CHAPITRE 6. LEGAL ASPECTS OF THE RISKS RAISED BY NANOTECHNOLOGIES IN THE FIELD OF MEDICINE

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CHAPITRE 6 : LEGAL ASPECTS OF THE RISKS RAISED BY NANOTECHNOLOGIES IN THE FIELD OF MEDICINE

Because "everything within us dances to the choreography of molecular mechanics"[1], understanding and mastering these mechanics is of fundamental importance in medicine. Nanotechnologies are the tools which allow us to see and act on this scale. They open up such prodigious new possibilities that if 'earth-shaking' events are expected in some fields of human activity, it is 'miracles[1] which are forecast in the medical field. It follows that nanotechnologies are in the course of revolutionizing not only the conditions of medical practice but also the very basis of the patient-doctor relationship by allowing a more pro-active and more individualised preventive medicine, built around the specific characteristics of each person.

All fields of medical activity are concerned. First of all the detection and identification of diseases, with quicker, more reliable, more accurate in vitro and in vivo diagnostic technologies, using for example nanochips or quantum dots; then the effectiveness of the treatment itself will be considerably reinforced by targeted drug delivery or the activation of nanoparticles at a distance; finally, alleviating disabilities or repairing organs and tissues will be improved through the use of newly-perfected, stronger and better tolerated materials, implanted biosensors, or even prosthetic human-machine interfaces… Seeing more clearly and detecting earlier, offering better treatment and healing more surely, and this, while reducing doses of medicine, therapeutic intolerance and patient discomfort, not to mention the costs of treatment and tests, this is the progress announced in the medical world some of which has already taken place. Research is progressing rapidly, supported by considerable financial investment and encouraged by public health policy confronted with population ageing and the inexorable rise of health costs.

The advantages of nanotechnology are thus undeniable. What is at stake henceforth is that the future of these developments should not be clouded by doubts about their harmless properties and reticence born of fragmentary knowledge about environmental or health impacts and by the absence of reliable data on their life cycle. Correspondingly, in counterpoint to the hopes raised by the new diagnostic and therapeutic possibilities, the practical introduction of

[1] Ted Sargent, The danse of molecules, Viking Canada, 2005 (trad. française, Bienvenue dans le nanomonde. Comment les nanotechnologies vont transformer notre vie, Dunod Paris 2006, p.29)

nanotechnologies in the health field has also occasioned a certain number of fears of varied kinds. Some of these fears concern directly the nanoparticles used in medicinal products or in medical devices whose harmless properties are yet to be proved, particularly in the long term. Beyond these questionings on the risks of damage to health, the size and probability of which have not been measured today, other preoccupations have appeared, more diffuse but just as certain, relating to the possible excesses or breaches of ethical code in the use itself of nanotechnologies.

No jurist can remain indifferent to these new tools of 'active life'[2] which may affect the social system and test the suitability and efficiency of current rulings. In this respect, more than in other fields no doubt, legal safeguards exist in the medical field, principles, rules and procedures, intended to guarantee the rights of patients, and which consist of explicit obligations for medical practitioners. These rights which proceed from the fundamental principle of respect for human dignity, structure medical relations founded for centuries on the famous Hippocratic injunction: "*primum non nocere, deinde curare*" ("*first do no harm, then restore to health").* These two precepts should help guide the answer to the dual challenge that the nanotechnologies present to the medical world through the toxic potential of nanoparticles on the one hand (I) and possible excesses in their use on the other (II).

I. THE UNCERTAINTY SURROUNDING THE TOXIC POTENTIAL OF NANO-OBJECTS FOR HEALTH : "PRIMUM NON NOCERE"

Nanoproducts are already out of the university laboratories and some have arrived on the market in the form of cosmetics or medicinal products[3]. Now, several environmental toxicology studies have demonstrated their dangers for animals[4] which has led to the questioning of their use in humans in the context of clinical trials or as a support for diagnosis or treatment[5].

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[2] Cf Hannah Arendt, The Human Condition, 1958.

[3] According to the inventory of Woodrow Wilson International Center for Scolars, more than 800 nanotechnology-based consumer products are currently on the market, in particular several healthcare products and cosmetics, http//www.nanotechnproject.org/inventories/.

[4] French Agency for Environmental and Occupational Health Safety (Agence Française de Sécurité Sanitaire de l'Environnement et du Travail (AFSSET)), Nanomaterials. Effects on the Environment and Human Health, 2006; Comité de la Prévention et de la Précaution, MEDD, Nanotechnologies, nanoparticules: quels dangers, quels risques, 2006; Institut de Recherche Robert-Sauvé en santé et en sécurité du travail, Health effects of nanoparticles, 2nd edition, Montreal, 2008; COM (2008) 366 final, Regulatory aspects of nanomaterials, 2008.

[5] Especially, European Medicines Agency (EMEA), Reflection paper on nanotechnology-based medicinal products for human use, June 2006; European Group on Ethics in Science and New Technologies to the European Commission (EGE), Opinion on the ethical aspects of nanomedicine, n°21, 17 january 2007.

This awareness of nanorisk presents a problem for jurists. To cope with such a risk, will it be enough to apply the existing regulatory framework or should we, in consideration of the specific properties of nanometric particles, develop new "nano-laws" as some already insist[6]?

In the present state of our knowledge in these matters, European and national authorities commonly accept that the current legal arsenal is sufficiently well armed to handle the risks of nanomaterials, in all relevant fields and even more so in medicine. The choice made, quite explicitly, in terms of a legal framework for nanotechnologies, has not been that of ad hoc regulation – which in any case would have required a time delay which would not allow the rapid development of the sector – but rather that of a progressive and flexible adaptation of the texts in force.

This pragmatic approach should lead to change, on the one hand, through the reinforcement of the legal corpus applying to research and medical activities and, on the other, through an immediate wider reflection on the suitability of damage compensation schemes which might arise from it.

A. The necessary reinforcement of the regulatory framework

The uncertainty surrounding nanotechnologies, like the importance of the dangers they entail, demands a precautionary approach which henceforth inspires all decisions and public arbitrations, but which remains familiar for health matters. To achieve the right measure in this context (optimising what is good and minimising harm), precise and rigorous rules for evaluating and managing risk have been long ago developped, and these rules, when faced with new technologies, must simply be fine-tuned.

1. Uncertainty, an inherent characteristic of the medical approach

Weighing up risks and comparing advantages, before starting treatment or undertaking surgery, are part and parcel of the daily life of a medical practitioner and at the same time the very essence of his practice. From its origins, medicine was founded on this comparison as soon as one higher reason alone could justify the *noli me tangere*. This reason is not built on certainty

[6] Cf J. Clarence Davies, Managing the effects of nanotechnology, 13 janvier 2006, Woodrow Wilson Center on Emerging Nnaotechnologies, 2006, in line.

but on the conviction, supported by confirmed knowledge or acquired experience, that the operative treatment on the body of another person, the intrusion upon his integrity, will have more beneficial effects than abstention. The art of permanently balancing benefits and risks, which concerns just as much medicinal products as a medical act itself, is, in the last analysis, none other than the precautionary principle forever inscribed in the art of medicine, which allows to intervene even in uncertain situations. It is a principle which imposes the consideration of hypothetical risk, unproven or non-authenticated risk, whose realisation could involve serious and irreversible consequences. Far from being a brake on innovation, the precautionary principle must signify a flexible approach through the adoption of proportionate and provisional measures which are revised in accordance with the development of our knowledge of risk. In the nanotechnologies and nanosciences of today it finds a privileged field of application[7].

Taking uncertainty into account, which has henceforth become a paradigm of the nano approach, is consubstantial to medical activity. The practice has always been an ontological given with which medical professionals must come to terms and which they integrate into each decision. It determines a certain number of binding ethical rules, enshrined in various European documents, which effectively constitute patient rights[8] : right to suitable treatment or to tests based on the supposition that the risks involved are not disproportionate to the expected benefits, right to a quality of treatment, right to safe medicinal products and safety in the medical acts themselves. It is precisely this permanent coexistence with risk, even potential risk, which has led in medical matters to the submission of health products to particularly exacting and rigorous rules and technical norms, and moreover, to making the patient's free and informed consent one of the pillars of medical relations. It follows that as soon as the patient agrees to undergo tests, treatment or operative treatment which inevitably include a certain element of danger, he or she should be informed and give consent in full knowledge of the risk involved. For these two reasons, the regulations which are currently applied to medicine appear well designed to face up to the hazards brought by nanotechnologies, with the reserve nevertheless that some of their applications must be adapted with the greatest of vigilance.

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[7] Commission Recommendation, 07/02/2008, Code of Conduct for Responsible Nanosciences and Nanotechnologies Research, C(2008) 424 final, COM(2008) 366 final; AFSSET, préc.; National Consultative Ethics Committee for Health and Life Sciences (Comité Consultatif National d'Ethique), Opinion n°96, Ethical questions raised by nanosciences, nanotechnologies and health, 27/03/2007, p.18; Haut Conseil de la Santé Publique, Avis relatif à la sécurité des travailleurs lors de l'exposition aux nanotubes de carbone, 07/01/09.

[8] Cf in particular, Convention for the protection of Human Rights and dignity of the human being with regard to the application of biology and medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.4.1997; European Charter of Patients' Rights, Rome, November 2002; Opinion of the European Economic and Social Committee on Patients'rights, (2008/C 10/18), 15/01/2008.

2. Limited adaptations of existing regulations

At present, nano-objects are not conceived as such by the law, as a specific legal category, but only through the legislation relating to the manufactured products which incorporate them[9]. Consequently in the field of health, the evaluation of their potential hazards is measured against current rules established for medicinal products or medical devices. In this context, the medical world's long experience with risk is expressed by the systematic application of regulations and well-tried methodologies which guarantee a high level of safety. To be placed on the market, health products must first undergo precise and exacting procedures strictly defined by the regulations, destined not only to guarantee their efficacy but also their quality and inocuity. The right to sell medicinal products is thus subordinated to a compulsory authorisation granted by competent European or national health authorities, which rely on international principles and standards and involve far reaching preclinical and clinical trials. The marketing authorization is refused in particular when it appears that the assessment of the therapeutic benefit-harm-risk profile is unfavourable, given the risks to the health of the patient or of the public, or when the therapeutic effect claimed by the applicant is either absent or unproved. This authorisation may always be modified or withdrawn if the original criteria are no longer respected or if some new risks are identified. These safeguard procedures as a whole come with a systematic obligation imposed on the manufacturer to inform and offer traceability, notably by means of package leaflets and by labelling, and by the introduction of a detailed risk management system and a system of pharmacovigilance.

Thus in the state of the present development of nanomedicine, this regulatory framework is considered appropriate at both European and national levels. The same holds true for the different regulations applying to medical devices, which also include before any marketing the demonstration of their conformity to the essential requirements of safety for patients and, a posteriori, follow up reporting activities and materiovigilance. Moreover, it is upon these rigorous foundations that some health products have already been placed on the market. There is also at present a consensus that it is not necessary to put dedicated regulatory structures into place for nanotechnologies, the existing authorities possessing the necessary skills, policing powers and expertise to handle most eventualities[10].

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[9] Communication, Commission of the European Communities, Regulatory aspects of nanomaterials, COM (2008) 366 finals, 17.6.2008.

[10] Cf. EGE, Opinion n°21, Ethical aspects of nanomedicine, 17/01/2007, 5.5.1. General issues: "The Group does not propose new broad regulatory structures that specifically deal with nanomedicine at this point. Changes should primarily be made within existing structures".

The refusal to single out nanoparticles for particular treatment must not be allowed, however, to prevent consideration of all as yet little known or unknown matters. In this respect, there is a consensus about the need to conduct not only further research into the toxicity and ecotoxicity of nanoparticles but also to adapt or even modify existing regulations[11] in relation to the uncertainty surrounding a number of effects and the long term development of nanoparticles. The current procedures, methods and protective measures must be reinforced under the control of the authorities in charge. It is thus a question of anticipating, in the name of the precautionary principle, a possible breach of the regulatory framework concerning either safety requirements or the respect of patient rights.

First, regarding to the **evaluation procedures undertaken before placing medicinal products and medical devices on the market**, a distinction must be made between soluble nanoparticles and/or biodegradables (in the form of liposomes, nanoemulsions...) and insoluble nanoparticles and/or biopersistants (fullerenes, carbon nanotubes quantum dots…). For the first of these, conventional risk assessment methodologies would seem to suffice and medicinal products in this form, moreover, have already been allowed on the market under the existing regulatory framework. By contrast, for the second, other parameters and supplementary analyses are necessary, taking into account the specific properties of nanomaterials. It is a fact that we still have a limited knowledge of the metabolism of medicines in the form of nanoparticles, of the conditions of their excretion, their capacity to translocate, their incidence at the immunological or genotoxic level, or of their carcinogenic potential in particular in the long term[12]. The biopersistance potential of anorganic compounds, given their capacity to cause a dangerous build up in the body, must be studied extensively in animals before any human application. The priority, therefore, must be to pursue research in order to adapt tests and if necessary, to update certain authorisations which have already been granted. In this respect, the National Academy of Medicine recommends that "*during the authorisation of nanomedicinal*

[11] The French Health Products Safety Agency (Agence Française de Sécurité Sanitaire des produits de Santé, AFSSAPS) underlines that if the evaluation of potential hazards related to nanomedicinal products must be conducted in accordance with the existing pharmaceutical legislation, "however, the methods of this evaluation must be adapted when necessary and the results must be expressed in relation with the particular characteristics of the nanoparticle structure", Recommendations for toxicological evaluation of nanoparticle medicinal products, septembre 2008, p.2 et p.7.

[12] The evaluation of this potential is debated: on the one hand, "it is clear that (...) NMPs could induce tumours, especially lung tumours. On the other hand, (...) carcinogenesis studies do not appear to be necessary in view of the current applicatios of NMPs (single dose in medicinal imaging, vectorization of anti-cancer drug)", AFSSAPS, p.8.

product marketing, an already authorised active principle must be considered as entirely new, susceptible to be of a different toxicity, if it is transported by a 'cargo ship' of a different kind"[13].

To conclude on this point, the evaluation of the toxicity of nanotechnologybased health products may be included without difficulty in the existing legislative framework; however, each time it is necessary, the methods for characterising the products, or of evaluating their quality or their safety, the norms and technical documents upon which the regulations and authorizations are founded, must be fine-tuned or reviewed, according to the characteristics and singular properties of each nanoparticle[14].

The next stage should be that of building nano-products as singular legal objects and, therefore, the elaboration of nano-regulations. This will come to pass notably through the development of normalisation – the first step of which has recently been made by the agreed use of terminology and precise definitions for nanoparticles[15]– but also through the possible creation of new legal categories. Indeed, nanotechnology allows to create innovative products, on the boundaries between of medicinal products and medical devices. If science finds this state of affairs acceptable, the law must insist on precise terminology in order to apply the corresponding regulations. Thus, in time, the complexification of nano-objects for health combining the action of mechanical, chemical and pharmacological properties and associating diagnostic and therapeutic functions, should lead either to amend the definition of medicinal product or to devise new classifications and, more hypothetically, to reconsider the regulatory framework[16]. Already certain procedures for testing, clinical trials, and surveillance have been reinforced for advanced therapy medicinal products[17].

In parallel to this construction of nano-products as legal objects,development should finally lead to a **reinforcement of the guarantees and protection offered to people in the context of medical relations and biomedical research.** Obtaining the free consent of a well-

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[13] Report Nanosciences et Medicine, December 2008, en ligne; see also, AFSSAPS, id. "In addition to the specific toxicity of the vectorized active principle, the structure in which it is contained could also considerably modify this toxicity. Consequently, it would often be preferable to consider the NMP as a distinct entity that needs to be evaluated as a largely new "total" drug substance", p.2.

[14] Nanotechnology-A report of the US FDA Nanotechnolgy Task Force, 25 july 2007; EMEA, Committee for medicinal products for human use, Reflection paper on nanotechnolgy-based medicinal products for human use, june 2006; AFSSAPS, fore-mentioned recommendations.

[15] ISO/TS 27687:2008, Nanotechnologies-Terminology and definitions for nano-objets, nanoparticle, nanofibre and nanoplate.

[16] As proves the Regulation (EC) n°1394/2007 of the European Parliament and of the Council, on advanced therapy medicinal products, 13 november 2007, which had to qualify and regulate the overlap between legal categories, JOUE 10 déc. 2007, p.121. This text is a lex specialis in relation to the directive 2001/83/CE.

[17] The Regulation n°1394-2007 which applies particularly to tissue engineered products, lays down specific additional rules for the authorization, monitoring and pharmacovigilance. In this way, a wide range of products is placed under an adapted and reinforced regime, for both the marketing authorization, traceability, patient follow-up and risk management. Many of these products are or will be from the nanotechnologies.

informed patient is indispensable and this after a faithful, clear and appropriate information. To be more specific, this obligation must be seen in particular terms, with regard to both the sheer size of what it is we have to learn and to the rate of acceleration of research in this field. In such a context, the European Group on Ethics raised the following questions : *"consent may not be too difficult to obtain -but when is it informed? And when is it free? Informed consent requires the information to be understood. How is it possible to give information about future research possibilities in a rapidly developing research area and to make a realistic risk assessment in view of many unknowns and the complexities?*"[18]. In the context of biomedical research, patient associations have consequently urged that the requirement of free consent should be strengthened by the granting of additional time for reflection and by the provision of accurate information on the degree of uncertainty concerning risks, to be made if necessary in the presence of a third party. In the same way, it is proposed that personal protection should be reinforced, notably by subordinating research to a specific authorisation from a competent health authority[19]. Beyond the observance of these procedural obligations, it is also paramount to ensure that ethical principles of research are well respected. But here too, the existing procedures will have to adapt to the singularity of the research involving nanotechnology: one the hand, the authorities and the committees charged with surveillance are not necessarily aware of the specific questions that it raises, and, on the other, the requirement that *"foreseeable risks*" for the participants *"are not be disproportionate to the potential benefits of the research*"[20] supposes that one is capable of evaluating risks… which the latest state of scientific knowledge does not allow.

It is thus not certain, as is denounced with increasing frequency, that the simple adaptation of current legislation will suffice to anticipate all the risks for the safety of patients, or to guarantee the preservation of free and truly informed consent, the pillar of research and medical relations. The same uncertainty weighs on the appropriateness of a posteriori event risk management systems, that is to say compensation systems for possible claims of damage.

[18] EGE, Opinion on the ethical aspects of nanomedicine, n°21, 17 january 2007, p.40.
[19] D.Thouvenin, in Nanomédecine: enjeux et pilotage, "Il me semble judicieux, pour ce type de recherches impliquant les nanotechnologies, d'appliquer les règles spécifiques du code de la santé publique à propos de la greffe et de la thérapie génique. Ce sont des domaines pour lesquels un avis d'expert est nécessaire et une autorisation expresse de l'AFSSAPS indispensable", en ligne.
[20] Oviedo, Convention on Human Rights and Biomedicine, art.16.

B. Creation of a new scheme for compensation of damages

Compensation systems on which tort suits could be made, in case of personal damage, are logically those which concern medicinal products and medical devices from production until post approval follow-up studies. Different claim scenarios could be envisaged: against the public health authorities for having delivered a marketing authorisation[21], against a sponsor of clinical trials[22], or against the producer of an incriminated health product[23]. However, none of these claims could cover damages whose cause could not be known at the moment of the trial, the therapy or the product marketing. Thus the risk/benefit balance, precondition to the grant of marketing authorization, could only include known risks, whether proven or potential, which are sufficiently well documented and judged plausible by the scientific community. In the case of hypothetical or unknown risks, the only obligations incumbent on public authorities in uncertain situations, in the name of the precautionary principle, are to keep themselves informed of the dangers, to pursue research and to take all necessary measures according to the discoveries made; as for professionals and health industrialists, they are required to introduce a rigorous system of product traceability and of vigilance. In this field, in France, the health scandals of recent decades have furnished lessons which have been learnt and public authorities, like the health industry itself, appear to be trying to anticipate any challenge by multiplying research programmes and protection measures for employees.

But beyond this field, uncertainty is so great, knowledge so sketchy, and damages will have such a hidden latency that if the nanoparticles were to prove health hazards, none of the legal systems in force today would allow the victims to obtain compensation through an incapacity to establish even the conditions of civil liability. First, it would be impossible for plaintiffs to invoke insufficient information, the condition of free and informed consent. Whether it is presented to participants in clinical trials, or to patients, information can only pertain to "foreseeable risks"[24]. Now, with nanotechnology, today it is not so much the frequency of supposed hazard which presents a problem as their very existence: only those risks which are known in the current state of planetary scientific knowledge and so identified by the

[21] Fault liability, for failure or deficiency.
[22] Presumed-fault liability, L.1121-10 CSP.
[23] Strict-liability, no fault liability: Council Directive 85/374/CEE, 25 july 1985 on the approximation of the laws, regulations and administrative provisions of the Members States concerning liability for defective products (transposée par la loi du 19 mai 1998, relative à la responsabilité du fait des produits défectueux, art.1386-1 et s. Code civil).
[24] Directive 2001/20/CE, 4 april 2001, on the approximation of the laws, regulations and administration provisions of the Members States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

medical community can constitute the basis of prospective risk information and for the moment all those implied by nano health objects have not been discovered.

Hoping to demonstrate the liability of the pharmaceutical manufacturers is unlikely to be more effective. In accordance with European and national laws, in most Member States, the producers can, in fact, escape liability through invoking the "development risk exemption"[25] which appears for the moment, in the light of our own knowledge, to be inseparable from the nano issue. Above all, even in the absence of a liability exoneration, torts suits which are based on the current use of nanotechnology will probably not succeed: the very characteristics of nanoelements (high reactivity and diffusivity, non-seizability…) just as much as ignorance concerning their long-term behaviour, should make it very difficult or even impossible to impute liability to one single person in charge or to prove specific causation. Indeed, it is generally a tricky matter to demonstrate that a health product is the principal cause of harm; nanoparticle forms can only intensify this state of affairs. Quite apart from the fact that many risks and potential effects are yet to be evaluated, not to say for many of them identified, it is difficult to see how the current legal rules could be applied in a context where elementary data are lacking (concerning bioaccumulation characteristics or the recombination of nanoparticles according to each patient's metabolism, concerning their life cycles and thus their biological fate…). Moreover, indirect exposure of victims to other nanoparticles present in the environment, by dispersion or release, should further dilute the relation between the damage and the nanoelement or medical device.

It is no doubt necessary here to change perspective. The use of nanoparticles and nanomaterials, from the moment that uncertainty remains concerning their toxicity, currently stands outside the control of traditional mechanisms for assessing civil liability. Starting from this point, the development of new aspects of "active life" must be accompanied at each instant by responsible and ethical consideration as the Commission's February 2008 *Code of Conduct* recommends[26]. More than ever before, the progressive and active dynamic spirit which motivates researchers and businesses must be inspired by one of the most essential dianoetic virtues, that is to say in Aristotelian terms: phronesis, "prudence" or "practical wisdom"[27].

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[25] Directive 85/374/CEE, art.7: "The producer shall be liable as a result of this directive if he proves:...(e) that the state of scientific and technical knowledge, at the time when he put the product into circulation, was not such as to enable the existence of the defect to be discovered;...".

[26] COM (2008) 424 final, Recommandation of 07/02/2008, on a Code of conduct for responsible nanosciences and nanotechnologies research.

[27] Ethique à Nicomaque, especially Livre VI, Ch.V. Cf see also, P. Ricoeur, Le concept de responsabilité. Essai d'analyse sémantique, Le Juste, Ed. Esprit, 1995, p.61 et s. In this respect, one of the first responsabilities of industry, scientists and public authorities is to promote research to improve knowledge on toxicological effects of nanoproducts and develop biodegradable products, therefore less aggressive to human health and environment.

In this way, all the excesses and transgressions in the use of nanotechnology could be anticipated. But to go further, recalling their mission and the very foundations of medicine to its practitioners should guide them as it guides health officials each time they are confronted with new usages made possible by nanotechnologies which lead them away from the path of fundamental principle. For if the potential is immense, so too is the risk of misuses.

II. WORRIES ABOUT POSSIBLE MISUSES OF NANOMEDICINE: "...DEINDE CURARE (THEN RESTORE TO HEALTH)"

It is no longer a question here of the nano object as a source of worry, but of the power and knowledge it gives its users. In this respect, the ethical and legal questionings of the intended aims in resorting to nanotechnologies are similar to those raised not long ago by biotechnologies. Predictions of a convergence in the information and cognitive sciences have reinforced fears surrounding those technologies which permit the manipulation of elemental bricks of matter. It has reached a point where some begin to see the Four Horsemen of the Apocalypse, the premise of total destruction of human identity if not of the race itself.

The reaffirmation of certain fundamental principles alone, presented at an international and national level as indispensable first steps, must serve to prevent all misuse of nanotechnologies. Their common basis is the principle of the human dignity. In this respect too, the art and practice of medicine has always been guided by the other part of the Hippocratic precept, which gives a guiding path in the confused maze created by the explosion of technological possibilities: "deinde curare". This evocation of the ultimate aim of medical care, which is at the heart of ethical duty even before being set down in law, to heal the mind and the body, is one of the sturdiest guarantees when confronted with the variety of temptations to misuse technological innovations.

A. The threats to private life and individual liberties

The risks that the current use of nanotechnologies present for the protection of fundamental rights and individual liberties are not new, since it is these kinds of risk which generally derive from the excesses or abuses of technical possibilities. The tools and devices concerned, such as diagnostic tests or RFID for example, even before being subject to debate

relating to nanotechnology, had already been the object of ethical questioning and given regulations. But the new potential that extreme miniaturisation offers has led to doubts about the appropriateness of this existing regulatory framework.

1. New diagnostic tools

Nanotechnologies have already transformed genetic and biological methodologies of analysis. The nanoscale devices can produce reliable and extremely accurate results both cheaply and rapidly through the examination of certain molecular markers. Thanks to these enhanced possibilities, the early diagnosis of undeclared diseases or simple predispositions and the access to genetic information are greatly facilitated. Biochips and biocaptors thus open the way to a decidedly more preventive and individually tailored medicine, defined on the basis of the features of each patient. These new possibilities have raised a certain number of questions and debate little of which is new or original as the same questioning was already expressed more generally about genetic testings. Their use is thus already established within a known legal framework, defined by the Universal Declaration on the Human Genome and Human Rights[28], the European Convention for the Protection of Human Rights and Fundamental Freedoms[29], the Oviedo Convention and its additional protocol of 27th November 2008[30]. The principles are reiterated in French law[31]. This precise and protective framework, elaborated for predictive genetic testings, can be applied without difficulty to techniques and devices developed for nanotechnologies. The regulations in themselves raise no problem which has not already received attention, whether it concerns the content of the information to be provided, the legitimacy of the use of these testings for disorders for which there exists neither treatment nor prevention, or the right of the patient to know or not to know.

Only the multiplication of predictive testings could present a problem as they have become more precise, quicker and easier to use. In practice, when the introduction of such tests has become current usage, we will be able to establish individual biological ID cards, at the risk of limiting the definition of human beings "*to the universe of their genetic or biochemical parameters*" as the CCNE underlines. Nevertheless, in medicine more than elsewhere,

[28] UNESCO, 11 november 1997, ONU 9 december 1998.
[29] European Convention on human Rights, Rome, 4 november 1950.
[30] Additional Protocol, concerning Genetic Testing for Health Purposes.
[31] Civil Code, art. 16-1 et 16-10: principles of respect for individual autonomy and integrity of the human body, requirement for express, informed and free consent, non discrimination based on genetic features, strict definition of the purposes of the genetic testing...

guarantees have been provided for patients. In the first place, the purposes of genetic tests are specified by law, which forbids doctors from prescribing testings which do not have a medical aim or a clinical utility[32]; secondly, tests must be carried out under the control of regulations and measures designed to protect the confidentiality of the personal data obtained. Finally, the divulgation of any information obtained in this context, notably to the profit of insurance companies or employers, is subject to penal sanction. The risks of going too far or misuse appear under control.

But, beyond these risks which are correctly understood by the law, the development of improved tools at the service of preventive and predictive medicine is in the course of modifying the very terms of the medical relation and the individual's attitudes to illness. Indeed, patients who are henceforth made aware of pathologies to come and to avoid, are by the same process confronted with their potential vulnerability and their responsibility, from the point of view of their own health and with regards that of society. Nationwide preventive campaigns could thus be organised based on the results; one can even imagine that uncooperative individuals, either because they are opposed to tests or because they refuse to adapt their behaviour to their genetic profile, might be financially sanctioned. Significant economies could thus be achieved but only to the detriment of respect for liberty and private life.

The same worries about making the control of the individual and of society much easier are expressed over the dazzling progress in identification techniques.

2. Nanotechnologies at the service of ubiquitous medical monitoring

The digitalisation of society is gathering pace and the majority of its procedures are in contradiction with respect for private life and individual liberties. Even more, the convergence of nanotechnologies and ICT promises increasingly powerful tools for monitoring and surveillance which are cheaper and, more especially, undetectable.

Currently, RFID has been the cause of the most controversy[33]. Indeed the miniaturisation of electronic components and the increase of storage capacities have transformed these devices

[32] Additional Protocol concerning Genetic Testing for Health Purposes, art.6: "Clinical utility of a genetic test shall be an essential criterion for deciding to offer this tests to a person or a group of persons". Art.16-10, Civil Code: "An examination of the genetic particulars of person may be undertaken only for medical purposes or in the interest of scientific reseach".

[33] About the RFID technology and its regulatory framework, Article 29 Data Protection Working Party, Working document on data protection issues related to RFID technology, january 19, 2005; EGE, Ethical aspects of ICT implants in the human body, Opinion n°20, 16 march 2005.

into highly efficient auxiliaries in patient monitoring but at the risk of undermining one of the bases of medical relations, the guarantee of secrecy. The systems which are challenged are more or less sophisticated and so the ethical problems are of uneven intensity. These devices can serve to identify the carriers, store information, or even contain a localisation function. All of them offer many interesting characteristics for health care: rapid and easy access to patient database files, increased safety in case of emergency, a reduction of medical error risks and surveillance of vulnerable patients such as handicapped children or those suffering from Alzheimer's disease. Experiments are currently underway in the United States.

From all these points of view, their use appears legitimate. Already, RFID patchs and implanted radio-tags can transmit the health bulletin of a patient from a distance[34]. But in parallel, these same techniques carry risks, perhaps for health and certainly for liberty, respect of private life and the confidentiality of personal medical data. Excluding those non invasive devices which are worn or carried, such as biomedical clothes, "smart" bracelets or 'exo captors', vigilance is of critical importance with regards the ICT implants whose size makes them almost invisible. The use of these miniaturised chips for health matters renews the ethical debate which they raise generally: it is in fact easy to pass from simple role of localisation or identification to the surveillance and systematic profiling of individuals. With nanometric size devices, traceability becomes invisible and permanent[35] and the protection of personal data is hazardous, aleatory. We rediscover here the three most tormented questions expressed by the CCNE in its opinion on biometrics : "*that of identity control sliding into the uncharted waters of data interconnection and its accumulation while the people involved remain unaware*"[36].

This technology, however, has not developed within a "legal wasteland". Quite the contrary, different international and European texts, and several national legislations, define the framework of its use under the simultaneous control of independent regulatory authorities and that of justice. Thus the European Charter of Fundamental Rights, following the directive 95/46/EC[37], has recognised as a fundamental right the protection of personal data. In France, the CNIL (Commission nationale de l'informatique et des libertés) has insisted that RFID technologies should submit to the stipulations of the 'loi Informatique et Libertés'[38]. But aware

[34] In 2004, the FDA approved the Verichip, an implantable RFID chip, used to facilitate medical record access in case of emergency, which is implanted in the subcutaneous tissue, in the triceps area.
[35] See Stéphanie Lacour, Ubiquitous computing et Droit: l'exemple de la radio-identification, in La sécurité de l'individu numérisé, L'Harmattan, 2009.
[36] CCNE, Opinion n°98, Biometrics, identifying data and human rights, 1997.
[37] Directive on the protection of individuals with regard to processing of persona data and on the free movement of such data, 24 october 1995.
[38] Loi n°78/17 du 6 janvier 1978 relative à l'informatique, aux fichiers et aux libertés (modifiée par la loi n°2004-801 du 6 août 2004).

of the deficiencies of the text in the face of the threats that nanotechnologies represent[39], the Commission has announced a variety of measures to reinforce the protection of the carriers of these miniaturised chips[40]. Moreover, a number of principles designed to limit the use of subcutaneous implants can be applied here, legal principles henceforth integrated in the civil code and based on respect for human dignity. One of them, the principle of respect for the inviolability and physical integrity of the human body expressly forbids any invasion which is not justified by medical necessity[41]. The EGE (European Group on Ethics) also mentions the principles of proportionality and of suitability which should guarantee that the implants are only used if they are really necessary.

The drafting of specific legislation is thus not indispensable. However, to remain effective and guarantee these principles, the techniques for controlling such activities must follow the progress of miniaturisation. The same vigilance is necessary with regard to implants or prostheses designed to remedy dysfunction or handicaps.

B. From handicap compensation to the improvement of human capacities

A physician, since Hammurabi (1728 B.C.), Hippocrates (460 B.C.), Galen (131B.C.), is the person who treats present or imminent illness even if he does not always manage to find a cure or prevent it. From this point, his behaviour is governed by this single finality which inspires his code of ethics and which, according to the law, is the only legitimate justification of his action upon the body of another. His mission must also be carried out for the service of all without favour. The reaffirmation of these essential aspects must lie behind the response to the ethical, legal and political challenges that nanotechnology presents, notably by the promise of a "post humanity", reserved inevitably to the few.

[39] Activity reports 2006 and 2007, n°27, p.71 et n°28, p.27-28.
[40] Clear and accurate information on the use of chips and on the means for data subjects to access their content; deactivation at the request of people, secure data to prevent any fraudulent access. With regard to the medical file, systematic data encryption should limit any risk of disclosure.
[41] Article 16-3: "There may be no invasion of the integrity of the human body exept in case of medical necessity for the person or excpetionally in the therapeutic interest of others".

1. About a few speculations on the new possibilities of "repair"

Many ICT devices for implantation in the human body are already used, from pacemakers to cochlear implants, and many nanotechnology projects are underway such as the production of biocaptors, ocular implants or artificial retinas. One of the most promising fields of research is the creation of neuroprosthesis to replace damaged neuronal structures and cerebral implants designed to treat pain, the symptoms of depression or illnesses like Parkinson's disease. Soon, thanks to nanotechnology, it will be possible to repair certain functional deficiencies, to remedy a physical handicap or brain damage. These prodigious hopes do not excuse us from not mentioning the crucial controversies of our time, quite the contrary; debates about these new possibilities for healing the body and perhaps even one day, the mind…

First of all, the intrusion into the brain raises particular fears relating to the capacity of doctors to appreciate "normality" in the functions of the brain. Others cite doubts about the protection of information obtained through increasingly sophisticated techniques for decoding mental activity. Finally, possible manipulations of thoughts or emotions would constitute an infringement not only of physical integrity but also of the dignity of the individual. Without descending to the level of an Orwellian vision of a manipulated world, it is indispensable to remain vigilant[42]. The current regulatory framework cannot for the moment provide answers for unexplored situations which depend consequently on the codes of conduct and ethical responsibility of the research scientists.

It is to be feared next that these new tools, developed though considerable investment and protected by a variety of patents, deepen the already disturbing gaps, not only between the North and the South, but even within the developed nations, between those who can and those who can't obtain access. It is not certain that the burden of developing all these technologies, some of which are extremely costly, can be borne by medical insurance systems, which constitutes a threat to the equality of access to healthcare, a right which is recognised for all patients and one of the first duties of the doctor. The allocation of funding in this field cannot afford to ignore the debate on the *social relevance* of each product.

Finally, these new possibilities of restoring certain physical or mental functions by artefacts raises questions about the notion of handicap and improvement, about what is normal and what is different, about what is acceptable for a society and what is not. The criteria used, however, unless one considers health as a purely biological state of conformity and ignores the

[42] See EGE, Opinion n°20, 5.3 and 6.4.4.

psychological and social aspects, are subjective. The development of these new devices must not be allowed to create a mindset whereby a handicap is a dysfunction, an "abnormality" to be systematically removed, to the point of stigmatising those who carry such impaired characteristics or who refuse a proposed improvement. This fear has already been expressed by pressure groups militating for the defence of the rights of handicapped persons. The respect for the autonomy of each person, as it is guaranteed under the law in particular in medical relations, should prevent the emergence any larval eugenicist tendency. It is this sense that the EGE proposed to limit the use of ICT implants for enhancement in two cases : "*To bring children or adults into the "normal" range for the population (normal meaning the conditions that generally prevail and that are not caused by genetic malfunction, disease or deficiency and lacking observable abnormalities), if they so wish and give their informed consent"; "to improve health prospects*", such as enhancing the immune system to be resistant to HIV for example[43]. In this way, the EGE are also trying to draw a frontier between what is concerned by therapy and what falls into the category of improving human capacities and no longer belongs in principle to the field of medicine…

2. From repaired man to "enhanced" man

Beyond the field of medical care, the convergence of NBIC (Nanotechnology, Biotechnology, Information technology and Cognitive science) will offer men in good health the highly attractive possibility, for our overexcited societies, of improving his complete physical and intellectual prowess by tissue engineering or implantation of biochips. From the exclusively therapeutic purpose of repairing damaged functions, we will pass to the enhancement of naturally healthy functions. In itself the improvement of performance is not a priori to be condemned as long as its sole aim the fulfilment of the individual. This progress must not, by contrast, become a means for dominating others[44], nor a form of alienation. Now, the temptation could be great for individuals under pressure from economic necessity or patterns of social conformity or for businesses looking for the ideal worker, to heedlessly resort to devices whose long term risks by definition are unidentified. Nanotubes could be, amongst other things, "*a means of improving the functional organisation of neuronal networks, through*

[43] Id.
[44] Cf. H. Chneiweiss, Office parlementaire d'évaluation des choix scientifiques et technologiques, Exploration du cerveau, neurosciences: avancées scientifiques, enjeux éthiques, 26 march 2008, p.10 et s., in line.

acting upon the synapses or on DNA"[45]. But in that case who would determine such a use and upon what criteria? If such processes became common, what might happen to those who stubbornly resisted? Wouldn't today's state of health be in danger of turning into tomorrow's handicap?

The question of the social and ethical responsibilities as well as liability of those in charge of healthcare will (or would) be raised then. In fact, there is a fine line between treating a disease, compensating for a handicap and enhancing performance and this frontier can be discussed. Here again, it is the very basis of the art of medical practice, built upon the widely shared conception of what "the state of health" means, which should resist the use of an invasive technique capable of undermining the integrity of the human body in the absence of a recognised medical purpose.

Thus the regulatory framework in force is sufficient. Its principles are precise but it remains sufficiently flexible to adapt to current developments. The legislative reminder of medical necessity and the practitioner's respect for the principles of their medical ethics, the checks and balances that one or the other constitute, as well as the evocation of the principle of patient equality, would appear to offer resistance to any movement astray led by nanodevices in the simple name of an "increase"[46].

For all others matters, we know since Canguilhem, that the distinction between normal and pathological is relative and that each epoch produces its own specific normality. The limits which cannot be crossed in medicine are fixed by the rule of law but also by the medical ethical code itself, based on preserving or restoring health. The notions of health or of medical necessity, however, cannot be legally defined. They are the result of developing scientific, cultural, social, not to say, economic attitudes as the lengthy OMS definition of health demonstrates *"state of complete physical, mental and social well-being and not only consisting in the absence of illness or infirmity"*. Certainly today "*no doctor tries to create a new race of men, with a new position for the eyes or the limbs*" and "*would never promise anything to the sick other than a return of vital functions to a satisfactory stat*e"[47]. But tomorrow new possibilities given to mankind to combine the natural and the artificial, will no doubt lead to new forms of life, translating these rebellion of the *"future man"* mentioned by Hannah Arendt,

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[45] J. Monzée, Les enjeux des nanotechnologies appliquées aux nanosciences, in La nanomédecine. Enjeux éthiques, juridiques et normatifs, Dalloz, 2007, p.72.

[46] In the same manner, the EGE has precised the principles which must govern the implantation of ICT devices for health purposes, principles which govern every medical action: an important objective, "like saving lives, restoring health or improving the quality of life", the necessity of the implant to achieve this objective; and "no other less invasive and more cost-effective method of achieving the objective", .n°6.3.

[47] G. Canguilhem, The normal and the pathological, (Le normal et le pathologique, PUF, 1966, II, p.193-194).

"*against human existence as it has been given*", and "*which he wishes to exchange, as it were, for something he has made himself*"[48]…

It will, then, be the responsibility of the relevant national and international political authorities to find agreement over the kind of values that can rule in our globalised world. From this moment on, a dual admission is called for: to be effective, the regulatory framework of nanotechnology must remain flexible over its technical rules. But to find social acceptance at large, this framework must also be built on a sustainable basis, on principles and fundamental values whose definition, demands and protection depend, indisputably, on public debate then on democratic regulation.

Toulouse, Avril 2009.

[48] The Human Condition, p.35.