Regulatory objectivity and the generation and management of evidence in medicine*

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The evolution of Western medicine since World War II may be described as a realignment of biology and medicine that has resulted in the emergence of new practices based on the direct interaction of biology and medicine. This development amply justifies the use of an apparent syncretism, the term biomedicine (Keating & Cambrosio, 2003). The post-war realignment of biology and medicine has in turn been accompanied by the emergence of a new type of objectivity. While philosophers of science have tended to treat objectivity as a logical, ahistorical category, recent work in the history of science has shown how we can in fact historicize the notion of objectivity and describe both different periods of scientific development and different kinds of scientific activity in terms of the forms of objectivity that they embody. (Daston, 1992; 1999a; 1999b; Daston & Galison, 1992; Galison, 1998; Porter, 1992; 1995). Building on this work, we claim in this paper that modern biomedicine incorporates a novel form of objectivity that we call regulatory objectivity and that is based on the systematic recourse to the collective production of evidence (Callon, 1991). By "collective," we refer to the kind of evidence that is produced, for example, by inter-laboratory studies, multi-center clinical trials and research consortia that develop collective devices such as mouse models of disease, genetic maps or clinical and laboratory guidelines (Vinck, 1992; Cassier, 1998; Cambrosio, Keating & Mogoutov, 2004). The notion of the collective production of evidence also includes those bodies of evidence that are embedded and archived in a growing collection of institutions such as open-access genome libraries and tissue banks.

Our claim, in a nutshell, is that unlike forms of objectivity that emerged in earlier eras — with which it now co-exists — regulatory objectivity consistently results in the production of conventions, sometimes tacit and unintentional but most often arrived at through concerted programs of collective action. These actions incorporate unprecedented levels of reflexivity, in the sense that biomedical practitioners in their debates and discussions take into account the conventional dimension of their endeavors. We do not claim, of course, that every single medical practice is now governed by regulatory objectivity, but we maintain that this form of objectivity corresponds to a new regimen of coordination of medical practices that increasingly operates as a condition of possibility for the very existence of these practices.

The emergence of biomedicine

Like the practices it describes, the term biomedicine is of relatively recent coinage. Although dictionary definitions exist prior to World War II, the general use of the term as a descriptor for Western medicine is mainly a post-war

phenomenon. The neologism is as much projective as it is descriptive. Reducing medicine to a branch of biology and creating a single homogenous science remains an ambition rather than a fait accompli. While the genomic sciences are presently the most high-profile purveyors of the proposed reduction, other sciences have since the Second World War aspired to reorder the material and discursive relations between these two domains. One need only recall the different research programs and agenda of life sciences such as biophysics, biochemistry, immunology, and molecular biology. The problematic nature of the project becomes apparent when the term is used in its polemical form to advocate a strict reduction of medicine to biology. On these occasions, defenders of the autonomy of clinical research have not hesitated to denounce the term as a smoke screen intended to hide the clinical origin of many biological breakthroughs and to divert funds from clinical to more basic research (Schechter, 1999).

And yet the term biomedicine is not simply a rhetorical device invented by, say, molecular biologists in the search of a larger slice of the medical research funds pie. Early use of the term in the immediate post-war era suggested that biomedicine would be some sort of hybrid of biology and medicine and not the reduction of one to the other. The hybridization was to be accomplished not only by the application of biological theories and methods to the problems of pathology but also by the creation of new domains of study involving the interaction of “normal” humans with “pathological” environments such as those resulting from radioactive contamination or space travel. The development of civil and military atomic research and the conquest of space provided the opportunity for the creation of a panoply of biomedical instruments that would soon find more mundane applications in clinical medicine not only in such fields as nuclear medicine but also in numerous automation programs that targeted both routine diagnostics activities and new endeavors such as the monitoring and screening of actual and potential patient populations.

By the 1960s, the term biomedicine had acquired a political and administrative meaning, as is indicated by the work of the prominent medical researcher and reformer, Lewis Thomas. In an often overlooked yet extremely insightful paper on the relations between technology and medicine written at the beginning of the 1970s, Thomas pointed out that, contrary to current wisdom, true “high tech” medicine would ultimately not be based on technologies derived from physics and chemistry such as X-rays and radiotherapy. These technologies, he argued, simply papered over our lack of understanding of the biological mechanisms at the origin of disease. The high-tech medicine of the future — a biomedicine — would be more likely to profit from a better understanding of disease mechanisms and would probably use newly emerging biological tools (antibodies, enzymes, hormones, and, more recently, genes) in both diagnosis and therapy. For this to occur, according to Thomas, it was imperative to fund fundamental and strategic research in order to overcome the institutional barriers that separated biological and clinical research (Thomas, 1972). As we now know, Thomas’ vision was largely turned into reality, albeit with unexpected twists and quirks, the most important of which

was the merging of physico-chemical and electronic instruments with biological technologies.

While Thomas placed biomedicine at the interface between the normal and the pathological, he did not explain what the socio-epistemic relations between the two domains should be. Several alternatives are available. One may choose, for example to view the relations between the normal and the pathological in terms of subordination leading ultimately to the reduction of the pathological to the normal. It is also possible to view the relationship between the two as one founded on the generation of relations of mutual enrichment within a novel space of representation and intervention. We would suggest that recent work in the history and sociology of the biomedical sciences tends to support the latter position (e.g., Löwy, 1996; Rheinberger, 1997; de Chadarevian & Kamminga, 1998; Gaudillière, 2002). Biomedicine differs greatly from the small-scale or largely programmatic attempts in the 19th century to link biology and medicine. The biomedicine that emerged in the post-war era features a complex interweaving of the diverse material and epistemic components of the life sciences. Although an occasionally overblown rhetoric claims that biology is the ultimate explanation of the origin and mechanisms of disease, biology has clearly not replaced, in the reductionist sense, pathology (Keating & Cambrosio, 2004a).

Indeed, multiple observations show that the last fifty years have seen the constitution of a biomedical space wherein the tools and experimental systems used in pathology and biology tend to deploy both normal and pathological entities interchangeably to the point where, more often than not, they largely overlap. In other words, despite the fundamental differences between physiological and pathological processes, the last fifty years have witnessed a convergence in the methods used to intervene in these processes and in the entities held to be the principal actors both in health and disease. Moreover, given the interchange of actors and methods, the biological or clinical relevance of deploying an experimental system in biology or pathology cannot be known in advance. A clinical trial tracking a biological, prognostic variable, for example, is equally likely to say something about the biology of human beings as about the pathology of the disease being studied.

Redefined as surrogate markers for pathological processes, biological variables (i.e., cell surface markers, chromosomes, genes, proteins, etc.), make possible both mass screening and the automation of screening techniques (consider the Pap test; see Keating & Cambrosio, 2005a; Kaufert, 2000; Casper & Clarke, 1998; Singleton & Michael, 1993). They thus redefine the relations between individual patients, pathological singularities and populations. Consequently, the automation of diagnostic activities represents more than the simple use of technologies to more rapidly achieve the same results as manual methods. Automation modifies the content of medical practices and the nature of the judgments that arise in these practices. It does so by supplanting qualitative analyses with quantitative analyses, by upsetting the relations between structure and function, and by resorting to computer generated representations that change both the type and means of circulation of biomedical entities (Baird, 2004; Keating, Limoges & Cambrosio, 1999).

At the institutional level, this transformation has been accompanied by an unprecedented rise in the public funds invested in biomedical research and by the creation of institutions like the National Institutes of Health in the United States. Less visible but equally significant changes include the expanded role accorded research in medical schools which, by 1980, awarded almost 40% of the Ph.D.s in the biological sciences (Rothstein 1987: 251). Similarly revealing was the 1995 change to the American Journal of Pathology which added the subtitle: Cellular and Molecular Biology of Disease. In keeping with the idea of biomedicine as an ongoing project, one of the current themes of the present direction of the NIH is to harness the knowledge in the life sciences produced at the NIH in a more direct fashion in the treatment of disease. The much vaunted "Roadmap" that is presently reorienting research at the NIH constitutes the latest stage in the continual realignment of biology and medicine and the persistent concern with the translation of biology into medicine that has animated numerous projects since the advent of biomedicine. To take just one example from the Roadmap, in recognition of the distributed nature of genomic biology on the one hand and the problems of organizing multi-center clinical trials, on the other, Roadmap designers propose that clinical research in turn will have to be reorganized and suggest that "clinical research needs to develop new partnerships among organized patient communities, community-based health care providers, and academic researchers. In the past, all research for a clinical trial could be conducted in one academic center; that is unlikely to be true in the future."[i]

With regards to routine clinical activities, the second half of the 20th century has witnessed (especially in Europe because of the devastation caused by the War) a transformation of hospital architecture. The pavilion system of architecture based on the segregation of patients into separate pavilions according to medical specialty was gradually replaced by so-called platform hospitals where high-rise patient towers sit on technical platforms containing highly automated analytic laboratories (Verderber & Fine, 2000). Most of the analyses are diagnosis-related, as a common feature of post-war clinical medicine has been the sharply increasing number of diagnostic tests. So many, in fact, that observers generally concur that diagnosis has in many instances outdistanced the therapeutic capabilities of clinical medicine, leading yet other observers to suggest that the diagnostic enterprise has achieved a relative autonomy with regards to other clinical objectives (Sournia, 1995). Similarly, isolated clinical specialists have, in many instances, been replaced by multi-disciplinary teams that are avid consumers of biological-diagnostic tests, and by a complex web of interdependencies between sub–areas of specialization (Gosselin, 1985). In the case of emerging domains, such as predictive genetics and cancer, the collective production of diagnosis has meshed imperceptibly with the collective production and management of medical judgment and medical decision-making (Bourret, 2005).

To sum up: as used in this paper, the term biomedicine refers to a material, institutional and epistemic configuration that cannot be reduced to medicine (the pathological) or biology (the normal). This novel configuration is properly described as biomedical to the extent that it is the result of the realignment

(not fusion) of practices concerned with the production of the normal and the pathological. Biomedicine offers, in other words, a new space of representation allowing for the coexistence of biomedical entities (antibodies, oncogenes, genetic signatures, etc.) that participate simultaneously in normal and pathological processes. As we will see in the next section, these biomedical entities function within a regulatory framework and their (re)production depends upon a network of conventions that express a new kind of objectivity. In this respect, the highly-publicized movement for evidence-based medicine (Daly, 2005; Timmermans & Berg, 2003; Weisz 2005) is but one of the many expressions of a deeper and more wide-ranging transformation.

Biomedicine and regulation

The central role assumed by diagnostic tests in biomedicine has prompted a growing concern about their reliability and utility. Numerous studies conducted by state agencies and professional bodies such as, in the United States, the Centers for Disease Control or the College of American Pathologists have contributed to the discussion and convinced legislators, health care providers and health care administrators that standards and quality control measures are urgently needed. Despite the seemingly mundane nature of such discussions, we must not forget that norms and standards of quality control are much more than a means of controlling the activities of diagnostic test technicians. They are part of a larger domain of activity, regulation, which contributes to the constitution of the entities and the practices that it regulates. The following example will make the recursive nature of these relations explicit.[ii]

Over the last thirty years, new biomedical entities known as cell surface markers have figured prominently in the diagnosis, prognosis and therapy of a steadily growing number of pathologies. The best known of these markers is CD4 whose detection serves to identify types of white blood cells such as macrophages and T4 cells that are the common targets of the AIDS virus. Numerous other markers (there are presently more than 200, all designated by the acronym CD followed by a number) play a major role in research and clinical domains as diverse as cancer — especially the leukemias and the lymphomas — transplantation, and diseases of the immune system. The markers are detected using specific antibodies tagged with fluorescent substances which, in turn, are measured by computerized equipment produced by a growing biomedical instrumentation industry. The domain of surface markers developed very quickly in the 1970s and a number of laboratories and commercial enterprises marketed antibodies with different names and different specificities. This quickly raised the question of which antibodies recognized which markers and consequently of inter-laboratory and inter-company comparability. In 1980, in order to resolve a situation that risked sliding into chaos, a group of researchers began organizing a series of international workshops to create a standardized nomenclature for use by clinicians, researchers and commercial enterprises (Cambrosio, Keating & Mogoutov, 2004).

Briefly, the system worked as follows: at regular intervals, new antibodies (or old ones requiring reclassification) were distributed to the hundreds of participating laboratories which, following testing, sent the results to be pooled for statistical analysis. Statisticians were thus able to define, on this basis, clusters of antibodies (hence the acronym CD for “cluster designation”) that reacted similarly and thus presumably attached themselves to the same cell surface marker (which received the same CD number). We are less interested here in the details of the system than the fact that in such a system, the CD numbers depend upon the establishment of an international network for the express purpose of creating the CD categories that separate one antibody and its corresponding cell surface maker from another. A single laboratory could not possibly establish the differences that make up the system. The system in turn depends upon the mobilization of a series of statistical and organizational conventions and standard laboratory protocols. The conventions not only separate one marker from another but make it possible to assign biomedical meaning to the CD category. The regulations, in other words, create the entities they regulate.

But there is more. As mentioned above, using antibodies with a CD designation entails the use of sophisticated laboratory instruments. Given that these instruments are produced by a variety of commercial suppliers, is it possible, clinicians and researchers asked at the time, that different instruments run by different operators in different institutions produce different results? It turned out that the answer was yes. Consequently, there is yet another network of rules, regulations and conventions that target the reagents used, the samples tested, the instruments and the instrument operator, and that must be followed if one wishes to compare, for example, blood samples taken from patients enrolled in multi-center clinical trials (Keating & Cambrosio, 1998). The absence of absolute standards in this field means that the establishment of conventions concerning the proper performance of the laboratory test in question is the only way of assuring that test results are comparable and that they attain the status of fact. What counts, in other words, is not whether or not the results produced by a particular laboratory are true, in some absolute sense, but whether or not they are compatible (within conventionally determined statistical limits) with results produced by other laboratories.[iii]

National and international organizations such as the World Health Organization are quite conscious of the significance of these different layers of regulation which run the gamut of formality from unofficial rules of thumb and different forms of internal quality control that allow a single laboratory to compare results over time, to external quality control measures that make possible inter-laboratory comparisons. Complex networks of regulation that mobilize intricate metrological infrastructures have thus been established in order to create, where possible, reference standards. In cases of unstable structures like blood, systems of control have been established that assure that laboratory analyses maintain a minimum of consistency between laboratories and over time.[iv] As the authors of one of these standardizing enterprises point out:

> A genuine assessment of accuracy is not possible without true reference standards which do not exist for any of the formed elements [cells] of the blood. The only available indicator of accuracy is therefore the degree of consensus on samples analyzed in different laboratories. (Kidd and Vogt: 4)

Readers of Canguilhem (1989) will recall that the normalization process does not presuppose the existence of a norm. Rather, norms are the result of normalization which entails the establishment of a set of conventions and, increasingly, the development of methods that provide the framework for the production of those conventions.

The following statement issued by the International Committee on Standardization in Hematology (ICSH) gives an idea of the kinds of problems confronting such an enterprise in the real world:

> A definitive method is one which has no known source of inaccuracy or ambiguity. A reference method is less certain than a definitive method but it is a clearly and exactly described technique which provides sufficiently accurate and precise laboratory data for it to be used to assess the validity of other laboratory methods. A selected method is one which is recommended for routine use having been shown to be sufficiently accurate and precise for its intended purpose and to be practical enough on the grounds of economy of labour and materials and ease of operation. Unfortunately even the selected method may be impractical under certain circumstances so that a simple routine method may be used albeit not recommended by ICSH. (Lewis 1990)

Our concept of regulatory objectivity is not restricted to the diagnostic phase of biomedicine that we have thus far emphasized. When a patient consults a medical practitioner or is admitted to hospital, s/he sets out on a non-linear trajectory divided into diagnosis, treatment, and evaluation stages where the results of one stage may feed back into a previous stage as when the results of therapy modify the initial diagnosis or prognosis (Berg, 1992). A diagnosis implies not only the examination of the patient and bodily samples; it also entails the existence of nosographical categories that allow clinicians to name the disease and to evaluate the results of various diagnostic tests (and, subsequently, of prognostic measurements and therapeutic interventions). Consider, now, the field of migraines: some of the most significant therapeutic advances in the past two decades owe their existence to the international classification of migraines which has made possible a whole series of novel clinical trials and created the grounds for their comparison (Popowycz, 2004). Nosographical entities are themselves subject to frequent redefinition implicating yet other biomedical entities. Consider, for example, the leukemias. Initially diagnosed on the basis of clinical and morphological criteria through the examination of stained cells and tissues under a microscope, they are presently defined in terms of cell surface markers (CD) and are currently in the process of being redefined in molecular biology terms (Keating & Cambrosio, 2000).

The redefinition of disease entities by means of biomedical entities also has recourse to what might be termed institutions of meta-regulation such as consensus conferences (Ferguson & Sherman, 2001) and groups or networks of experts that establish clinical guidelines and recommendations (Castel & Merle, 2002; Burgers, Grol, Klazinga, Mäkelä, & Zaat, 2003; AGREE Collaborative Group, 2000) that have varying degrees of force (Willems, 1998). Numerous critiques have denounced these initiatives as a form of unwanted meddling in medical practice (even though it is physicians themselves who are usually behind such undertakings) and studies have raised doubts about the extent to which recommendations and guidelines are actually followed. Because methods of achieving consensus are frequently local and informal, efforts are currently underway to develop and promote international guidelines for producing guidelines (Graham, Beardall, Carter, Tetroe & Davies, 2003; AGREE Collaborative Group, 2000). Despite such difficulties that call into question its practical import, our notion of regulatory objectivity retains its validity in this domain as well. Even if nobody followed clinical guidelines or recommendations, and even if clinicians were guided by sheer intuition, clinical diagnosis and intervention would still call upon normal and pathological entities and procedures whose clinical existence and meaning depend upon regulatory objectivity.

Biomedicine and regulatory objectivity

As previously noted, recent historical studies have transformed objectivity into a subject of historical inquiry. They have shown how different historical periods have produced different types of objectivity which have subsequently persisted either as autonomous forms or in combination with other types of objectivity. Thus, whereas the objectivity of a statement was once guaranteed by the knowledge and experience of the author of the statement, later periods have tended to privilege mechanical or instrumental objectivity that replaces experts' subjectivity with mechanically produced inscriptions (Daston & Galison, 1992; Baird, 2004). Similarly, Daston (1992) has described the emergence of a type of objectivity predicated upon the absence of any viewpoint or perspective and which culminates in the systematic recourse to quantitative measures (Porter, 1992; 1995). Each form of objectivity stands in opposition to some other form of (equally historically contingent) subjectivity and embodies a distinctive moral economy (Daston, 1995).

Elements of these different types of objectivity — collective expertise, scientific instruments and their inscriptions, and statistical measurements — have played and continue to play a central role in the development of modern biomedicine. We wish, however, to claim that biomedicine now incorporates a new type of objectivity based on regulation and systems of conventions (Thévenot, 1984; 1997; Dodier, 1995).[v] These conventions are constitutive not only of clinical practices but also of the knowledge emerging from both clinical and laboratory settings. The CD example is just one instance of how the production of biomedical knowledge has been redefined by the establishment of new modes for the production and management of

knowledge that are based on regulatory objectivity. Similar forms of regulatory objectivity are expressed in such knowledge creation projects as the aforementioned multicentered clinical trials or in the more recent bio-clinical collectives involved in cancer genetics (Bourret, 2005; Bourret, Mogoutov, Julian-Reynier, & Cambrosio, submitted) and genomic medicine more generally.[vi]

Some readers might object that the configuration that we have described is not new. This is true to the extent that regulatory objectivity implicates systems of measure and standardized objects such as the metric system, high purity chemical reagents (Analytical Reagent Grade or Analar), electrical standards and so on, whose invention dates back to the 19th century and which are also based on conventions (Schaffer, 1992; O'Connell, 1993; Gooday, 2004). In this regard, regulatory objectivity could be construed as little more than a pre-condition of mechanical objectivity. Our view of regulatory objectivity is not, however, restricted to the establishment of standard measures. It incorporates the use of these measures as a basis for clinical judgment. Thus, for example, the establishment of standards allowing clinicians to identify pathological cells (blasts) in the blood of leukemia patients has led to the creation of standard criteria for the definition of specific stages of the disease (the blast crisis). These stages are then used as a means to render objective clinical judgments in clinical trials. There has therefore been a reversal of objectivity: whereas mechanical objectivity displaces the bearer of objectivity from the human expert to the object, regulatory objectivity displaces the focus from objects back to human experts, or, rather, to collective forms of human expertise combining people (clinicians, researchers, administrators, patients, …) and objects (entities, instruments, tools, techniques, …) connected by specific coordination regimens. Depending on the domain under consideration, these human and non-human elements are attributed a differential weight (Dodier, 1995). In a field like surgery, for instance, in spite of the development of surgical instruments that embody specific operating techniques, the face-to-face transfer of operating skills plays a crucial regulatory role at the expense of more impersonal tools such as guidelines (Schlich, 2002). Similarly, animal models and clinical trials do not perform the same regulatory function in surgery as compared to oncology. More generally, the various sectors of medical science and practice may differ substantially in the degree to which they incorporate regulatory objectivity.

The heuristic value of our approach thus lies in the fact that it allows us to investigate not only the dynamics of different forms of regulation but also the constitution of the entities and processes that are the subject of regulation. Regulatory objectivity targets not only specific instruments or practices and individual representations but also those configurations of practices, instruments, knowledge, and clinical expertise known as biomedical platforms (Keating & Cambrosio, 2003). The notion of regulatory objectivity also enriches our understanding of medical history. The well-known developmental sequence according to which medicine moves though a series of stages or types running from bedside medicine to clinical and laboratory medicine (Ackerknecht, 1968; Jewson, 1976; Pickstone, 1994) can now be extended to

include the latest stage of multi-centered medicine, a stage saturated by convention-based forms of regulation. Its predecessor in this scheme, laboratory medicine, relied heavily on mechanical objectivity which proposed that there were indeed “true measures” that corresponded to the quantitative characteristics of the substances present in the body. Under the regime of regulatory objectivity, biomedicine suspends the search for “true values” and replaces it with the establishment of conventions. As we previously mentioned with regards to laboratory standards, for biomedicine it is less important to arrive at a truth (analytic or otherwise) than to ensure compatibility between different laboratories and different hospitals. As one of the participants at a conference on the international harmonization of in vitro tests pointed out, it is a question of providing consistent resources for “patients [who] travel globally, acquire global diseases and will eventually request global healthcare” (Carneiro, 2001: 17). In this sense, regulatory objectivity also reflects the values of globalization and free information flow that has driven international standardization since World War II (Timmermans & Berg, 2003: 17).

Within the framework of regulatory objectivity, the way in which practitioners reach a consensus is as important as the object of the convention. It might be argued that, henceforth, regulation has its own dynamic as demonstrated by the emergence of “regulatory science” (Bodewitz, Buruma, & De Vries 1987) as an interface between top-down and bottom-up forms of regulation. Regulatory objectivity is thus more than a simple metrological infrastructure (Star & Ruhleder, 1996) of the kind that permeated mechanical objectivity. Those implicated in the regulation of biomedical practices are not bureaucrats but scientists and clinicians whose work uses the same tools and know-how utilized in the practices themselves; the work, as we have seen, is recursive. Regulation generates results, raises questions and produces phenomena whose significance feeds back into the practices that are the subject of regulatory activities. Regulation is also at the centre of the production and maintenance of biomedical platforms which are the motor of contemporary biomedicine.

Systems of evidence

As we have seen, regulatory objectivity is based on the use of a variety of different systems for the production of evidence (clinical trials, consensus conferences, etc.) that are linked to standard substances and standard practices (quality control procedures, practice guidelines, clinical recommendations, etc.) which are themselves organized into systems; a single measure, in other words, has no meaning when isolated from other measures in the system. The systems themselves can in turn be articulated within a larger system. In spite of potential variations between medical domains, the formal procedures that constitute evidence-based medicine, for example, explicitly recognize a hierarchy between different systems of evidence and their components: a randomized double-blind clinical trial is considered of greater value than a non-randomized clinical trial or an expert opinion. In other situations, such hierarchies remain implicit. Of critical importance is that, regardless of the level of formalization, the tools used to

produce objectivity are not handled on an individual basis but function as components of a larger system and are explicitly understood to do so.

Clinical medicine, which to inattentive observers may appear somewhat homogeneous, is, in reality, shot through with multiple differences (Berg & Mol, 1998) and clinical practice consequently presupposes the ability to correlate different systems of evidence. Doctors, of course, have in the guise of clinical judgment always evaluated different kinds of evidence on an individual and informal basis. Such processes, however, are now increasingly collective, specialized and formalized (Gosselin, 1985; Berg, 1997; Mol, 2002, Bourret 2005). Consider the relatively simple example of prostate cancer diagnosis. In the course of making such a diagnosis, the practitioner draws together clinical signs (rectal exam), biochemical laboratory tests (PSA test), and histopathological examinations following surgical biopsy. Each of these different kinds of evidence calls upon different specialties and techniques. In turn, the results are interpreted both sequentially and conjointly. A high PSA level may be cause for a biopsy but does not alone signify cancer. Regulatory objectivity seeks out not only correlations between the different components of the diagnosis, but also seeks standards that allow such comparisons to be made. This includes not only setting out the conditions that must be respected in order to produce reliable test results, (quality control, etc.) but also the conditions that define the relations (within a clinical context) between the different diagnostic elements as well as the consequences of such relations on clinical judgment. In the case of prostate cancer, PSA tests, the most recent of a panoply of tests in this domain, are presently the subject of much regulatory work. The target is not so much the individual patient as the collective patient or, in other words, the population of potential patients on whom the test will be used. Present regulatory investigations consequently go beyond individual clinical judgments and establish conventions based on biology and biological know-how. At the same time, the PSA test, as a biological test and not as a determinative diagnosis displaces the question of the diagnosis of the cancer patient. By opening up the possibility of monitoring a biological variable in a population, the PSA test sets up the possibility of prevention through the calculation of risk and thus leads the clinician into a dense thicket of statistical and biological conventions. Such calculations may end up undermining the very premises on which PSA testing in based (Stamey, Caldwell, McNeal, Nolley, Hemenez, & Downs, 2004).

In addition to its impact on research, diagnosis, treatment, prognosis and screening, regulatory objectivity has had a profound effect on the reward system or the moral economy (Daston, 1995) of modern medicine and research. The change in scale engendered by collective research practices has provoked numerous questions about the proper distributions of credit in research publications. The distributed nature of the biomedical research enterprise raises further issues of trust or, as Hardin (2002) would caution, trustworthiness, with respect to data production and interpretation (e.g., Hilgartner, 1998). While we can go no further here, there is no doubt an interesting story to be told about the conventions that guide and maintain the trustworthiness of a single datum along the interpretive trail from its origin through the various data managers (a recent invention), into a medical journal

(which routinely employ their own statisticians to check data) and on into a consensus conference (e.g., Healy, 2004).

Conclusion

In conclusion, we would like to emphasize that our analysis touches upon a domain that is not merely socio-epistemic but that broaches a number of political, economic and ethical controversies. In the last case, many present discussions in medical ethics (for a recent example, see Richman 2004) are unable to account for the dynamics of medical practice insofar as they reduce the latter to a physician-patient encounter which they denounce as "de-humanizing" thus treating the objectivity of laboratory medicine as a form of mechanical objectivity. This attitude displays a remarkable lack of reflexivity, since ethical problems as they are framed today, far from leading an independent existence in the realm of transcendental human values, are the historically contingent products of the clinical research enterprise itself (Keating & Cambrosio, 2005b). We would, thus, treat ethical debates as one of the elements entering into the constitution of contemporary biomedical practices as defined by regulatory objectivity (Tournay, 2005).

With regards to the socio-economic aspects, we have noted that the tools used to manage and produce conventions are articulated within different systems of evidence. The latter, in turn, make possible interventions that are perceived as having an outside source (state or otherwise). Much has been written of late about the evaluation, rationalization and quality of health care (Hafferty & Light, 1995; Mossé, 1998; Setbon, 2000; Robelet, 2001). The concern for the quality of health care delivery has lately been informed by recognition of the heterogeneity of medical practice and, in particular, of significant inter-hospital and inter-regional variations in clinical decisions. As Robelet (2001) has noted, the heterogeneity of medical practices becomes a problem for administrators and practitioners when it is construed as an indicator of sub-standard performance in terms of both economics and the overall goal of ensuring the temporal and geographic continuity of medical care. According to Robelet (1999), the application of systems of quality management signals a profound transformation in the mode of regulation of medical practice, namely the decline of professional self-regulation and the rise of industrial modes of regulation.

No one would deny that medicine faces "external" interventions that are experienced by doctors as a loss of power. We would suggest, however, that these interventions are made possible by the development of a number of endogenous regulatory practices that, taken together, make up what we have termed regulatory objectivity and that are inextricably linked to the development of modern biomedicine. This claim does not amount to yet another attempt to separate the wheat of medicine and science from the chaff of politics and society. Rather, we seek to delineate the mutually constitutive roles politics and medicine play in producing both medical and social practices.

Tools like medical records make hospital work possible, but simultaneously facilitate and foster administrative or judicial audits (Berg, 1996; Howell, 1995). Any biomedical action including those undertaken by a solitary practitioner presupposes the existence of a range of conventions concerning the entities (bacteria, viruses, antibodies, genetic mutations, etc.) at work in pathological processes. These entities define the types of events that must be taken into consideration when diagnostic and prognostic routines are deployed, whether individually or collectively. Therapeutic interventions in turn presuppose an equally wide range of conventions with regards to pharmacological substances. These myriad interlocking conventions create the conditions for a clinical objectivity that relies on the existence of entities produced and maintained far outside the intimate encounter between doctor and patient (Bourret, 2005). Regulatory objectivity thus aligns the clinic with other socio-technical domains and links clinical questions with those of public health (Berlivet, 1999) in novel ways that break down the porous barriers between medical and political institutions and give rise to hybrid initiatives. In this respect regulatory objectivity operates on a different plane and in a different mode from those suggested by analysts who treat all regulation as a form of rationalization imposed upon medicine from without.

Endnotes

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[i] http://nihroadmap.nih.gov/clinicalresearch/index.asp (last access: December 2004).

[ii] Our example concerns the clinical practice known as immunophenotyping. The remarks made there are equally applicable to more recent practices, such as the use of molecular probes and microarrays (Keating & Cambrosio, 2004b).

[iii] Attempts to harmonize international regulations in the in-vitro diagnostic field have revealed interesting differences between United States and Europe. The US tends to accept as inevitable the differences between methods and American regulators limit themselves to efforts to create conventions to compensate for differences. The Europeans, however, insist that it is better to undertake a search for “analytical truth” which can be achieved through the use of reference substances and the establishment of a chain of traceability linking the samples on which measures are taken (Powers, 2000).

[iv] Unlike the standardization of the Wassermann test analyzed by Fleck in the 1930s, present-day tests no longer require a “thought collective”; it is sufficient to have a consensus group. The difference between the two resides in the fact that the latter arrives at a consensus in a self-conscious and explicit manner. In this regard, we can consider the standardization of the Wasserman test as part of the beginnings of regulatory objectivity.

[v] Berg, Horstman, Plass, & van Heusden (2000) have already drawn connections between medical practices and different types of objectivity but have, despite considerable intuition and insight, restricted themselves to the somewhat marginal case of insurance medicine. We treat the question as fundamental to the development of biomedicine as a whole.

[vi] See, for example, the plans set out in Collins, Green, Guttmacher & Guyer (2003).

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