex decisions, it remains limited to issues that are deemed important with regards to challengeable elements of some given medical technologies. It does not propose a method that would allow highlighting of every ethical issue that could arise from any given health technology in defined health care settings (p. 12 of this guide). One example of this restrictive use of ethics is that some methodological approaches involved in medical, economic and public health choices are not being subjected to any ethical assessment because they are deemed scientifically sound and efficient (p. 9 of this guide).

Thus, this guide proposes a descriptive ethics approach, but it does not provide a thorough inclusion of ELSI into HTA. Ethics is mobilised separately, on the fringe of an assessment process that remains independent. It is not questioned by ethical analysis.

NICE

In 2012, the UK Health and Social Care (HSC) act legally recognised the National Institute for Health and Care Excellence (NICE) but left the details of the agency's mission and functioning to be included in a Charter framed and governed by regulations (s. 232 & 242, HSC act). In 2013, these NICE regulations were adopted and prescribed the publication of a NICE Charter in order to provide guidance on procedures and consultations in carrying out NICE's mission. NICE regulations s. 3 (*hard law*) and NICE Charter s. 19 & principles on social value judgement section 3.2 (*soft law*) also prescribe the inclusion of some form of "ethics of" HTA by requesting that the agency publish some procedures for dealing with its members' conflicts of interest and refers to mandatory independence and transparency of stakeholders as well as procedural principles to follow.

Moreover, the Charter further adopted by NICE (69) represents *soft law integrated in hard law*. With regards to "ethics in" HTA, the Charter indicates that NICE should ensure that value judgments made in relation to recommendations and decisions do in fact reflect the values of the UK society. It establishes a Citizens Council to inform the agency of the public's point of view (Section 21). The aim of this 30 member Council is therefore to provide a broad public perspective on overarching moral and ethical issues that should be taken into consideration in the agency's decisions and recommendations. In addition, a Guide was produced to address the social value judgments that should be made in the process of developing NICE recommendations in the context of HTA, especially when NICE has to make choices on effectiveness and cost-effectiveness (61). This Guide builds on reports and recommendations from a Citizens Council and also refers to, among other things, the four principles of bioethics, different theories of justice and fundamental rights/values (e.g., non-discrimination and equality), that are all relevant to healthcare decision-making. This *soft law* initiative outlines the need to include ELSI in NICE's HTA methodology without targeting it to specific appraisals. In a way, it represents some sort of inclusion of ELSI in the field of HTA without applying it systematically throughout the HTA process.

Discussion

The case study clearly demonstrates that the social role of HTA varies according to the legal agencies' mandates involved and thus confirms that within two of the three agencies studied, the ultimate goal defined by law is scientific assessment. It is only in the legal mandate of INESSS that there is a requirement for making an ethical evaluation in the actual HTA process. This

prerequisite is clearly linked to the requirements of appraisals and recommendations, and for the need to give reasons to support final decisions. In contrast, the legal mandates of HAS and NICE clearly confirm the post-war social contract between science and governance in regulatory law whereby science, by its assessments, speaks the truth to decision-makers.

The need for taking ELSI into account in regulatory law is fulfilled differently by the different agencies analysed. In fact, the “ethics of” HTA matters for the three agencies studied and each has voiced the importance of excellence, independence, openness, scientific rigor and transparency. This contrasts with the “ethics in” HTA statements, which are handled quite differently. In one agency (NICE), ELSI are addressed by a general discussion between citizens. Although this solves the democratic deficit problem, such an approach does not have a direct impact on the actual assessment part of HTA. HAS proposes a different approach supported with an optional ethical evaluation guide that focusses on the diversity of ethical arguments applicable to the technology being assessed. Such evaluation remains an add-on to the assessment. INESSS’ statutory law requires the integration of an ethical evaluation in the HTA process, but this requirement has not yet been fulfilled and is an indication of the difficulty of integrating ethical evaluation in the usual HTA process.

The approach of these agencies towards the fact/value dichotomy and the value-ladenness of the HTA process stems from their stand on assessment and appraisal. The NICE approach takes the social values that are expressed by the Citizens Council into account and considers that the scientific assessment of HTA should thus integrate the social values identified in its final goal. Since HAS has proposed a guide for ethical evaluation of HTA, it has also specified that the value-ladenness found in assessments should not be the object of the ethical evaluation. Therefore, the approach of science speaking the truth to power is not open to debate. What distinguishes the INESSS approach is that it is clearly oriented towards being discursive, aiming to justify the best decisions in a given context. The value-ladenness of all decisions made in the HTA process should therefore be clearly spelled out.

The democratic deficit identified in the criticism of the pact between science and regulatory law is addressed directly by the Citizens Council of NICE, and also, to a different extent, through the general public’s involvement in INESSS’ consultations and scientific activities, while HAS does not have such requirements. Nevertheless, there is much discussion in the literature on the necessity of patient involvement in the HTA process and on the different local initiatives that have been put into place to fulfill this need. However, a tension remains between taking patients’ perspectives as data for assessment or as resources to be considered for ethical evaluation and appraisal.

Conclusion

Our review of literature and our case study clearly show that the debate between EHSI/ELSI observed in technological assessment is essentially reproduced in HTA. In the literature studied, the five main themes of this debate are replicated: EHSI/ELSI distinction, assessment/appraisal, fact/value dichotomy, neutrality/value-ladenness and democratic deficit. The case study indicates that the main trend still remains the pact between science and regulatory law. Our results demonstrate that, through their existing practices, these three agencies seem to circumscribe their social role further than their constitutive laws. They also show that the social demand for integrating ELSI, and more precisely that of ethical evaluation into HTA, are accounted for primarily through soft law. In one instance, hard law redefines the social role of HTA by integrating EHSI/ELSI in the requirement for appraisal and in the reasons for grounding recommendations. This highlights the importance of the role of social actors in the context of regulatory law, and in defining, structuring and operationalizing the integration of ELSI into HTA. Nevertheless, without a clear political re-examination of the HTA agencies’ statutes that proposes the integration of both ELSI and EHSI into HTA, ethical evaluation will remain essentially an add-on to the evaluative process.

Remerciements

Nous, les auteurs, attestons que 1) chaque auteur a contribué à la conception et au design ou à l’analyse et à l’interprétation des données et à la rédaction de l’article ; 2) chacun a approuvé la version soumise ; et 3) le contenu n’a pas été publié et n’est pas envisagé pour une publication ailleurs. Les auteurs souhaitent remercier Louise Corbeil pour son travail éditorial sur le manuscrit. Ce travail a été soutenu par les Instituts de recherche en santé du Canada (J.P., numéro de subvention 142187).

Conflits d’intérêts

L’un des évaluateurs externes, Isabelle Ganache, est directrice du Bureau Méthodologies et éthique à l’Institut national d’excellence en santé et en services sociaux (INESSS), et elle aide ses collègues de l’ETS à intégrer l’éthique dans leurs évaluations

Acknowledgements

We the authors, attest that 1) each author contributed to the conception and design or analysis and interpretation of data and the writing of the paper; 2) each has approved the version being submitted; and 3) the content has not been published nor is being considered for publication elsewhere. The authors wish to thank Louise Corbeil for editorial work on the manuscript. This work was supported by the Canadian Institutes of Health Research (J.P., grant number 142187).

Conflicts of Interest

One of the peer-reviewers, Isabelle Ganache, is Director of the Methodologies and Ethics Office at the National Institute of Excellence in Health and Social Services (INESSS), and she assists HTA colleagues with integrating ethics into their evaluations.

Responsabilités des évaluateurs externes

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Reçu/Received: 21 Mar 2019

Publié/Published: 20 Jul 2020

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