

Regulatory objectivity and tests systems in medicine: The case of cancerology

Alberto Cambrosio

Social Studies of Medicine, McGill University, Montréal / alberto.cambrosio@mcgill.ca

Peter Keating

Département d'Histoire, Université du Québec à Montréal, Montréal / keating.peter@uqam.ca

Pascale Bourret

Université de la Méditerranée et INSERM UMR 379, Marseille / pbourret@univ-aix.fr

Abstract: The evolution of Western medicine since World War II has resulted in the emergence of new practices based on the direct interaction of biology and medicine. The post-war realignment of biology and medicine has been accompanied by the emergence of a new type of objectivity, regulatory objectivity, which is based on the systematic recourse to the collective production of evidence. Unlike the objectivity forms that emerged in earlier eras, regulatory objectivity consistently results in the production of conventions, sometimes tacit and unintentional but most often arrived to, by means of concerted programs of action. The conventions produced by regulatory objectivity create the conditions for a clinical objectivity that relies on the existence of entities and protocols produced and maintained far outside the intimate encounter between doctor and patient. By establishing endogenous forms of regulation, regulatory objectivity operates on a different level and in a different mode from those suggested by analysts who treat all regulation as a form of rationalization imposed upon medicine from the outside.

Key words: biomedicine, objectivity; regulation, evidence, conventions.

Resumen: La evolución de la medicina occidental desde la Segunda Guerra Mundial ha resultado en la emergencia de nuevas prácticas basadas en la interacción directa entre biología y medicina. El realineamiento de la biología y medicina de la posguerra ha sido acompañada de la emergencia de un nuevo tipo de objetividad, objetividad regulatoria, que ha sido sustentada sobre el recurso a la producción colectiva de la evidencia. A diferencia de las formas de objetividad que emergieron en épocas tempranas, la objetividad regulatoria repercute de manera consistente en la producción de convenciones, algunas veces tácitas y sin intencionalidad, pero frecuentemente arriba a través de programas concertados de acción. Las convenciones producidas por la objetividad regulatoria crean las condiciones para una objetividad clínica, que confía en la existencia de entidades y protocolos creados y mantenidos fuera del encuentro íntimo entre doctor y paciente. Estableciendo formas endógenas de regulación, la objetividad reguladora funciona en un plano y en un modo diferente de aquellos sugeridos por los analistas que tratan toda la regulación como una forma de racionalización impuesta sobre la medicina de fuera.

Palabras clave: biomedicina, objetividad, regulación, evidencia, convenciones.

Introduction¹

This text takes up again and rereads a certain number of subjects we have analyzed in some of our previous works. There are two main confirmations in the origin of this work. To begin with, the explicit confirmation in Keating and Cambrosio (2003) mentions that during the second half of the XX century we have seen a realignment of the relations between biology and medicine, and with this, the beginning of a new configuration of the clinic and laboratory practices, called biomedicine. Next, the confirmation that far from considering the notion of objectivity as a logic category and therefore, ahistoric, we can describe and analyze the emergence, in different periods and dominions, of different kinds of objectivity (Daston, 1992, 1999^a, 1999b; Daston and Galison, 1992; Galison, 1998; Porter, 1992, 1995). On the base of these two confirmation, we move to the hypothesis that biomedicine entails a new kind of objectivity—a regulatory objectivity—, founded on the systematic use of the sample collective production procedures, as well as the introduction of conventions, in the context of long reflexive practices (Cambrosio, *et al.*, 2006).

Regarding the emergence of biomedicine in the post-war period, we limit to verify the correspondence with a new institutional and scientific activity that, different form the long programmatic tentatives of the XIX century of relating medicine and biology, is characterized by a high degree of material and epistemic (techno scientific) imbrications of different components of the sciences of life. Even a rhetoric, which has sometimes being excessive, has upgrade the rank of biology to that of the ultimate

¹The research for this text was financed by the following institutions: Instituts de Recherche en Santé du Canada (IRSC/CIHR), Conseil de Recherches en Sciences Humaines du Canada (CRSH/SSHRC) and the Fonds Québécois de Recherches sur la Société et la Culture (FQRSC) and the INSERM (France).

A preliminary version was presented at the Colloquium V ESOCITE. The original version in French of this paper was published in: Tournay, Virginie [ed.] (2006), *Vers de nouvelles formes d'action publique en matière de santé. De la production à l'institutionnalisation des savoirs médicaux*, Paris: Presses Universitaires de France. The authors thank PUF for the permission to publish the Spanish translation. The translated Spanish version belongs to Antonio Arellano Hernández

explanation of the origin and mechanisms of diseases, biology has not, evidently, replaced, in the reductionist sense of the term, pathology (Keating and Cambrosio, 2004). Biomedicine has —to say something graphically— surrounded medicine; at least judging the amplitude taken by the “paramedic” practices as the pre-diagnosis biological test, the population test and the patents’ therapeutic monitoring (Sournia, 1995). However, biomedicine, as long as it is a project directed to merge biology and medicine into a differentiated conjunction, presents an unfinished side, unceasingly recommenced each time a new approach (immunology, molecular biology) redesigns the boundaries of life’s knowledge and each time medical advances or laboratory breakthroughs make scientists and medics to produce new alignment ways between normal and pathological.

In the medicine where biomedicine is explicitly positioned itself in the interphase between the normal (associated to biology) and the pathological (associated to the clinic), constitutes a biomedical space in whose core are the very instruments, entities and experimental systems without the possibility of knowing, *a priori*, about the kind of results —biological and/or clinical— that its use ends in. The progressive emergence of such an inter-phase can be empirically illustrated. So, if the inter-citations network among the journals on cancer (Cambrosio *et al.*, in press) is analyzed, it can be observed that in 1980 this network was formed by two large series characterized by the density of citations relating them: the first has several journals that reveal a medical domination, and the second, dominated by research. In 2000 it is observed the presence of a third series located between the first two, which corresponds to a kind of research called “translational”, this combines medical, technical as well as laboratory entities’ elements. Moreover, after the semantic networks that relate the concepts extracted from publications’ titles and abstracts in the dominion of cancerology, the emergence of this new inter-phase is precisely located.

In the core of the biomedical space, the biological variables are redefined as pathologies’ markers. Moved in the core of automated systems (Baird, 2004), these markers have allowed the development of tests in bulk as the *Pap test* (Keating and Cambrosio, 2005; Kaufert, 2000; Casper and Clarke, 1998; Singleton and Michael, 1993), redefining by doing so the matter of

the relations among individual patients, pathological singularities and populations. These biomedical entities function based on regulations and their (re)production depends now on a collective process of tests production and on a series of conventions that mention the arrival of a new kind of objectivity. Recent phenomena, highly advertised, such as the said movement of the evidence-based medicine (Daly, 2005; Timmermans and Berg, 2003) are not, from this point of view, more than epiphenomena of this leading wave.

A pro biomedicine collective turn

Two elements characterize the emergence of biomedicine: the role of regulation and the transformation of the collectives that the practices and knowledge in this dominion produce. Regarding the first aspect, it is enough to think in the multiplication of the inter-laboratories studies, multi-centered clinical tests, as well as the emergence of cooperative groups and medical networks, of research and collective production of genetic maps (Gaudillière and Rheinberger, 2004), of diseases' animal models or even of medical and laboratory medical "guidelines". Let us take the case of the clinical tests of cancer. In the United States, the first aleatory clinical test on this dominion (for leukemia) was performed in 1954 by the National Cancer Institute (NCI). From the decade of 1960, most of the clinical tests would be performed by cooperative groups, gathering thousands of medics and researchers: in 2002, an army of close to 10,000 medic-researchers located in almost 3,000 institutions was registered in the NCI; this group organized about 160 Phase II tests every year, with an average of 100 participating institutions per test (Christian *et al.*, 2002). In Europe it can be observed an equivalent process. So, the Organization for Research and Treatment of Cancer (EORTC), founded in 1968 and following of the Groupe Européen de Chimiothérapie Anticancéreuse (GECA), created in 1962 by 17 researchers from six countries; in 2002 approximately 2,500 medic-researchers affiliated to close to 300 hospitals in 32 countries participated in the EORTC activities (Meunier and van Oosterom, 2002).

Regarding the second element, it can be considered that the development of these collectives is not limited to the enlargement of these networks. In

his ethnographic study on cancer's genetics in France, Bourret (2005) has shown that the process goes hand in hand with a transformation of the activities of the collectives, whose, within each hospital, take the decisions referred to the activities, such as the genetic council and the eventual clinical follow-ups. It is then, at the same time, the emergence of new kinds of "de-territorialized" bio-clinic collectives that take on the practices that imply the decision taking and the medical judgments, producing informal and formal regulations that nourish their activities, redefining and stabilizing the bio-medical entities mobilized by them.

As in the case of the emergence of a medical inter-phase, it is possible to follow empirically the location, development and content of these collectives work. Besides the ethnographic nature surveys, the fact that we are faced to distributed collectives makes it necessary the use of methods that allows discerning their particular configuration. So, Bourret and others (2006) have examined the emergence of a French biomedical collective of cancer genetics using a cartographic analysis of co-authoring relations among the members of the Grupe Génétique et Cancer (GGC), a study of the semantic networks of the content of their publications and, in the end, an heterogeneous cartography of relations among the human and non-human actant in the collective's core.

The GGC, group affiliated to the Fédération Nationale des Centres de Lutte contre le Cancer, gathered almost all the active French researchers and medics in this dominion, presenting it as a collective that covers the spectrum that goes from fundamental research to the medical practice and passing through applied research; all of this involved in public actions, purely at the medical recommendation preparation level, of the participation in collective experience exercises and of other regulation forms. The GGC far from corresponding to the scientific societies' model or to a lobbying group and the sanitary authorities appears as an example of the new bio-clinical collective; of which we have studied its emergence and dynamics. For this, we have analyzed the publications and their members from the end of the 1970's (before the creation of the group) until the present day, dividing this period into four subsets being, respectively: i) the first works of the future members of the group; ii) the creation of the first informal relations among

these people with the emergence of the first clinical activities; iii) the official creation of the group and, at an international level, the linkage studies consortium (which related genomics and ailing), and the identification of the cancer predisposition genes; and iv) the creation of a national network of clinics of cancer genetics and the emergence of these activities regulation problems.

If the collaborations' cartography in the first period (1969-1986) is analyzed, it is seen a series of collectives located in particular cities and clearly a large conjunction of collaborators affiliated to the Centre International pour la Recherche sur le Cancer, established in Lyon, a group of cytogeneticists and hematologists located in Paris, as well as a series of teams located in other cities (Lille, etc.). This kind of geographical fragmentation persists during the second period (1987-1991), even if it is observed the establishment of relations among these different local sets as well as the increase in the number and amount of collaborations within the latter. During the third period (1992-1996), there is an important fall in this situation: the collaborators' network is now a tightly knitted set, and the zones that can be distinguished about the map do not obey a geographical logic anymore, rather, logic of research. In this way it can be distinguished a group that corresponds to the works on breast cancer, and a smaller conjunction that gathers the medic-researchers who work on colon cancer and pediatric oncology. Finally, in the course of the fourth period (1997-2001) the collaborators network is presented as an integrated whole, the GGC works ever since as a de-territorialized collective.

Cartography of the GGC activities content shows a parallel transformation of the semantic network that characterizes these activities. During the first period the presence of cytogenetics and virology is confirmed, centered in the analysis of the first oncogens, being in the more familiar for the contemporary cancer genetics observers: genetic relations' studies, identification of cancer predisposition genes, mutation analysis, characterizations performed by a strong presence of works on breast cancer and the BRCA1 and BRCA2 genes. In the most recent period several issues directed to the regulation of the practices in the dominion of cancer preventive medicine appear in the semantic network. If these are combined,

in the same chart, the collaboration and semantic networks, a very interesting phenomenon can be seen: during the initial periods, the network tends to be structured by human entities, this is, by medic-researchers who direct a set of colleagues with whom they collaborate on different subjects; whereas in during the most recent periods, non-human and purely the terms of “breast cancer” and “mutations”, the ones that act as structural poles vis-à-vis of other network nodes.

Regulation and biomedicine

After having illustrated the collective turn of biomedicine, we will mention a second constitutive element of this configuration, to know: regulation. We have mentioned the commitment of GGC during the last years, in the initiatives directed to determining the conditions that rule the practice of cancer predictive genetics, but also the content, the judgments and the decision taking processes (for more details see Bourret, 2005). We have to mention that the relation between biomedicine and regulation is further the particular case of the dominion we are analyzing here.

After a patient goes to a doctor's office, or is admitted into a hospital, he or she is committed to a trajectory that is not necessarily lineal —diagnosis establishment, therapeutic intervention and the evaluation of the latter's result— but many times these stages are mixed, in medicine, for example, the evaluation of the results from an given intervention can be used as a diagnosis or even more, when the diagnosis can be established based on the announced or available therapeutic interventions. The diagnosis does not only imply the examination of samples (blood samples or others) but also the existence of nosologic categories —frequently redefined based on the use of new biomedical entities (Keating and Cambrosio, 2000)— allowing naming the disease and concluding the diagnosis process. So, leukemia, formerly diagnosed based on clinical and morphological criteria (microscopic cell examination) are from now on defined by means of immunologic methods that allow defining the markers located on the surface of the cells and, more recently, thanks to molecular biology methods.

The adaptation and redefinition of nosologic categories through the assistance of new biomedical entities also passes through the resource that

can be called meta-regulation institutions, as for example, the consensus conferences (Ferguson and Sherman, 2001) or the experts' networks who, according to the modalities of each country, they establish "practice regulations" and "clinical recommendations" (Castel and Merle, 2002; Burgers *et al.*, 2003; AGREE Collaborative Group, 2000) to the deontological statutes (Willems, 1998). Several studies have constantly informed these different initiatives as examples of external interference in the medical practices (despite the fact that these are well received by the doctors) and have also presented some doubts regarding the mobilization and adhesion degree that these arise among the health professionals. This does not invalidate our argument about the role played by the regulation. Indeed, even if not a single medic follows the practices preconized by the clinical recommendations, and even if every medic assumes not obeying but his clinical intuition, the latter cannot be displayed if does not comply with the condition of passing through the mobilization of entities and procedures that own their existence and signification to the introduction of conventions, in the context of formal and informal activities that operate as a regulation layer.

Due to space, we will limit this to the dominion of diagnosis. The increasingly relevant role diagnostic tests play in the biomedicine core have given space to multiple interrogations regarding the reliability and precision of these tests. Several surveys taken by state organizations or professional associations have fed these interrogations and convinced the legislative power, as well as administrators and professionals of health about the urgency of establishing standards and quality control measurements. This kind of regulation is not limited to the vigilance and sanction of eventual irregular behaviors from the laboratories; on the contrary, this regulation is constitutive of entities and practices that ensure regulation. We will explain this affirmation through an example.

During the last decades, new biomedical entities known as cellular surface markers, have occupied an increasing space in the diagnosis, prognosis and therapy of a series of pathologies (Cambrosio *et al.*, 2004). These markers are detected through the use of a particular kind of antibodies combined with fluorescent substances, which at the same time are detected

and measured thanks to computing systems. The dominion of the surface markers have been quickly developed, and several laboratories and commercial companies have issued antibodies under different names, not knowing very well if the recognition spectrum of such and such antibody was cut or with the uncertainty of the existence of such and such surface marker. In order to end with this situation that was about to turn chaotic, a group of researchers was in charge of organizing, from the 1980's, a series of international workshops directed to the creation and updating a nomenclature of makers known and used by all the scientists, medics, clinics and commercial firms.

To sum up, the work consists on the fact that the antibodies are distributed to the participant laboratories (several hundreds) at regular intervals; these laboratories, after the antibodies have been tested, gather the results for a statistical analysis. The latter allows establishing antibodies clusters (from there the acronym CD (cluster of designation), regrouping the antibodies that work in similar ways and that make us think of the existence of a cellular surface marker, equally designed by the same number of CD. What interests us here is not so much to enter to this complex system, but to mention the fact that in such system the existence of antibodies and CD markers depend, for practical ends, on the establishment of a network in charge of sanctioning and updating the categories that depend on the mobilization if a series of conventions (statistical, organizational, textual, etc.). These conventions allow establishing the boundaries of each category of CD, and besides, defining and stabilizing the biomedical signification.

But things do not stop there, another regulation layer concentrates and concretes the other reagents used, the manipulation of the analyzed samples, the equipment used and commercialized by the companies, as well as the operators of the instruments and the conditions of their use (Keating and Cambrosio, 1998). The non-existence, in this dominion, of absolute external standards makes that the establishment of conventions that allow judging the quality of the performance of a given laboratory will be the only criterion that allows attributing a factual value to the results produced. The important thing is not the fact that the results produced by a laboratory are "correct" results, but, above all, that these are compatible —to the interior of certain

statistically defined margins— with the results produced by other laboratories.²

National and international organisms, such as the WHO, are conscious of the importance of the role of these different regulation layers; parting from the internal quality control that makes it possible to ensure that the measures taken by a single laboratory from different epochs are compatible to the external evaluation of the results' quality, opening the way to the inter-laboratories comparisons.

So, the complex regulation networks have been put into practice supported by a metrologic infrastructure destined to create reference standards in the cases where this is possible, as well of controls that guarantee the analyses a minimum degree of consistence, diachronic and synchronic in the cases of “unstable” substances control, as it is blood. Here we can find the idea presented by Canguilhem (1972), that the normalization process does not imply the existence of a norm; on the contrary, the norms are the result of a normalization process. The latter implies, obviously, the establishment of a series of conventions and every time more, of methodologies that govern the development of the conventions.

Biomedicine and regulatory conventions

Several historic studies, cited at the beginning of this text, have transformed the notion of objectivity into a historical object: different times have produced different kinds of objectivity that coexist and, therefore, recombine without necessarily be replaced. So, it has been possible to describe the emergence of a mechanical objectivity directed to replace the subjectivity of the experts for the mechanic inscriptions generated by the instruments

²In the context of international regulations harmonization tentatives in biomedical issues it is interesting to note the existence of some divergences between Americans and Europeans. Whereas the former ones tend to accept as unavoidable the presence of differences among methods and limit themselves to claim the verification of conventions that allow compensating these differences, the latter insist in the search of an “analytical true”, thanks to the use of reference substances linked by a traceability chain of the samples over which the measurements are done (Powers, 2000).

(Daston and Galison, 1992; Baird, 2004), as well as the formation of a type of objectivity that is defined by the absence of every point of view or perspective (Daston, 1992), and that finds its apotheosis in the systematic resource of the quantitative measurements (Porter, 1992, 1995).

In our analysis of the emergence of biomedicine there are elements of these different kinds of objectivity —mainly on the role of the instruments and statistics. But farther this confirmation, we affirmed that biomedicine incarnates a new type of objectivity (Berg *et al.*, 2000) founded on the regulation and a system of conventions (Thévenot, 1985). These conventions govern the production of knowledge as well as the performance of the clinical practices; in this sense the production of biomedical facts is, at the same time, redefined by the introduction of new modalities of production and management of knowledge, as the examples on multi-centre clinical tests networks demonstrate, of the cancer genetics and of the CD.

The regulatory objectivity as we conceived it is not limited to the establishment of standard measurements but rather it extends to the use of these measurements to fund the judgments supported by the conventions. For example, the establishment of standards that allow identifying and measuring the presence of pathologic cells (Blastos) in leukemia, lead to the creation of standard criteria to define a particular state of this disease (blastic crisis), that are soon used as one of the parameters that make it possible to produce an objective clinical judgment in the development of clinical tests. There is, to say something, a return to the objectivity: being at first directed to the displacement of experts, individual or group, toward the objects; now, this displaces the objects toward the bio-clinical collectives.

The regulatory objectivity, as we have seen it, rests on the use of a series of production systems of tests coupled to standards of substances and practices, organized in more extensive systems and outside which an isolated measure does not have any signification. The formal procedures that regulate the “evidence based on medicine” establish an explicit hierarchy among the different testing systems: a clinical test done randomly and at blind-peers, for example, is considered more evidential than a non-randomly done test or than a mere expert’s opinion. The essential thing, however, is that the different instruments that work to produce objectivity do not make

the object of an individual treatment but, on the contrary, are retained was components of variable geometry conjunctions. The condition of possibility of the medical practice, as a conjunction impregnated by the differences (Berg and Mol, 1998) resides in the correlation between different tests systems.

Let us take a relatively simple example, extracted from leukemia or lymphomas diagnosis. The confirmed clinical signs, after a medical, examination, lead to a first kind of cito or histopathological exam of a blood sample or of a biopsy. These exams are from now generally followed by surface markers' analysis by immunologic methods, as well as by other layer of analysis provided by molecular biology (Southern Blot at the beginning of the 90's, technique that is added to the Polymerase Chain Reaction in 2000, and more recently, the use of DNA chips). Each one of these interventions provides different specialties and techniques, and produces results that may, in certain circumstances, seem contradictory and of which the signification must be determined as a whole. In the case of the regulatory objectivity, research of correlations and alignments among different diagnostic elements demands a research of standards that allows performing such correlations. This does not only include the definition of the conditions to be respected in order to produce reliable results (quality control, etc.), but of the conditions that regulate the set in relation, in the medical frames of different kinds of diagnosis, as well as the consequences of such relation on the production of medical judgments. The latter, by the return effect, affects the evaluation of the tests production systems. In the example we have just mentioned, mainly when it is about DNA chips, objective of regulation is not systematizing the individual medical reunion, but regulating the collective patient (the population of potential diseased people), to whom the tests are intended to apply. It is, to a certain extent, of exceeding the individual clinical judgment and to set conventions included in the knows and the biological know-how, displacing the medical interventions of clinical consultation in presence of a declared diseased, to a prevention founded on the calculation of risks, on a domain, passing through the statistical and biological conventions. In such chart, the way the debates reach the production of a consensus is as important as the

consensus itself. We can say that regulation generates a dynamic that is its own, as it is shown the development of a regulatory science (Bodewitz *et al.*, 1987). This implies more than a simple metrologic infrastructure that has led the development of the mechanical objectivity (Schaffer, 1992; O'Connell, 1993; Tournay, 2005). The personnel involved, directly or indirectly, in the regulation of biomedical practices is not formed by bureaucrats, but scientists and medics whose works move the very instruments and know-how displayed in other biomedical practices. Regulation generates results, proposes questions and produces phenomena whose signification has effects on the content of the practices that are subject to regulation. To sum up, the regulation work is in the centre of the production and functioning of the medical platforms (Keating and Cambrosio, 2003), that are the engine of the contemporary biomedical enterprise.

Conclusion

We would like to highlight the fact that our analysis implicates a dominion where the implications are not only socio-epistemic but that are, similarly, transferred to the political, economic and ethical debates and controversies. Regarding the last issue, we will only mention that a large number of current debates on medical ethics (for a recent example see Richman, 2004) do not have the power to give account of the dynamic of the contemporary medical practice, as these are reduced to the study of the medic-patient encounter, and declare the objectivity in laboratory medicine as “de-humanizing”, assimilated to the mechanical objectivity.

To the encounter of numerous analyses that, in recent years, associate the proliferation of rationalization and evaluation practices of the medical attention with the intervention of external forces, whether these are political or economic, directed to the change of professional self-regulation to industrial modalities of regulation (Hafferty and Light, 1995; Mossé, 1998; Setbon, 2000; Robelet, 1999, 2001), we would like to highlight, as a conclusion, that the condition of possibility of these “external” interventions has to be looked for in the development of a series of endogenous regulation elements that correspond to what we call regulatory objectivity and that are

hardly separable from the medical project itself. Indeed —further the development of management instruments of the hospital work that, as the biomedical file, give place to interventions of an administrative or juridical nature (Berg, 1996; Howell, 1995)—, every medical performance, even in the exercise of an individual consultation implies the existence of a series of conventions that concern the involved entities (germs, viruses, antibodies, genetic mutations) in the pathological processes, and also defining the kind of events that take place in the diagnostic and prognostic routines. On the other hand, the therapeutic interventions presuppose the existence of a series of conventions that concern pharmacological substances. The set in relation of these two processes has enabled the emergence of a clinical objectivity that appeals to a series of entities produced outside the verbal exchange between doctor and patient. The regulatory objectivity from now on links the clinical with other domains (such as histopathology) and refers, merely, to matters of public health (Berlivet, 1999), crossing that way the boundaries, which have never been very well established between medicine and politics. But it works in a very different way to that which presumes the analyses that attribute every regulation to the rationalization of the biomedical project.

Bibliography

AGREE Collaborative Group (2000), “Guideline development in Europe. An international comparison”, in *International journal of technology assessment in health care*, vol. 16.

Baird, Davis (2004), *Thing knowledge: a philosophy of scientific instruments*, Berkeley, CA: University of California Press.

Berg, Marc (1996), “Practices of reading and writing. The constitutive role of the patient record in medical work”, in *Sociology of health and illness*, 18.

Berg, Marc y Annemarie Mol [eds.] (1998), *Differences in medicine. Unraveling practices, techniques and bodies*, Durham: Duke University Press.

Berg, Marc *et al.* (2000), “Guidelines, professionals and the production of

objectivity. Standardisation and the professionalisation of insurance medicine”, in *Sociology of health and illness*, 22.

Berlivet, Luc (1999), “Argumentation scientifique et espace publique. La quête de l’objectivité dans les controverses autour des ‘risques de santé’”, in François, Bastien y Erik Neveu [eds.], *Espaces publics mosaïques. Acteurs, arènes et rhétoriques des débats publics contemporains*, Rennes: Presses Universitaires de Rennes.

Bodewitz, Henk *et al.* (1987), “Regulatory science and the social management of trust in medicine”, in Bijker, Wiebe *et al.* [eds.], *The social construction of technological systems*, Cambridge, MA: MIT Press.

Bourret, Paul (2005), “BRCA Patients and clinical collectives: new configurations of action in cancer genetics practices”, in *Social studies of science*, vol. 35.

Bourret, Paul *et al.* (2006), “A new clinical collective for french cancer genetics: a heterogeneous mapping analysis”, in *Science, technology & human values*, vol. 31.

Burgers, Jako *et al.* [for the AGREE Collaboration] (2003), “Towards evidence-based clinical practice: an international survey of 18 clinical guideline programs”, in *International journal for quality in health care*, vol. 15.

Cambrosio, Alberto (2004), “Mapping collaborative work and innovation in biomedicine: a computer-assisted analysis of antibody reagent workshops”, in *Social studies of science*, vol. 34.

Cambrosio, Alberto *et al.* (2006), “Regulatory objectivity and the generation and management of evidence in medicine”, in *Social science & medicine*, 63.

———, “A paraître. Mapping the emergence and development of translational cancer research”, in *European journal of cancer* (in press).

Canguilhem, Georges (1972), *Le normal et le pathologique*, Paris: Presses Universitaires de France.

Castel, Patrick and Ivanne Merle (2002), “Quand les normes de pratiques deviennent une ressource pour les medecins”, in *Sociologie du Travail*, vol. 44.

Casper, Mónica and Adele Clarke (1998), “Making the pap smear into the

'right tool' for the job: cervical cancer screening in the USA, Circa 1940-95", in *Social studies of science*, vol. 28.

Christian, Michael *et al.* (2002), "A central institutional review board for multi-institutional trials", in *New England journal of medicine*, vol. 346.

Daly, J. (2005), *Evidence-based medicine and the search for a science of clinical care*, Berkeley, CA: University of California Press.

Daston, Lorraine (1992), "Objectivity and the escape from perspectiva", in *Social studies of science*, vol. 22.

Daston, Lorraine and Peter Galison (1992), "The image of objectivity", in *Representations*, vol. 40.

Ferguson, John and Charles Sherman (2001), "Panelists' views of 68 NIH Consensus conferences", in *International journal of technology assessment in health care*, vol. 17.

Galison, Peter (1998), "Judgment against objectivity", in Jones, C. y P. Galison [eds.], *Picturing science, producing art*, New York: Routledge.

Gaudillière, Jean and Hans Rheinberger [eds.] (2004), *From molecular genetics to genomics. The mapping cultures of twentieth-century genetics*, London: Routledge.

Hafferty, F. and D. Light (1995), "Professional dynamics and the changing nature of medical work", in *Journal of health and social behavior*, num. 35 [Extra issue: Forty years of medical sociology].

Howell, Joel (1995), *Technology in the hospital. Transforming patient care in the early twentieth century*, Baltimore: The Johns Hopkins University Press.

Kaufert, Patricia (2000), "Screening the body: the pap smear and the mammogram", in Lock, Margaret *et al.* [eds.], *Living and working with the new medical technologies: intersections of inquiry*, Cambridge, UK: Cambridge University Press.

Keating Peter and Alberto Cambrosio (2005), "The production of biomedical measures: three platforms for quantifying cancer pathology", in Jorland, Gérard *et al.* [eds.], *Body counts: medical quantification in historical and sociological perspectives*, Montreal: McGill-Queen's University Press.

_____ (1998), "Interlaboratory life: regulating flow cytometry", in Gaudillière, J. and I. Löwy [eds.], *The invisible industrialist: manufacturers*

and the construction of scientific knowledge, London: Macmillan; New York: St. Martin's Press.

_____ (2000), "Real compared to what?: diagnosing leukemias and lymphomas", in Lock, M. *et al.* [eds.], *Living and working with the new medical technologies. Intersections of inquiry*, Cambridge: Cambridge University Press.

_____ (2003), *Biomedical platforms. Realigning the normal and the pathological in late-twentieth-century medicine*, Cambridge, MA: MIT Press.

_____ (2004), "Does biomedicine entail the successful reduction of pathology to biology?", in *Perspectives in biology and medicine*, vol. 47.

Meunier, F. and A. van Oosterom (2002), "40 years of the EORTC: The evolution towards a unique network to develop new standards of cancer care", in *European journal of cancer*, vol. 38 (Suppl. 4).

Mossé, Philippe (1998), "La rationalisation des pratiques médicales. Entre efficacité et effectivité", in *Sciences sociales et santé* vol. 16, num. 4.

O'Connell, Joseph (1993), "Metrology: the creation of universality by the circulation of particulars", in *Social studies of science*, vol. 23.

Porter, Theodore (1995), *Trust in numbers. The pursuit of objectivity in science and public life*, Princeton, NJ: Princeton University Press.

Robelet, Magali (1999), "Les médecins placés sous observation. Mobilisation autour du développement de l'évaluation médicale en France", in *Politix*, vol. 46.

_____ (2001), "La profession médicale face au défi de la qualité. Une comparaison de quatre manuels qualité", in *Sciences sociales et santé*, vol. 19, num. 2.

Schaffer, Steve (1992), "Late victorian metrology and its instrumentation: a manufactory of Ohms", in Bud, R. and S. Cozzens [eds.], *Invisible connections. Instruments, institutions, and science*, Bellingham, WA: SPIE Optical Engineering Press.

Setbon, Michel (2000), "La qualité des soins. Nouveau paradigme de l'action collective?", in *Sociologie du Travail*, vol. 42.

Singleton, Vicky and Mike Michael (1993), "Actor-networks and ambivalence: general practitioners in the UK Cervical Screening Programme", in *Social studies of science*, vol. 23.

Sournia, Jean (1995), *Histoire du diagnostic en médecine*, Paris: Éditions de Santé.

Thévenot, Laurent (1985), “Les investissements de forme”, in *Cahiers du centre d’études de l’emploi*, vol. 29.

Timmermans, Stefan and Marc Berg (2003), *The gold standard. The challenge of evidence-based medicine and standardization in health care*, Philadelphia: Temple University Press.

Tournay, V. (2005), *Produire des biens publics médicaux: Contribution pragmatique à une sociologie de l’action publique*, Thèse de doctorat, Science-Politique, Université de Paris I-Sorbonne.

Willems, Dick (1998), “Outcomes, guidelines and implementation in France, the Netherlands and Great Britain”, in Boyle, P. [ed.], *Getting doctors to listen. The ethics of outcome research in practice*, Washington, DC: George Kennedy University Press.

Alberto Cambrosio. He works at McGill University, Montreal, Canada. His lines of research are: sociology of the biomedical practices and innovations, in particular the relation between laboratories and clinical activities. His most recent publications, along with some other authors are: “A new clinical collective for French cancer genetics: a heterogeneous mapping analysis”, in *Science, Technology & Human Values*, 2006; “Regulatory objectivity and the generation and management of evidence in medicine”, in *Social Science & Medicine*, 2006.

Peter Keating. He works at the Université du Québec à Montreal, Canada. His lines of research are: history of the post-war biomedicine, mainly clinical research on cancer. His most recent publications, along with some other authors are: “Regulatory objectivity and the generation and management of evidence in medicine”, in *Social Science & Medicine*, 2006; “Cancer clinical trials: new style of research, new forms of risks”, in *Les cultures du risque (XVIe-XXIe siècle)*, 2006.

Pascale Bourret. He works at the Université de la Méditerranée and INSERM UMR 379, Marseille, France. His lines of research are: innovation

in the genetics and biomedicine fields and their relations with the social transformation of the medical work and diagnosis. His most recent publications, along with some other authors are: “BRCA patients and clinical collectives: new configurations of action in cancer genetics practices”, in *Social Studies of Science*, 2005; “A new clinical collective for French cancer genetics: a heterogeneous mapping analysis”, in *Science, Technology & Human Values*, 2006.

Sent to dictum: August 27th, 2006.

Approval: October 06th, 2006.