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Neonatal Screening of Cystic Fibrosis in France: a socio-material configuration of biomedical diagnosis and therapeutics

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Neonatal cystic fibrosis screening (CF NBS) has been a subject of debate in the majority of Western countries since the Crossley discovery of an early biological marker: immunoreactive trypsinogen (IRT). On the basis of criteria established by Wilson and Jungner in 1968, the incidence rate and gravity of this disease ranked it as a serious candidate for a global screening programme. Despite the advances in medicine that increased the life expectancy of CF patients, the absence of a curative treatment and the low specificity of the biological marker used in the diagnosis largely contributed in curbing the widespread use of this screening test. Reservations were finally overcome with new advances in both domains: with the introduction of systematic neonatal cystic fibrosis screening (CF NBS) instituted by the public health authorities since 2002, France became the first country in the world to adopt nationwide screening.

We will discuss (1) the birth of an expanded collaborative and interdisciplinary network of biomedical and therapeutic entities in the sense that the sector was structured *via* the systematic Neonatal Cystic Fibrosis Screening (CF NBS) programme instituted by the government since 2002, the creation of Resource and Expertise Centres for Cystic Fibrosis (CRCM) at national level, followed by the institutionalisation of a well-ordered global care offer covering the patient, the family and the social network. (2) The highly controversial principle of CF NBS; a tolerated waiving of the regulatory requirement for informed consent in disease screening, and contested in its utility¹.

¹ This paper is based on a research programme bringing together health professionals (doctors, nurses, geneticists, psychologists...), sociologists and statisticians. The study entitled 'Factors favouring or limiting the implementation of practice recommendations for CF diagnosis announcement following neonatal screening' (Facteurs favorisant ou limitant la mise en œuvre des recommandations d'annonce du diagnostic de la mucoviscidose suite à un dépistage neonatal), jointly financed by the association 'Vaincre La Mucoviscidose' and the 'Fondation de France', was launched in February 2008. It was conducted in two phases: 1. questionnaires in the 34 CRCM in France, 2. individual interviews and *focus group* sessions in 15 CRCM.

A socio-material perspective in technology, organization, and constitutive entanglement

For this presentation, we opted for a methodological standpoint centred on *socio-material configurations*. The last two decades have produced a number of particularly stimulating conceptual advances permitting the emergence of a sociological representation of technoscience: the most convincing examples being *actor-networks* (Callon 1986; Latour 1992, 2005)², *object-centred sociality* (Knorr Cetina 1997)³, and *material agencies* (Barad, 2003, Leonardi, P.M., S.R. Barley. 2008)⁴. These concepts challenge and transcend the great canonical division between the human and the material by considering them as symmetrical. Our analysis is characterised by its focus on the entanglement of these two levels in the sense that social relationships and materialities are mutually constitutive in the formation of human agents. The material properties of artefacts (bodies, clothing, accessories, protocols, equipments, labels, instruments, software and software packages) actively participate in the constitution of actor cooperation and entity coordination and represent an infinite number of potential points of contact that can materialise in space and time. This constitutive entanglement allows us to trace the socio-material configuration regimen for a given artefact, in this present case the point of intersection between CF NBS and CF diagnosis, molecular biology and medicine and the rationalisation of knowledge and professional practices in biomedical and clinical innovation. More specifically, the concept of *sociomateriality* (Mol, 2002, Suchman, 2007)⁵ for these authors signifies the interactivity of the social and the material in the constitution of everyday organisational and professional life, forming heterogeneous couplings, ground-breaking amalgamations that associate and dissociate depending on conditions and circumstances and, in this theatre of perpetual metamorphosis, give rise to unprecedented configurations and reconfigurations (Orlikowski, 2007)⁶.

Using this theoretical base together with empirical data obtained during the course of our research, we opted for an analysis of the constitutive entanglement between mass neonatal screening technology and diagnosis announcement practices based on the recommendation protocols for good medical practice. The initial aim of this research was to examine the positive and/or negative impacts of these announcement recommendations, defined by a

² Callon, M. (1986), 'Some elements of a sociology of translation: Domestication of the scallops and the fishermen of Saint Brieu Bay' in *Power, action and belief: A new sociology of knowledge?* J. Law (ed.): 196–233. London: Routledge. ; Latour, B. (1994), 'On technical mediation: Philosophy, sociology, genealogy'. *Common Knowledge* 3/2: 29–64. Latour, B. (2005), *Reassembling the social: An introduction to actor-network theory*. Oxford: Oxford University Press.

³ Knorr Cetina, K. (1997), 'Sociality with objects: Social relations in postsocial knowledge societies'. *Theory, Culture & Society*, 14/4: 1–30.

⁴ Barad, K. (2003). "Posthumanist Performativity: Toward an Understanding of How Matter Comes to Matter," in *Signs: Journal of Women in Culture and Society*, vol. 28, no. 3, Spring ; Leonardi, P.M., S.R. Barley. (2008), Materiality and change: Challenges to building better theory about technology and organizing. *Information and Organization*, 18, 159-176.

⁵ Mol, A. (2002), *The body multiple: Ontology in medical practice*. Durham, NC: Duke University Press. ; Suchman, L. A. 2007 *Human-machine reconfigurations: Plans and situated actions*. Cambridge: Cambridge University Press.

⁶ Orlikowski, W. J. (2007). Sociomaterial Practices: Exploring Technology at Work. *Organization Studies*, 28(9): 1435-1448 ; Orlikowski, W.J., S.V. Scott. (2008). Sociomateriality: Challenging the separation of technology, work and organization. *The Academy of Management Annals* 2(1) 433-474.

multidisciplinary working group under the initiative of the French association ‘Vaincre La Mucoviscidose’ (VLM), on cystic fibrosis diagnosis announcement practice. During the course of our research, however, the reality of clinical medical practice and care team organisation obliged us to question the very principle of mass neonatal screening.

Establishing recommended practice protocols is not simply a tool at the service of the medical teams that will implement them to formalise procedures, coordinate services and trades, determine terminology or manage teams’ observance of external and internal rules. In view of the specificity of each CF Centre, the recommendation protocols once materialised are in fact equally revelatory, and in a quasi chemical manner, of how each entity is run and organised and how resources are managed. We will add that the introduction of recommendation protocols reveals more complex, diversified work situations regarding announcement procedures than the mere fact of implementing incentive standards or the mere fact of non-compliance with accepted good practice. Compliance with the recommendation protocols allows us to explore the crucial aspects of diagnosis procedures and communication between health professionals and families. Even more, it invites us to turn our attention to the ethical debates raised by CF NBS that have entered this rare disease into public health policy. We will see that the challenge faced by these health professionals gravitates around the information delivered during the diagnosis announcement consultation and the ethical debate generated by neonatal screening, the announcement procedure and the follow-up treatment. The one-to-one interviews revealed that these two factors are problematic and perturb the health professionals concerned.

The analysis is divided into two phases. First, we describe the socio-technical NSB programme and outline its impacts by retracing its materiality, the significant moments in its history and subsequent developments followed by the controversies provoked and fuelled by this technology (1). Secondly, we describe the configurations and reconfigurations generated by CF NBS focusing on two specific areas: (2): the creation and dissemination of a good practice recommendations doctrine and a standardising corpus and the tension between informed individual consent to screening and the quantitative management of neonatal screening results.

1. The genealogy of CF NBS: a history of continuous alternation between biomedical entities and the joint exploration of pathology and normality, deviation and conformity.

As an introduction, it is important to look back at the genealogy of screening, its equipment and more especially, the continuous alternation between *biomedical* conventions concerning the *entities* (genetic mutations, biomarkers) involved in both pathological change and normal physiological variations, and the *systems* that establish, temporarily standardise and partially regulate recommended practice and the clinical procedures in diagnosis and prognosis.

In the first place, the genealogy of a technology imposes a coordinated exploration of the constitutive waiving (or deviation) from the rules that have governed the approval of cystic fibrosis as a candidate for neonatal screening.

1. 1. A joint exploration of rule waiving and tolerance to deviations

Neonatal screening (NBS) is a mass screening, secondary prevention policy⁷ aimed at detecting one or several often congenital disorders in all neonates in a given country. To be eligible for neonatal screening, a disease should meet a number of criteria approved by the World Health Organisation; criteria taken from the taxonomy established in 1968 by Wilson and Jungner: 1- the condition sought should be an important public health problem; 2- it should present a recognised latent or early symptomatic phase prior to or at the onset of clinical symptoms; 3- the natural history of the condition should be adequately understood; 4- there should be an accepted preventive or curative treatment available; 4- a reliable early detection test should be available at its latent phase; 5- the test should be acceptable to the population in general and subject to the consent of the person being tested, or the parents in the case of a child, who should equally be clearly informed as to the nature of the test, the meaning of the results and therapeutic possibilities; 6- the screened patient must have the possibility of being examined, treated and benefit from follow-up care in high performance medical structures; 7- the screening programme must be a continuing process; 8- the cost of screening should be moderate and not exceed the cost of treatment (1). Adapted to neonatal screening, one should retain that the disease should constitute a serious health problem with an early symptomatic stage, be sufficiently prevalent (over 1/20 000 births), and accessible to efficient treatment in its pre-clinical phase. It should be detectable by means of a rapid, cost effective test with a low false-positive incidence (to avoid unnecessary parental stress and high resource consumption) and a false-negative rate that is virtually nil and applicable on a large scale (over 800, 000 births per year in France). The screening process should be acceptable to parents and, in the event of a positive result, include a rapid second-tier DNA mutation analysis to identify the genetic anomaly responsible, as is the case for cystic fibrosis screening. Positive results should systematically lead to the immediate provision of adequate follow-up care so as to improve prognosis and finally, all instituted screening programmes should be regularly evaluated.

A national screening programme was organised from 1978 with the agreement of the CNAMTS, the National Health Insurance Fund for Salaried Workers and the French Association for the Screening and Prevention of Handicaps in Children (AFDPHE) with three aims: equal access to screening and therapeutic treatment for all neonates; screening test efficiency with maximal detection of sensitivity and specificity; utility, or in other words that CF NBS should be directly beneficial to the neonate.

Five diseases are currently included in the national neonatal screening programme: hyperphenylalaninemia and congenital hypothyroidism since 1978, congenital adrenal hyperplasia since 1996, drepanocytosis among children potentially at risk (African and West Indian) first introduced in the French West Indies and Guyana then in metropolitan France, and cystic fibrosis since 2002. Neonatal screening for toxoplasmosis is not included as it is only justified under specific circumstances and is not part of the AFDPHE mass screening programme. Cystic fibrosis is a congenital autosomal-recessive disorder with a relatively high rate of prevalence (1/4600 births). The screening test measures the dose of immunoreactive

⁷ Population-based public health program applying preventive medicine in defined regions to reduce infant morbidity and mortality from certain biochemical and genetic disorders by using presymptomatic detection/diagnosis with dried blood specimens from newborns analyzed in central laboratories employing automated procedures linked to clinical follow-up systems. Allen and Farrell (1996). *Adv Pediatrics* 43: 231-270.

trypsinogen in blood serum⁸. In the case of elevated IRT values (> 65µg/L), the diagnosis is validated by a search for mutations on the ‘cystic fibrosis transmembrane conductance regulator channel’ (*CFTR*) gene. This search examines approximately 30 potential mutations covering 90% of those most frequently observed in France, the most frequent (70%) being the *F508del* mutation. A sweat test is then prescribed to verify the disease’s phenotypic expression (mutation penetration). A sweat chloride concentration level higher than 60 mmol / L is considered abnormal. In the case of a positive diagnosis, the infant is referred to a Resource and Expertise Centre for Cystic Fibrosis (Centre de Ressources et de Compétences pour la Mucoviscidose: CRCM) for the provision of global multidisciplinary care associating a specialised paediatrician, paediatric nurse, physiotherapist, nutritionist, psychologist and a geneticist biologist. The aim is thus to ensure the parents are informed, to provide advice for healthy living, avoid infections and regularly monitor the child.

The dissemination of CF NBS has not been homogeneous and has been implemented with variations according to country, region or province. Cases of noncompliance with the Wilson and Jungner criteria cited above have appeared as a result of technological advances and medical benefits that have successfully enrolled others to the cause. In effect, neonatal screening for cystic fibrosis (CF NBS) fails to comply with the Wilson and Jungner criterion stating that neonatal screening should lead to an effective curative treatment. It implies that treatment would permit affected neonates to be brought back to normal health, yet to date there exists no specific curative treatment for cystic fibrosis even if the utility of screening is increasingly based on solid medical arguments (if one adheres to professional literature written by reputed experts in cystic fibrosis). These experts are all globally favourable to the principal of mass screening, but somewhat sensitive to its quality, technological advances and the new diagnostic and prognostic dilemmas generated by its implementation.

1. 2. *The endless rhetorical questions regarding CF NBS and its validity*

The CF NBS debate remains heated on both sides of the Atlantic, both in America and northern Europe. This is confirmed by the quantity and profundity of publications in specialised paediatric journals reviewing the Wilson and Jungner criteria and the emergence of new screening criteria over the past forty years (see the in-depth evaluation by Andermann A, Blancquaert I, Beauchamp S, Déry V., 2008)⁹, and the time and efforts invested in creating a new set of recommendations and guidelines aimed at optimising procedures¹⁰. The course followed by this literature testifies to the work of convergence and aggregation achieved through the intermediary of consensus conferences¹¹.

⁸ The screening test is performed 3 or 4 days after birth and measures the IRT (immunoreactive trypsin) level in the blood. A few drops of blood, are collected from the baby’s heel on Guthrie paper. A second sample is used for DNA analysis in order to confirm the diagnosis and determine the form of cystic fibrosis present.

⁹ Andermann A, Blancquaert I, Beauchamp S, Déry V., (2008), Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the past 40 years. *Bull World Health Organ.* Apr; 86(4):317-9.

¹⁰ Comeau AM, Accurso FJ, White TB, et al. (2007), Guidelines of implementation of cystic fibrosis newborn screening programs: cystic fibrosis foundation workshop report, *Pediatrics.* 119:e495–518.

¹¹ Farrell PM, Rosenstein BJ, White TB, Accurso FJ, Castellani C, Cutting GR, Durie PR, Legrys VA, Massie J, Parad RB, Rock MJ, Campbell PW 3rd; Cystic Fibrosis Foundation.

Concerning the benefits of neonatal screening for CF patients, if it appears impossible today to conduct a scientifically rigorous study proving that early diagnosis increases patients' life expectancy, an improvement in nutritional and respiratory states can be confirmed, at least in the first ten years of a child's life. It also demonstrates that neonatal screening eliminates trial and error diagnoses, costly for the health system and highly stress provoking for the families, and favours the optimal organisation of care for all those affected. As for the biological marker used in screening, its sensitivity has been considerably improved by associating it with a DNA analysis to search for mutations on the cystic fibrosis gene (*CFTR*). Introducing molecular biology techniques in a neonatal screening strategy, however, gives rise to a certain number of problems.

It has created dissent among health professionals with the eruption of heated disputes between biologists, geneticists and paediatricians, between field clinicians and research laboratory staff. Beyond the scientific arguments and competing hypotheses concerning mass neonatal screening, we note an invisible though sensitive split between those upholding elevated meta-principles, those using persuasive arguments to justify treatment practices, and those lobbying to obtain perennial financing for clinical research and the creation multi-disciplinary structures. These different groups are manifest around organisations and networks, both national and international, but equally invisible in the form of pressure groups advocating the perpetuation or abandonment CF NBS. A specialist in the field summarises this co-evolution of institutional (screening and treatment units), techno-scientific (biological markers, instrumentation and knowledge), regulatory (assembling and standardising diagnosis and care practices) and socio-professional (protagonist aspirations and trajectories) dimensions:

“As a professional involved in patient care, the implementation and generalisation of systematic neonatal cystic fibrosis screening in France and advances in screening methods that I sincerely hope for, I am aware of existing ambiguities. I am a firm believer in the benefits of neonatal screening but I'm also aware that this belief is not based on indisputable scientific proof concerning the extent and nature of the value it adds. I am equally fully aware that professionals, including clinicians and researchers by necessity always develop rational arguments that, not surprisingly, are in perfect coherence with inexpressible desires strongly related to their professional interests”¹².

On one hand, the scientific discovery of biomedical entities (*CFTR* genes), incorporated into systematic screening equipment and policies, provides new opportunities for clinical practice. On the other hand, CF delimitations and nosological categories, redefined following advances made by specialists in contact with patients and their families, have fuelled the debate regarding the causes of CF and possible curative treatments. *In fine*, they have contributed in opening up new avenues of questioning for molecular biological research, genetics and also clinical medicine.

The interviews carried out for this research clearly demonstrated that, in broaching the diagnosis announcement procedure and its associated torments, health professionals questioned the validity of NBS and were aware of the controversies. Within the restricted

2008 Guidelines for diagnosis of cystic fibrosis in newborns through older adults: Cystic Fibrosis Foundation consensus report. *J Pediatr*. Aug;153(2):S4-S14.

¹² Extract from correspondence with the authors of this paper.

sphere of cystic fibrosis, and although present in the minds of the professionals concerned, this question of validity appears to be in the process of being resolved. A panel of practitioners concluded that research on CF NBS had established that the benefits outweighed the risks and more especially, that screening programmes should be organised and controlled, implicitly suggesting the need for medical management¹³. One of the pioneering practitioners in the field, highly reputed in North American academia, emphasised the importance of shifting the focus from endless debates on ‘should we screen?’ to ‘how should we screen’.¹⁴ He insisted that it was high time to become proactive by renewing the focus on prevention as rapidly as possible in order to provide a more appropriate and individualised therapeutic approach: “This new era is also characterized by the predominantly ambulatory care, rather than recurrent hospitalizations, and a fundamentally pre-emptive philosophy in which we strive to prevent both malnutrition and chronic infections through routine clinical management. I want to emphasize that this does not necessarily mean more treatment but, rather, more appropriate treatment and potentially less of a therapeutic burden for children and their parents”¹⁵. The same author suggested that, both beyond and in addition to the clinical argument, the debate should be oriented towards fundamental human rights as one of the corner-stones of current and future good biomedical practice in an attempt to ease the tensions surrounding the diagnosis ‘odyssey’ for parents and health professionals alike¹⁶.

2. Characterising two types of configuration: the regulation of diagnosis announcement practices, the tension between subjects’ consent to screening for the good of their health and public health population management

Two characteristic socio-material configurations appear in the light of this study and the data produced (in terms of figures and accounts given by the actors concerned): (1) the differentiated and contingent accommodation of announcement protocols in CF centres that emerge as necessary operational entities at ground level and thus act as nodal political actors; (2) the tension between individual consent to screening and mass population genetics.

2. 1. The differentiated accommodation of announcement protocols by CF centres and health professionals

Since the beginning of the 1990’s, France has been going through the process of rationalising health practices, both medical and paramedical, that has included the introduction of Opposable Medical References (RMO) a health information system and inevitably, under the guise of management, the incorporation of standardisation and certification schemes. In retrospect the impact has been somewhat contrasted.

¹³ Grosse SD, Boyle CA, Botkin JR, et al. Newborn screening for cystic fibrosis: evaluation of benefits and risks and recommendations for state newborn screening programs. *MMWR Recomm Rep.* 2004;53(RR-13):1–36 ;

¹⁴ Farrell P.M., (2004), “Cystic fibrosis newborn screening: shifting the key question from “should we screen” to “how should we screen?”, *Pediatrics* , n°113, p. 1811-1813.

¹⁵ Farrell, P. M. (2007); The Meaning of "Early" Diagnosis in a New Era of Cystic Fibrosis Care, *Pediatrics*, January 1, 119(1): 156 – 157 ; Sims EJ, Clark A, McCormick J, et al. Cystic fibrosis diagnosed after 2 months of age leads to worse outcomes and requires more therapy. *Pediatrics.* 2007;119:19–28.

¹⁶ Farrell P.M., (2008, Is newborn screening for cystic fibrosis a basic human right?, *Journal of Cystic Fibrosis*, Volume 7, Issue 3, Pages 262-265 (May 2008).

In the case of cystic fibrosis, achieving standardisation *via* guidelines is singular. The cystic fibrosis neonatal screening programme was instituted almost 40 years ago. Although subject to numerous controversies, the benefits of screening, at least in the medium term and notably at nutritional and/or respiratory level, are clearly demonstrated by arguments supported by an accumulation of data, screening programme evaluations and authoritative texts punctuating academic and professional life in the field of cystic fibrosis and rare diseases¹⁷. In fact, the interest of practicing this type of screening is reiterated in the light of experience obtained in France and abroad. The results are nevertheless closely correlated to the quality of the follow-up care delivered to the affected child by specialised medical teams. Neonatal screening for CF thus only has meaning if it is associated with continuous, specialised care. It is for this reason that the generalisation of CF NBS to the whole of France in 2002 was accompanied by recommendations regarding the provision of follow-up care for the affected child in specialised CF centres, subsequently officialised by the public health authorities.

The specific problem posed by cystic fibrosis, however, is more complex; not all children carrying the mutation are seriously affected, there is no curative treatment for the disease and the diagnosis is first announced to the parents creating deep anxiety because no-one can predict how the disease will evolve. It is in this very context of mass CF NBS that we were able to consider that clearly outlined and systematised diagnosis announcement procedures could represent a therapeutic advantage. The diagnosis announcement confirms the child's entry into the disease; it marks an alteration in the child's status hitherto identified as a 'sick child' in the eyes of the child concerned, in the eyes of the family and society in general. In other words, if the diagnosis announcement recommendations are embedded in a therapeutic project with a family and social dimension, but also in a broader more extensive context that constitutes the structuring elements of the provision of care for this rare chronic disease in the French context, the screening test and confirmatory diagnosis 'equip' the announcement procedure. Like other examples of innovation in the industry and service sectors, regulatory schemes in the health sector over the past ten years have been a driving force in stimulating innovation, the acquisition of skills and the formation of new specialists. The formulation and dissemination of recommendations to 'improve' the diagnosis announcement procedure, in parallel with the generalisation of CF NBS, are both innovative schemes: they incite professionals and their organisations to elaborate new trade practices and propose new directions for the delivery of care. However, beyond this structuring factor provided by technology and standardisation, an institutional framework was essential for the deployment and implementation of this screening technology and the normalisation of 'good practice' recommendations. The advantage of standardising professional practice should be understood in this sense rather than in terms of prescriptive constraints; professional recommendations and medical practices determined by a set of rules conferred with a legal capacity that become justificatory in the event of deviations and infringements. As the etymology of the word 'recommendations' suggests, the corpus of post-screening announcement recommendations is considered here as being simply advisory, a collection of wise formulas and proposals devoid of constraints.

In the case of CF Centres (CRCM) it is clear that 'good practice' standards have become opportunities for action. It should be noted that this is already the case in the field of

¹⁷See for example; Roussey M., Deneuille E., Munck A., (2007), « Le dépistage néonatal de la mucoviscidose en France et dans le monde. Organisation, bénéfices, difficultés. État des lieux en 2007 », *Journal de pédiatrie et de puériculture*.

oncology¹⁸, type 2 diabetes¹⁹, asthma and breast cancer screening²⁰, and insurance medicine in the Netherlands²¹. In the case of cystic fibrosis, these standards were for the large part established by the CF Centres in collaboration with the central authorities and built up into a common base so as to bring different professional segments into convergence²².

These standards were then adapted to local circumstances and the actors concerned were able to assess and assimilate them during the recent experimental phase. As the protocol does not pose a threat to proven practice, does not take up too much time, resources and means to the detriment of the clinic and contact with patients and families, it is easy to understand that the professionals concerned globally consider it as being to their advantage. In a certain manner, by becoming involved in the dynamics of elaborating and disseminating the protocol, these multidisciplinary organisations mobilised themselves to avoid being subject to external rationalisation.

These different factors resulted in limited compliance to national (and increasingly international) recommendations in favour of more local arrangements negotiated between physicians and the main trade segments exposed to the announcement procedure. We were able to observe that paediatricians, pneumologists, gastroenterologists, the ICE, and more recently, psychologists and other trades (physiotherapists, nutritionists), tended to become specialised in cystic fibrosis (and occasionally chronic diseases), by gaining qualifications (through job loyalty and stability, in-house training, seniority in the CF Centres) and by professionalising themselves more or less early on. Concerning the patients, families and medical teams alike, the 'regionalisation' of care coordination has been concomitant with the appropriation of the recommendations. This largely explains the discrepancies between actual team practice and the national protocol regarding the diagnosis announcement procedure and, taking into consideration organisational, historical, demographic, and resource contingencies, the differences (or variable evolutions) between CF Centres.

The creation and dissemination of the national diagnosis announcement recommendations protocol, and the paradox is only apparent, involved setting up singular dynamics that contributed in clarifying localised clinical practices and the certification of CF Centres, and

¹⁸Castel, P., & Merle, I. (2002). Quand les normes de pratiques deviennent une ressource pour les médecins. Le cas de la cancérologie, *Sociologie du Travail*, Vol. 44, n°3, p. 337-355 ; Castel, P., (2009). What's Behind a Guideline? Authority, Competition and Collaboration in the French Oncology Sector, *Social Studies of Science*, Vol. 39, No. 5, 743-764.

¹⁹Bachimont J., Cogneau J., Letourmy A., (2006), « Pourquoi les médecins généralistes n'observent-ils pas les recommandations de bonnes pratiques cliniques ? L'exemple du diabète de type 2 », *Sciences Sociales et Santé*, Vol. 24, n° 2, p. 76-102.

²⁰Urfalino P., Bonetti E., Bourgeois I., Dalgarrondo S., Hauray B., (2001), *Les recommandations à l'aune de la pratique. Le cas de l'asthme et du dépistage du cancer du sein*, Paris, Centre de Sociologie des Organisations.

²¹Berg M., Horstman K., Plass S., Van Heusden M., (2000), "Guidelines, professionals and the production of objectivity: standardization and the professionalism of insurance medicine", *Sociology of Health & Illness*, Vol. 22, p. 765-791.

²²Vailly J., (2004). « Une politique de santé "a priori". Le dépistage néonatal de la mucoviscidose en Bretagne », *Sciences Sociales et Santé*, Vol. 22, n°4, p. 35-60; Vailly J. (2006), "Genetic screening as a technique of government: the case of neonatal screening for cystic fibrosis in France", *Social science and medicine*, Vol. 63, n°12, p. 3092-3101.

resulted in the ‘territorialisation’ of public action to the detriment of centralised, impersonal or bureaucratic regulations for the specific health domain that cystic fibrosis has become.

The institution of CF NBS, the structuring of CF Centres and the diagnosis announcement recommendations protocol reflect the standardisation of care for this orphan disease. This standardisation does not infer the homogenisation or alignment of practices. The general movement towards standardisation has encountered two unexpected effects in comparison with initial aims:

- the introduction of the new NBS technology and protocol aimed at systematising practices has encouraged professionals to elaborate innovative interdisciplinary roles and explore novel means of sharing medical, paramedical and supporting trades;

- the emergence of what can be qualified as *small or medium scale singularities management* (according to active patient list size) in the operational CF Centre entity; a form of management requiring both professional and organisational skills, to date largely unknown, and still in the embryonic stage. This type of management emerged in a hospital environment and was constituted from *large scale care management*, a bureaucratic configuration that consequently operated on routine, mastered skills and depersonalised services.

1. 2. *The tension between individual consent to screening and mass genetic management*

The ‘the voluntary consent of the human subject’ is today one of the cornerstones of good biomedical practice. The aim of instituting CF NBS was ultimately the ‘individual, direct, and immediate interest of the sick child’ (Ardailou, Le Gall, 2007)²³. By this very fact, concrete situations and their resulting dilemmas are dealt with at CF Centre level and rely on the experience of health professionals in CF diagnosis announcement. The HAS²⁴ report, an evaluation of the NBS programme after five years operation, highlights several areas for improvement thereby adding fuel to the controversy opposing those in favour and those against NBS.

In a broader context, these programmes concord with the movement advocating that individuals should take charge of their health and that of their families and feel personally ‘responsible’. In association with this politico-moral framework, the ‘production of subjects’ capable of making choices in genetic counselling situations has been underlined by several researchers in the social sciences; in this context, voluntary consent to neonatal screening is an agent-level typicality of a well described form of modernity. The first characteristic of modernity is to underline its belief in the power of reason and the rational act (Touraine, 2005, p. 121)²⁵. Through this profession of faith in a world entirely rationalised by human acts, a fundamental assertion is equally expressed: that of an individual subject with the capacity of investing in the creation of his own world and producing the significations that

²³ Ardailou R., Le Gall J.-Y., (2007), « Le dépistage néonatal généralisé par des tests d’analyse biologique », *Gynécologie Obstétrique & Fertilité*, 35 367–374 ; Comité Consultatif National d’Éthique (CCNE), « Avis 97 : Questions éthiques posées par la délivrance de l’information génétique néonatale à l’occasion du dépistage de maladies génétiques (exemples de la mucoviscidose et de la drépanocytose) », ronéoté, p. 7.

²⁴ « Le dépistage néonatal systématique de la mucoviscidose en France : état des lieux et perspectives après 5 ans de fonctionnement », Rapport de la HAS, janvier 2009.

²⁵ Touraine, A., (2005). *Un nouveau paradigme pour comprendre le monde d’aujourd’hui*, Paris, Fayard.

will give meaning to his existence (Gauchet, 2003)²⁶. In terms of social analysis, it imposes a representation of human organisation as being simultaneously governed by an overshadowing definition of instrumental rationality, a double emblem of progress and its prospects, of production and consumption (imposing a global, external code of meaning), and the assertion that an individual is the author of his own life, supported by a major component: subjectification, or in other words the transition to an intentional order. This presentation, in the form of a new subjectification of health, however tends to occasionally level out disparities between social groups, assimilate practice with rhetoric and neglect inherent tensions and uncertainties. Furthermore, it fails to cross the question of voluntary consent in genetics with that of population management.

The attempt at rationalising health care practices *via* recommendations is associated on the one hand with a definitional change that has converted the notion of ‘patients’ and their families to one of clients and subjects undergoing treatment, and on the other hand, an extensive and structuring management trend in institutions that find themselves caught in a stranglehold of financial constraints. On one side it is considered legitimate (and even desirable) to give greater consideration to seriously affected individuals and their families and on the other, public policy urges for standardisation (occasionally in a blind imitation of the industrial model) and shakes up existing models through demanding interrogations: what financial means, qualifications and perennial structures justify the evaluated importance of rare diseases and the burden they represent? As if our modern society felt continuously obliged to be in accordance with itself; what is the value of life in chronic and incurable diseases (by definition incommensurable)? What means is a society prepared to invest in to meet the care needs of these patients? The definition of public health finds itself ‘seized’ by this dual interrogation.

The change in the perception of a chronically ill patient²⁷ is a major, influential phenomenon apparent in the diagnosis announcement recommendations, NBS hold on public health policy and the nature of exchanges between health professionals and patients. In other words, the redefinition of the patient and the disease goes hand in hand with a change in the way a society views its chronically sick and, in a trivial but nonetheless realistic manner, its evaluation of human life and the ‘price’ of suffering in a child. The profession of faith as proof of the majority’s commitment to the rare disease cause, and more especially the actors exposed (patients, families and health professionals), find themselves up against the temptation to apply the ‘parsimony’ principle in the rationalising management discourse. We place ourselves at the intersection between the higher considerations asserting the sacredness of all that touches on the protected spheres of intimacy and human life (chronic illness, incurability, sterility, sexuality and also the worthiness of a life with projects for the future), and material and monetary considerations and the balance between costs, burdens, profits and benefits. The increasing interest for chronic diseases, and more recently orphan diseases in post-industrial, secularised societies, justifies the increasing preoccupation with these diseases in social life and its major institutions (the family, the hospital, the school and insurance) directly implicated in the economic and emotional evaluation of an individual’s existence: the birth and death of a child, then the birth, development, maturity and death of an adult. In other words, the emotional value attached to the death of a child, the evaluation of trauma as suffered by the family concerned, have evolved according to the social and cultural

²⁶ Gauchet, M., (2003). *La condition historique*, Paris, Stock.

²⁷ Baszanger I., (1986), « Les maladies chroniques et leur ordre négocié », *Revue Française de Sociologie*, Vol. 27, n°1, p. 3-27.

redefinition of the place given to the modern family in the material and emotional economy. Fixing a value on the suffering of a ‘priceless’ child has shifted through the increasing contribution of science and ‘*evidence-based medicine*’. The challenge is in estimating the inestimable, but what human price can be fixed on the breakdown of a couple to whom the physician presents the diagnosis results? What cost proposed for the uncertainty regarding the possible clinical expression in a mild form of cystic fibrosis? What value behind the fact that an uncertain outcome corresponds to a lack of compensatory treatment? This difficult evaluation has been accompanied by a redefinition of the modes of financing allocated to the care of incurable diseases and the fundamental research necessary to bring the disease under control: from public financing to private financing by donations (collected via the ‘Virades de l’Espoir’). This implies both working on the acceptance of caring for a rare disease by an extended community and an emotional transformation on the part of the families concerned that need to redefine the meaning attached to a good life ‘worth’ living despite the knowledge of its fatal outcome.

This debate on pricing the priceless child hit by cruel fate can appear somewhat out of place. In our study, the interviewees regularly reminded us that estimating the cost of delivering care and political choices in public health matters were part of their activity. They emphasised that in the case of mild forms of cystic fibrosis, team deliberations on the diagnosis announcement and the information to be delivered was very closely related to the cost of medical treatment (too costly, not too costly) and the emotional weight to be borne by the family. Yet, history reveals that this is not a first and the sociology of economics has highlighted the way in which social values played a determining role in estimating the degree of investment to be made. Childhood, and the value given to its status, feelings imparted to the child, the growing sacralisation of childhood throughout the XX century and the compassion for the poor unfortunate innocent are markers inscribed in modernity²⁸.

A research on the genealogy of the neonatal screening for cystic fibrosis in Brittany had established that the birth of CF Centres was associated with ‘an a priori public health policy’ for cystic fibrosis and the institution of CF NBS in 2002²⁹. The emergence and dissemination of disease-specific public policy was all the easier to introduce since it was in accordance with public opinion and medical advances meaning that the terms used in the debate were easier to accept. Today, a demanding question concerns the future development of neonatal screening and its application using effective methods and also on *ex-nihilo* procedures to be created for the equivocal, mild forms of cystic fibrosis with new ways of managing these difficult cases. It should be reminded that the problem surrounding the positive diagnosis of cystic fibrosis in these equivocal forms has already be raised and questions asked as to the necessity of treating these neonates, the type of counselling to be delivered and families’ requests for prenatal screening. The profundity and subtlety of the ethical debate and the doubts concerning clinical procedures experienced by health professionals is incontestable.

²⁸ Zelizer V., (1994), *The Social Meaning of Money: Pin Money, Paychecks, Poor Relief, and Other Currencies*, Basic Books; Zelizer V., (1985), *Pricing the Priceless Child: The Changing Social Value of Children*, Princeton University Press.

²⁹ Vailly J., (2007), « Dépister les nouveau-nés : évolutions, débats et consensus », *Médecine /Sciences*, Vol. 23, n°3, p. 323-326 ; Vailly J. (2008), “The expansion of abnormality and the biomedical norm: neonatal screening, prenatal diagnosis and cystic fibrosis in France”, *Social Science & Medicine*, Vol. 66, n°12, p. 2532-2543.

The extreme difficulty of practicing the diagnosis announcement can justify creating a protocol of recommendations that uphold both ends of the chain: calming the family and allowing medical teams to distance themselves whilst at the same time valorising their principles and skills; the ability to listen, empathy, availability and continuity. The announcement ordeal is in equal measure to the stakes at play in 'pricing' childhood, to the continued concern for the value of life and the promises it holds in view of the constant progress allowing subjects to increase their life expectancy, at least in the collective sense for those suffering from a chronic disease. Moreover, one should remain attentive to the fact that the diagnosis announcement plunges these patients and their families into a more or less long-term and intense story that immobilises the lives of all concerned. The round of uncertainties concerning the symptoms and the weight of the treatment draws up a picture of life that is very different to that which prevails in the case of acute illness. Finally, the fact that these patients succeed in building-up their identities through childhood, then through adolescence and adulthood, destabilises the specialised medical organisations and their appreciation of the balance between risk and benefits or cost and benefits.

These considerations highlight the effect of tensions occasioned by advances in medical practice, fundamental research and technological programmes in the case of cystic fibrosis.

In our study carried out among health professionals, and equally our review of professional literature published over the last decade, these doubts and concerns over the balance between costs and benefits and the revisable relationship between risk and benefits and by extension the dilemmas addressed to public health policy makers, are recurrent and preponderant. We are faced with an interaction between economic factors (rationalisation, restriction, profitability) and non-economic factors (coordination organised between structures, inter-disciplinary cooperation within CF Centre teams, educational therapy to enable families to alter their views and practices in the face of CF). The question of CF NBS and diagnosis announcement recommendations aimed at improving the provision of care is situated at the crossroads between (1) the market and the cost of treatment, or the physical price, (2) the professional skills and responsibilities concerning the work of the medical teams, or the price of a high level commitment to a worthwhile cause (3) personal values and morals associated with childhood, or the symbolic price.

To conclude

This journey has clearly revealed the existence of uncertainties shared between the health professionals, the patients and their families. All concerned share the common fate of those involved (specialists and laymen alike) in caring for or suffering from rare 'orphan' genetic diseases. They are mutually engaged in what could be termed a primitive accumulation of scientific knowledge on the one hand, and autonomous and therapeutic skills on the other. This is what enables cystic fibrosis to exist in the specialised field of paediatrics, and beyond with adult cystic fibrosis, within the operational organisation of CF Centres, hospitals and more broadly, in public health policy.

The question surrounding the diagnosis announcement recommendations that initiated this research concerned the problem of the collective apprenticeship of announcement efficiency standards and the delivery of information to parents faced with a traumatic life event. It constitutes a specific case with broader implications: the challenges facing public policy in terms of management and ethics, the standardisation and internationalisation of procedures relating to medical innovations. More and more, random clinical trials and consensus

conferences provide the tools, framework and discipline for diagnostic and therapeutic strategies. Recent studies are not unanimous in their conclusions; some will insist on the inconvenience of standardising practices and imposing legislative, regulatory and prescriptive constraints to check practitioners' autonomy³⁰; others will emphasise that the introduction of practice guidelines procures legitimacy for the work among the public whilst leaving room for interpretation and personal judgment³¹ and favouring coordination between the different actors whilst facilitating individual work³². There are situations, however, in which standardising practice proves difficult to achieve because it is dealing with a new domain with imprecise diagnosis and prognostic techniques and more especially, in health situations whose singularity place them beyond any thought of total objectivity. This is the case concerning the cystic fibrosis diagnosis announcement or collective acts concerning highly uncertain choices such as decisions to terminate life in neonatal intensive care³³.

Our study shows that, in a context of uncertainty characterised by the absence of strict scientific norms and reduced or random clinical practices, the actors elaborate their own cognitive criteria. Faced with diagnostic typology and prognostic uncertainty, health professionals react by partly relying on announcement recommendations. They seek to domesticate rather than avoid these uncertainties by creating imperative knowledge from their own clinical practice together with formal reflexivity (staffing) and informal exchanges concerning experiences to evaluate and validate. Decisions are largely structured by the local context from which they emerge.

These results are an invitation to devise new ways of approaching the question of diagnosis announcement recommendations. From this point of view, the study would contribute to international works on the creation of guidelines, standards, rationalisation programmes and legal imperatives. More particularly, it reveals how the actors arrange themselves, in what ways and with what motives, with the uncertainties that constrain them but that nevertheless provide opportunities to transform the type of reflexion and principles governing practice. Health professionals feel the need for procedures in situations of uncertainty; the corpus of diagnosis announcement recommendations is a solution that helps forge a kind of a minimal doctrine in order to progress and stabilise an announcement procedure. At the same time, the confrontation between the recommendations and concrete situations forms an area of reflexivity on the practical ethical dilemmas arising from CF NBS that affect one or other area of the diagnosis announcement.

³⁰ Ogien A., (2001), « Le système RMO, la maîtrise des dépenses de santé et les paradoxes du contrôle », *Revue Française des Affaires Sociales*, Vol. 4, n°55, p.51.

³¹ Berg M., (1995), "Turning a practice into a science: reconceptualizing postwar medical practice". *Social Studies of Science*, Vol. 25, p. 437-76; Berg M., Horstman K., Plass S., Van Heusden M., (2000), op. cit. ; Timmermans S, *Sudden death and the myth of CPR*. Philadelphia, Temple University Press, 1999.

³² Castel P., Merle I., (2002), op. cit.

³³ Orfali, K. (2004). Parental role in medical decision-making: fact or fiction? A comparative study of ethical dilemmas in French and American intensive care units, *Social Sciences & Medicine*, 58(10):2009-2022; Orfali K & E. J. Gordon (2004). Autonomy gone awry: A cross cultural study on parents' experiences in neonatal intensive care units. *Theoretical Medicine and Bioethics*, 25:329-365 ; Paillet A., (2007), *Sauver la vie, donner la mort. Une sociologie de l'éthique en réanimation néonatale*, Paris, La Dispute.