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## **LIABILITY ISSUES IN PERSONALISED MEDICINE: A COMPARATIVE PERSPECTIVE**

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### **Abstract**

In the light of current European Regulations, both on emerging technologies and on new medicines, a whole life cycle regulatory approach towards products is suitable. Following this perspective, it is increasingly necessary to investigate in advance both the applicable *ex ante* regulations, in order to manage risks for humans and *ex post* protection approaches for those injured by innovative medical products.

This essay describes the main liability issues connected to the new personalised therapies. The liability issues emerge on a two-fold profile.

The first issue deals with the allocation of liability for potential damage consequent to a hybrid sale-service transaction. The complex nature of this transaction is, in fact, typical of drug lifecycle management (prescription, preparation, use, etc).

The second issue pertains to the examination of the essential elements of the *facti specie* of damage within the condition of intrinsic techno-scientific uncertainty. Unavoidably, this condition characterises personalised medicine, because of a lack of clinical expertise.

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## 1. European and American Regulations for Personalised Medicine: An Introduction

The functional characteristics of so-called smart therapies are creating new challenges for the already complicated field of medical liability.

Personalised or individualised therapies derive from the convergence of progress reached in different fields of technology, science and particularly in modern genetics.<sup>1</sup> This convergence contributes to a biological clinical variability of pathologies.<sup>2</sup> Biological drugs, pharmacogenomics, and drug delivery systems implemented by nanotechnology are all included in the expression “personalised medicine”. Some of these products are already in use while other are only submitted to trial (e.g. gene therapy).<sup>3</sup>

The meaning of the expression “personalised medicine” varies depending on the different medical specialties within which it is used.<sup>4</sup> Therapeutic applications have different aims but what they have in common is that all their treatments are configured on the biological and biomolecular features of the individual patient. They all are based on genetic data collection and its study and use.<sup>5</sup>

Currently, the sole definition of “personalised medicine” is expressed by the US *Genomics and Personalized Medicine Act 2008*, s 2(2):

(2) Personalized medicine is the application of genomic and molecular data to better target the delivery of health care, facilitate the discovery and clinical testing of new products, help determine a person’s predisposition to a particular disease or condition, and identify any targeted prevention strategies for that predisposition.<sup>6</sup>

An official European definition is not available. However, a number of European regulations are in place to control these kinds of product including Council Regulation (EC) 1394/2007 on advanced therapy medicinal products, amending Council

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<sup>1</sup> The use of “individualised” instead of “personalised” is suggested by the Nanobio-RAISE project. See [www.nanobio-raise.org](http://www.nanobio-raise.org).

<sup>2</sup> On the interaction between modern science and technology, examined by several authors, see L Noah, *Law, Medicine, and Medical Technology: Cases and Materials* (2<sup>nd</sup> ed) (New York: Foundation Press, 2007) and M Shapiro, “Is Bioethics Broke? On the Idea of Ethics and Law ‘Catching Up’ with Technology” (1999) 33 *Indiana Law Review* 17-162; S Cotta, *La sfida tecnologica* (Bologna: Il Mulino, 1968), at 36; I Pavone, “Diritti dell’uomo e genetica” in *Enciclopedia Giuridica Treccani* 12 (Rome: Istituto della Enciclopedia Italiana, 2007) 1-6.

<sup>3</sup> There are still a lot of critical issues in the use of gene therapy. They are due to technical problems but also to legal and ethical problems. International regulations have so far admitted only certain kinds of use of gene therapy (along a somatic line, not along a germinal line). See also I Pavone, “Aspetti giuridico-internazionali dell’ingegneria genetica” in V Della Fina (ed), *Discipline giuridiche dell’ingegneria genetica* (Milan: Giuffrè, 2008) 167-202.

<sup>4</sup> M Herder, “Patents and the Progress of Personalized Medicine: Biomarkers Research as Lens” (2009) 18 *Annals of Health Law* 187-229, at 188.

<sup>5</sup> Genetic data could reveal the characteristics of personal identity. See P Zatti, “Dimensioni ed aspetti dell’identità nel diritto private attuale”, in G Alpa and P Zatti (eds), *L’identità nell’orizzonte del diritto privato (seminario di studi, Padova, 21 April 2006)* in Suppl 4 *La Nuova Giurisprudenza Civile Commentata* (2007) 1-11, at 2.

<sup>6</sup> *Genomics and Personalized Medicine (US) Act 2008*, s 2(2).

Directive (EC) 2001/83/EC, and Council Regulation (EC) 726/2004 (hereafter the Regulation).<sup>7</sup> Council Directive (EC) 120/2009 followed the latter Regulation.<sup>8</sup>

The Regulation is a *lex specialis* compared with Council Directive (EC) 2001/83 on the Community code relating to medicinal products for human use:<sup>9</sup> it adds regulations respecting the Directive and it is specifically devoted to advanced therapy medicinal products (ATMP).

For the first time, the Regulation attributed legal relevance to the concept of combined medical products.<sup>10</sup> This underlined European awareness of the fact that the most recent medical products share this characteristic.

The combined product notion has an American origin.<sup>11</sup> It originated with the federal law of Ninety which is specifically dedicated to biotechnological products.<sup>12</sup>

The main difficulties arise from the impossibility of classifying the new combined products within the categories of traditional medical products. Consequently, it is necessary to define new and adequate criteria to identify both the applicable legal discipline and the technical standards required.<sup>13</sup>

Art. 2 of the Regulation uses the expression “advanced therapy medicinal products” to refer to gene therapy medicinal products, somatic cell therapy medicinal products, and tissue engineered products.

Even if there is no general definition of personalised medicine, all the definitions about the different products, the subject of the Regulation, have a common feature. They all use biological material incorporated into drug devices. The uncertainty about risks deriving from the innovative personalised approach is also a shared feature.

Regarding last aspect, recent international legal doctrine observes that because of the incorporation of advanced biomedical products in the human body the impact of unavoidable risks for humans has to be managed. Because of this factor regulatory issues must be addressed in advance.<sup>14</sup>

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<sup>7</sup> [2007] OJ L324/121. An analysis of the Regulations is proposed by BR Dorbeck-Jung, “Governing Nanomedicine: Learning from Regulatory Deficiencies of European Medical Technology Regulation” (2009) 94 *Notizie di Politeia* 41-57.

<sup>8</sup> Commission Directive (EC) 2009/120 amending Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use as regards advanced therapy medicinal products [2009] OJ L242/3.

<sup>9</sup> [2001] OJ L311, at 67. Directive as last amended by Council Regulation (EC) 1901/2006 ([2006] OJ L378, at 1).

<sup>10</sup> BR Dorbeck-Jung, see note 7 above.

<sup>11</sup> During the preliminary phases of the enactment of the *Safe Medical Device Act*, the US Senate decided to add a final note to the statute, remarking that “devices impregnated with biologically-active materials, medical devices, implantable drug pumps and biological sensors, and therapeutic devices used in conjunction with drugs for the extra-corporeal treatment of diseases”. See *Safe Medical Device Act (US) 1990* (Pub. L No 101-629, s 16, 104 Stat. 4511, 4526); see also 21 USC 353 (2000). On this topic see MD Kramer, “Combination Products: Challenges and Progress” (2005) *Regulatory Affairs Focus* 33-36.

<sup>12</sup> Definition issues are addressed by the FDA. It instituted the *Center for Biologics Evaluation and Research* (CBER) and the *Office of Regulatory Affairs* (ORA) for defining and evaluating biotechnologies. See <http://www.fda.gov/>.

<sup>13</sup> The Regulation suggests the use of the primary mode of action in order to identify the nature of product.

<sup>14</sup> See R Brownsword, “What the World Needs Now: Techno-Regulation, Human Rights and Human Dignity” in R Brownsword (ed), *Human Rights* (Oxford: Hart Publishing, 2004) 203-234; R

From an economic point of view, the distribution of responsibility for damages will be affected according to the risk created by the different stakeholders. In case of damages, the obligation will interest the persons involved in proportion to their ability to guarantee a patient's safety.<sup>15</sup> This possibility is not legally clear in the case of risks connected to the pharmaceutical progress under examination.

Finally, an important English initiative about these issues must be taken into account. The Nuffield Council on Bioethics held a consultation from April to July 2009 in order to provide background information on some issues related to "personalised" healthcare which a working party is considering. In autumn 2010, the Nuffield Council will publish a report on "Medical profiling and online medicine: the ethics of 'personalized' healthcare in a consumer age".

The Nuffield working party especially wishes to identify and consider the ethical, legal, social, and economic issues that arise in the application of new health and medical technologies that aim to deliver highly individualised diagnostic and other services. The working party will use case studies to describe and analyse developments in medical research and practice and other factors arising from the development of personalised healthcare. To do this it will particularly look at:

- (a) arguments about the scientific significance, reliability and predictive value of particular personalised services;
- (b) implications for equity in health in relation to who will benefit most from particular personalised services, and for whom they may be harmful;
- (c) the impact of personalised services offered by private providers;
- (d) the tensions that might arise between increasing expectations for highly tailored care with the need to provide healthcare for all in the NHS;
- (e) the extent to which personalised services can be offered as part of a fair and efficient operation of private and public healthcare systems;
- (f) confidentiality and privacy issues in relation to the control, transmission, and storage of personal health data;
- (g) any impacts on the doctor-patient relationship;
- (h) whether current regulation is appropriate.<sup>16</sup>

It should be noted that the phenomenon the Nuffield Council will analyse is wider than the specific one considered here. This data shows a possible future development of the issue: from personalised techniques in clinical care to a personalised health care system. This "trend" is also emphasised by the US Department of Health and Human Services (HHS) in the report "Personalized Health Care: Pioneers, Partnerships, Progress".

The HHS underlines that

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Brownsword, *Rights, Regulation, and the Technological Revolution* (Oxford: OUP, 2008); R Brownsword and K Yeung (eds), *Regulating Technologies* (Oxford: Hart Publishing, 2009); T Murphy (ed), *New Technologies and Human Rights* (Oxford: OUP, 2009).

<sup>15</sup> For the Italian "law and economy" approach see R Cooter et al, *Il mercato delle regole: Analisi economica del diritto civile. I Fondamenti*, 2<sup>nd</sup> ed (Bologna: Il Mulino, 2006), at 204.

<sup>16</sup> These aims are described in the same Consultation Paper.

personalizing and better targeting care practices based upon individual needs and health indicators is one possible solution to help defray growing cost and quality challenges....The concept of personalized health care is very broad, integrating our growing knowledge of genetics and biomarkers and their role in treatment selection with HIT, principles of evidence-based practice, and health quality and performance improvement approaches. In essence, personalized health care would combine the best available information from a variety of sources in an actionable manner so that physicians and patients can make appropriate health care decisions and enhance use of individual patient data in health practice.

## 2. The *Facti Specie* of Damage and Risk from Biologics

Uncertainty as an element that can complicate the analysis of the *facti specie* is not an unexplored subject. There is frequent debate about the threshold of socially tolerable risk. Identifying the subject liable for injuries that come from an unknown cause is also common.<sup>17</sup>

There are many examples that show the way the European Union considers risks in the evaluation of innovative products. The ATMP Regulation exemplifies how risks could be taken into account in the adopted risk-benefit test for risk management purposes.<sup>18</sup>

Moreover, the policy adopted by the European Medicines Agency exemplifies awareness that the premise that a “zero” risk notion is not the correct scenario to start from.<sup>19</sup>

In the face of the objective impossibility of eliminating risks, it is necessary to explore which legal “instruments” are in place to distribute these risks.<sup>20</sup> Within this progressive framework, personalised medical therapies add new questions about the governance of risk. These kinds of therapies have intrinsic and peculiar risks which are associated with the use of human biological material. Harmful risk could be manifested in different ways, such as the lack of biocompatibility of the therapy with the individual human body. From the *ex ante* regulatory perspective, legislative provisions that regulate the specific risk connected to the use of biological material are not easy to find.

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<sup>17</sup> See the Italian Supreme Court case. Cass. (13 April 2007), at n 8826, *Responsabilità civile a prevdenza* (2007), at 1824; *Giurisprudenza Italiana* (2008), at 63; and *La Nuova Giurisprudenza Civile Commentata* (2007) at I, 1428.

<sup>18</sup> See Provision n 20:

Follow-up of efficacy and adverse reactions is a crucial aspect of the regulation of advanced therapy medicinal products. The applicant should therefore detail in its marketing authorisation application whether measures are envisaged to ensure such follow-up and, if so, what those measures are. Where justified on public health grounds, the holder of the marketing authorisation should also be required to put in place a suitable risk management system to address risks related to advanced therapy medicinal products. Council Regulation (EC) 1349/2007.

<sup>19</sup> <http://www.ema.europa.eu>

<sup>20</sup> See L Khoury, *Uncertain Causation in Medical Liability* (Oxford and Portland, OR: Hart Publishing, 2006), at 1 and G Alpa and M Andenas, “Fondamenti del diritto privato europeo” in *Trattato Iudica-Zatti* (Milan: Giuffrè, 2005), at 422.

However, on the European level, a reference criterion might be found in art. 168(4) (a) of the Treaty on European Union (Lisbon Treaty) (formerly art. 152 (4) (a) of the Treaty on European Union (Nice Treaty)) that settles the competence of Council by affirming:

measures setting high standards of quality and safety of organs and substances of human origin, blood and blood derivatives; these measures shall not prevent any Member State from maintaining or introducing more stringent protective measures.<sup>21</sup>

The evaluation from the *ex post* perspective shows that there are many implications for the investigation of risk associated to the use of biological materials. Some of them emphasise issues that are already the object of debate (i) while others are new (ii).<sup>22</sup>

(i) The aspects connected to the exploration of the typical legal elements of the *facti speciei* of liability lie within the first issue. First, there are the typical problems that characterise the analysis of the causality in uncertain circumstances.<sup>23</sup> Many other issues are, in fact, connected to causality and they have been affected by considerable changes. Regarding these changes, one exemplifies an especially important point. This is the convergence between natural and human causes of damage.

Given the influence that a patient's individual biological features might have in determining the success of personalised therapies, it is necessary to understand the relevance of natural factors (if they exist) in causing an injury from the use of medical therapy in terms of causality.

The Italian legal system has already faced this issue with a recent judgment which breaks from the past. An Italian case, Cass. civ., 16 January 2009, n 975 (Corte di Cassazione), concerned a patient who died of a heart attack after an operation for an epidural block. The Court had to establish if the heart attack was caused by the pathology (a hemorrhage) connected to the operation or by an autonomous cause connected to the patient's previous case history. The Court accepted that, in case of convergence or concurrence between a natural cause and a human one,<sup>24</sup> there were no reasons to hold the author of the human cause of damage responsible in connection with the further natural cause.

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<sup>21</sup> See AM Farrell, "The Politics of Risk and EU Governance of Human Materials" in S Ramshaw and M Flear (eds), "European Law, New Technologies and Citizens" (2009) 16 *Maastricht Journal*, 113-137. See also FD Busnelli, *Bioetica e diritto privato: Frammenti di un dizionario* (Torino: Giappichelli, 2001), at 217.

<sup>22</sup> The new issues (ii) concerns the protection of privacy about a patient's use of genetic information and another is connected to the traceability of biological material. The correlation between the use of genetic data and *privacy* is not analyzed here. On this issue see LM Franciosi, "Identità genetica e ricerca di forme alternative di tutela nell'esperienza statunitense" in G Alpa and P Zatti (eds), *L'identità nell'orizzonte del diritto privato (seminario di studi, Padova, 21 April 2006)* Suppl 4 *La Nuova Giurisprudenza Civile Commentata* (2007) 1-11; GZ Kohlmeier, "The Risky Business of Lifestyle Genetic Testing: Protecting against Harmful Disclosure of Genetic Information" (2007) *UCLA Journal of Law and Technology* 1-43 .

<sup>23</sup> For an Italian analysis of causality in uncertain circumstances see R Pucella, *La causalità "incerta"* (Torino: Giappichelli, 2007), at 164.

<sup>24</sup> A "natural cause" usually means that the pathology derives from human factors (diseases; personal peculiarities, etc).

So far, Italian judges have not agreed about the solution of the irrelevance of natural causes when the production of damage comes from both, not interdependent, human and natural causes. This trend appears to be more innovation-oriented than the precedent one. In considering this new issue, judges are taking the principle of equity into account and they are emphasising that there are no legal or logical reasons for making the author of the human cause necessarily bear all the consequences of the damage.

Art. 2055 of the Italian Civil Code, meanwhile, does not provide a valid pretext, because it regulates the hypothesis of verifying the existence of causality between several human causes of damage.<sup>25</sup>

Generally, for injuries arising from technology, in circumstances where the technology was used when its particular risks were not known, the issue of reasonable foreseeability of damage is particularly relevant.<sup>26</sup> It depends on the state of knowledge and expertise in the field and many physicians currently lack expertise when using treatments based on genetic profiling.<sup>27</sup> At the moment, many genetic tests are not as easily available as the diagnostic tests that physicians usually use.

With the rapid increase of personalised diagnostic tests and new scientific information, even the standard of diligence required will change rapidly.<sup>28</sup> The physician, who will not adjust his or her ways of considering the genetic profile of a patient when preparing a therapeutic programme, will face the risk of claims presented by his or her patients. Because of this omission, the physician would not have foreseen the possible negative clinical reactions of the therapy. The patient could argue, therefore, that the physician should have adopted a different therapy in the light of his specific genetic profile.

If we consider the other protagonists in the development of personalised medicine, such as the manufacturers of new products, it is possible to find some earlier attempts to control risk. Art. 14 of the Regulation is dedicated to the “control of efficacy, adverse reactions and governance of risks after the approval” and provides, not only that the request to put the product onto the market must respect the requirements of

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<sup>25</sup> Cass. civ., 16 January 2009, n 975. Art. 2055 established that “Se il fatto dannoso è imputabile a più persone, tutte sono obbligate in solido (1292) al risarcimento del danno. Colui che ha risarcito il danno ha regresso contro ciascuno degli altri, nella misura determinata dalla gravità della rispettiva colpa e dall’entità delle conseguenze che ne sono derivate (1299). Nel dubbio, le singole colpe si presumono uguali”.

<sup>26</sup> See Cass. civ., 21 January 2009, n 10741, *Il Foro Italiano* (2010), at I, 141, with notes by AL Bitetto, “Fecondazione assistita, malformazioni fetali e ristoro del ‘bebè prejudice’”, at 155-312. See also F Di Ciommo, “‘Giurisprudenza normativa’ e ruolo del giudice nell’ordinamento italiano” (2009) *Contratto e Impresa*, at 537, (note by Galgano) and R Pucella, “L’incerta causalità nella prospettiva del civilista” in R Pucella and G De Santis (eds), *Il nesso di causalità: Profili giuridici e scientifici* (Padova: Cedam, 2007) 93-123, at 93 and L Khoury and S Smyth, “Reasonable Foreseeability and Liability in relation to Genetically Modified Organisms” (2007) 27 *Bulletin of Science, Technology & Society* 215-232.

<sup>27</sup> See GE Marchant, “Personalized Medicine and the Law” (2007) 12 *Arizona Attorney*, at 44.

<sup>28</sup> On genetic tests see D Memmo, “Test genetici, medicina predittiva, privacy” in A Cicognani and S Pelotti (eds), *Il Dna nella società attuale: test genetici, disastri di massa, identificazione criminale: Atti del XX Congresso Nazionale dei genetisti italiani, Bologna, 9-11 settembre 2004*, (Milano: Giuffrè, 2006) 13-28, at 16-20; E Stefanini, *Dati genetici e diritti fondamentali: profili di diritto comparato ed europeo* (Padova: Cedam, 2008), at 4 and A Santosuosso, “Genetica, diritto e giustizia: un futuro già in atto” in A Santosuosso et al (eds), in *I giudici davanti alla genetica* (Pavia: Collegio Ghislieri, 2002), 20-35, at 34.

pharmacovigilance (arts. 21-29 of Council Regulation (EC) 726/2004),<sup>29</sup> but also describes detailed measures to guarantee the control and efficiency of therapies in critical cases.

In summary, the authorisation to market a product will have to include a description of a system to manage risk adopted by the manufacturer in order to identify, prevent and minimise risks connected to advanced therapies. Manufacturers will also have to include an evaluation of the efficiency of the system.<sup>30</sup>

### 3. Allocating Liability in “Hybrid Sale/Service Transactions”: A Difficult Task

The allocation of liability gives rise to new open questions related to the individualisation of responsible persons. Many are involved: medical facilities (private or public), the physicians apply the therapies, the researchers who study the patient’s genetic profile, and those who decide the therapy.

Moreover, difficulties arise from the fact that these kinds of medical treatments involve a kind of “mixed” transaction which consists of a professional service combined with the supply of a product.

The close relationship between a professional service and a supply (the supply of a device) involves another problem. Sometimes when a medical device is implanted it is difficult to establish when the product remains autonomous and identifiable as a device and when it becomes an inseparable part of the patient’s body.<sup>31</sup>

The Italian scenario relating to this topic has not yet received much attention. However, the issue is already well known in the United States, where case law has judged cases of damages differently following the execution of hybrid sale/service transactions.<sup>32</sup>

Medical professionals in the US who provide cosmetic medical products, such as breast implants, are engaged in hybrid transactions involving both the sale of a product and a service. In most circumstances, American courts address sales/service hybrid transactions by allowing cases strictly for product liability. For several reasons,

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<sup>29</sup> Council Regulation (EC) 726/2004 of 31 March 2004 laid down the Community’s procedures for the authorisation and supervision of medicinal products for human and veterinary use and established a European Medicines Agency (Text with EEA relevance); OJ L136, at 1.

<sup>30</sup> Council Regulation (EC) 726/2004, art. 24, s 3.

<sup>31</sup> A Querci, “Protesi mediche tra regolamentazione di sicurezza e responsabilità da prodotto: l’onere della prova tutela il consumatore” (2008) *Danno e responsabilità* 290-296; and G Guerra, *Regole e responsabilità in nanomedicina: Profili giuridici delle tecnologie biomediche avanzate* (Padova: Cedam, 2008), at 201.

<sup>32</sup> American jurisprudence emphasises the necessity of evaluating hybrid transactions when they involve physicians. See RB Adler, “Device Dilemma: Should Hospitals Be Strictly Liable for Retailing Defective Surgical Devices?” (1994) 5 *Albany Law Journal of Science & Technology* 95-130; JW Poppell, “When is a Sale a Sale, and a Product a Product? Missouri Health Care Providers and Strict Product Liability Claims” (1994) 63 *University of Missouri at Kansas City Law Review*, 283-308; KB Meyer, “Silicone Breast Implants and Hospital Liability: A New Forum for Hybrid Transactions” (1995) 99 *Dickinson Law Review*, 434 - 449; C Pleicones, “Tort Law: Passing the Essence Test: Health Care Providers Escape Strict Liability for Medical Devices” (1999) 50 *South Carolina Law Review* 444-463.



however, most jurisdictions exempt medical professionals engaged in hybrid transactions from strict product liability.<sup>33</sup>

US stakeholders have emphasised interpretative doubts. These doubts relate to the contrast behind this kind of transaction: it is necessary to examine if the professional service is predominant in comparison with the supply or the medical product (personalised therapies).

Many consequences result from the choice of the liability regime. If a health facility is considered as part of the distributive channel of the medical product, the moment of delivery of a product is predominant. The health facility would be able to recognise the legal requirements of product liability.<sup>34</sup> However, a different conclusion is reached if the physician's professional service is prevalent in order to use the therapy.

The solution usually adopted by courts (given the medical nature of the service, American courts have usually excluded applying a strict liability regime to physicians' services<sup>35</sup>) has been criticised by stakeholders who tend to allocate strict liability to the physicians every time damage is caused by products used in the medical workplace.<sup>36</sup>

Within the Italian context the issue is topical because it could be inherent to the debate about the nature of health facility liability, as a distinct liability with respect to the employee physician's professional liability. In recent Italian bills, the liability of hospitals for violations of assistance and organisational duties has to be independent from the physician's service.<sup>37</sup> The use of a defective product on the patient could be interpreted as a violation of the "duty to protect the patient" which the medical facility is obliged to observe. Based on this kind of obligation, the hospital has to "supply" the patient a safe and adequate medical product. In this way, risks for defective products would be allocated to hospitals and so not fall on employee physicians. On the contrary, there would be the risk that professionals will be held responsible on the basis of typical duties derive from medical facilities that belong to the health authority. Consequently, physicians would be liable for torts caused by a failure in structural organisation or by the defectiveness of medical products used inside the hospital.

### 3. A "Tool" of Surveillance for ATMP: The Traceability Issue

To complete this preliminary description of the legal issues relating to personalised medicine, it is necessary to delineate that the European Lawmaker allocates a duty of traceability to the subjects using biological materials for medical purposes.

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<sup>33</sup> The analysis is done by RL Cupp, "Sharing Accountability for Breast Implants: Strict Products Liability and Medical Professionals Engaged in Hybrid Sales/Service Cosmetic Product Transactions" (1994) 21 *Florida State University Law Review* 873-889.

<sup>34</sup> *Bell v Poplar Physicians Group* (1994) 879 SW 2d 618 (MO Ct App.). In the state of Missouri any exception is admitted in order to apply the strict liability regime to medical facilities. So far, within this kind of interpretation, both the strict liability regime and the provisions of implied warranties of merchantability and fitness (ss 2-314 and 2-315 of *Uniform Commercial Code (UCC)* are applicable).

<sup>35</sup> See e.g. *Hershley v Brown* (1983), 655 SW 2d. 671, 674 (MO Ct App.). Also JW Poppell, see note 32 above.

<sup>36</sup> RB Adler, see note 32 above.

<sup>37</sup> See Bill "d.l. Bianchi n 1183 2008" and "d.l. Gasparri n 863 2008". These are analysed in R De Matteis, "La responsabilità sanitaria tra tendenze giurisprudenziali e prospettive de iure condendo" (2009) 25 *Contratto e impresa* 541-551.

By traceability, art. 15 of the Regulation means that

the holder of a marketing authorisation for an advanced therapy medicinal product shall establish and maintain a system ensuring that the individual product and its starting and raw materials, including all substances coming into contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport and delivery to the hospital, institution or private practice where the product is used.

The rationale behind traceability is the guarantee of a medical product's safety above all when medical products are composed of biological resources. Within the medical sphere, there is not yet a consistent bibliography on the issue of legal consequence for breach of duty, possibly because traceability is a new legal duty.<sup>38</sup>

The Regulation emphasises the need for complete traceability of patient, products and materials as an essential provision in order to control medicines for advanced therapies. In the words of the Regulation, the object that has to be "traceable" is different from the one (cells and human tissue) described in Council Directive (EC) 2004/23/CE. The traceability of the medicinal product for advanced therapies is also different from that (human blood and its components) provided by Council Directive (EC) 2002/98/CE. At the same time, the traceability system designated by the Regulation must be a coherent system. This means that it has to be compatible with the pre-existing traceability systems regulated in other pre-existing regulations.<sup>39</sup>

Art. 15 of the Regulation establishes that the hospital, or the subject authorised to market the therapy, has to make arrangements for the traceability system. This system has to include the traceability of all the substances that enter into contact with cells and tissues through origin, fabrication, storage, transport and delivery to the hospital where the product will be used. Following the European Commission's latter "Detailed guidelines on good clinical practice specific for advanced therapy medicinal products", the individual product should be traceable through the sourcing, manufacturing, packaging, storing, transport, delivery to the hospital/institution/private practice administration to the subjects, reconciliation and destruction or final disposition.<sup>40</sup>

When the therapy is used in a phase of a clinical trial, the hospital where the medicine is used organises and monitors the traceability system. This is done in order to archive key information to allow connections to be made between every product and the patient. The hospital therefore has a duty to guarantee knowledge about the origins of the materials used within the medical service for patients.<sup>41</sup> Moreover, the same

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<sup>38</sup> See Council Directive (EC) 2006/86/EC which implements Council Directive (EC) 2004/23/CE concerning the traceability and the notification of adverse reactions in the use of biological material and human cells ([2006] OJ L294/32).

<sup>39</sup> Consideranda 22 of the Regulation provides that the traceability system must respect the provisions of the Council Directive (EC) 95/46/CE ([1995] OJ L281, at 31). This Directive was modified by Regulation 1882/2003 ([2003] OJ L284, at 1).

<sup>40</sup> Commission (EC), "Detailed guidelines on good clinical practice specific to advanced therapy medicinal products" ENTR/F/SF/dnD (3 December 2009), 35810.

<sup>41</sup> The concept has been used in several French judgments, see e.g. Civ 1er (9 November 1999) *Bulletin des Arrêts de la Chambre Civile de la Cour de Cassation*, at I, 300; D. 2000 Jur. 117, with a note by P Jourdain, who refers to the concept of "obligation de sécurité". See also Cass. (7 November 2000) *Bulletin des Arrêts de la Chambre Civile de la Cour de Cassation*, at I, 279; D. 2001 Somm. 2236 with

hospital must preserve the data about biological materials for at least thirty years after the product's expiry date.

Even if it has not yet been fully explored, the liability profile derives from the obligation of traceability and is described as an obligation that is allocated to the hospital. This obligation has to be numbered along with those relating to organisational matters. The consequence is that an injured patient who cannot identify the original components of a therapy because of the lack of a traceability system could initiate a notable legal action based on art. 101 of the Italian Consumer Code.<sup>42</sup> This provision protects consumers.<sup>43</sup>

### 3. Conclusions

The previous pages give a preliminary description of liability issues implicated in personalised medicine from two perspectives: (i) the outline of the peculiarities of the *facti species* of damage; (ii) the identification of the "actors" that could be potentially involved in claims for damages.

The first perspective demonstrates that risk associated with the use of human biological material will complicate the legal evaluation of the case.

The second perspective shows that the creation of personalised therapies requires by its very nature the involvement of many specialists. Medical professionals providing personalised medicine are increasingly engaged in hybrid transactions involving both the sale of a product and a service. There is a close connection between the supply of a therapy and the necessary medical performance. Consequently, the issue of which rules of tort affect physicians and producers of these therapies in this kind of claim for damage will constitute an important issue for a future research agenda.

Investigations about the circumstances in which the risks implicit in new therapies have to be considered and about who will respond for injuries will contribute to the understanding the effects of tort law on innovation in medical sciences and practice.<sup>44</sup>

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a note by P Mazeaud, at 3085, and observations by M Penneau and Y Lambert-Faivre, "La réparation de l'accident médical" (2000) *Dalloz hebdomadaire: chroniques*, at 570.

<sup>42</sup> Art. 101 (Title V, The provision of public services, ch I, Public services) of the Italian Consumer Code, establishes that

1. The State and the Regions, within the sphere of their relative powers, shall guarantee the rights of those using public services by the proper and day-to-day implementation of the letter and spirit of current enacted law. 2. All dealings with users shall be conducted with due respect for predetermined and adequately publicized standards of quality. 3. Users shall be entitled, via the democratic process, to participate in the procedures for determining and assessing the quality standards provided for by legislation. 4. Legislation requires the providers of certain public services to draw up charters, using specific implementation programmes, diversified according to the sector.

<sup>43</sup> On the applicability of art. 101 of the Italian Consumer Code for a default in the organisation, R De Matteis, see note 37 above. See also Cass. civ., 2 April 2009, n 8093 (2010) *Danno e responsabilità*, at 56.

<sup>44</sup> An in-depth legal analysis about the effects of tort liability for negligence, defective products and medical malpractice on innovation is proposed by G Parchomovsky and A Stein, "Torts and Innovation" (2008) 107 *Michigan Law Review* 285-316.