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ARTÍCULO

Regulating Biobanks: An ethical analysis of the Spanish Law and the new challenges of the bigdata-driven biomedical research

Regulando los biobancos: un análisis ético de la ley española y los nuevos retos de la investigación biomédica con datos masivos

Regulant els biobancs: una anàlisi ètica de la llei espanyola i els nous reptes de la recerca biomèdica amb dades massives

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Abstract

In the European landscape, Spain represents a positive reference point when it comes to biobank regulation. Indeed, at the beginning of XXI century, the Spanish legislation has promptly responded to challenges posed by new biotechnologies and advances in genomics in the field of biomedical research by enacting in 2007 the *Ley de Investigación Biomédica* in order to keep up with the paradigm shift. Over the past 10 years, this Spanish framework along with the *Real Decreto* 1716/2011 has hold the merit to tackle the most controversial ethical issues related to use of human samples and personal data in biomedical research and biobanking (e.g. broad consent, secondary uses, governance, etc.). However, today the regulation of biomedical research and biobanks has to deal with big data, artificial intelligence and data-intensive research which have brought a number of challenges and controversies. The aim of this paper is two-fold. First, I will analyse from an ethical point of view the merits of Spanish regulation on biobanking in order to draw some lessons for the still unregulated situation in other Member States. Secondly, I will discuss the big data paradigm shift in biomedical research and question if the ethical and legal framework introduced the Spanish law at the beginning of the century is still able to hold the ground with the new contextual and societal challenges. In this respect, I will identify some opportunities for implementation and suggest strategies to achieve them in the specific context of biobanks.

Keywords: Biobanks; regulation; principles; bioethics; data-driven biomedical research; Spain.

Resumen

En el panorama europeo, España representa un punto de referencia positivo en lo que respecta a la regulación de los biobancos. De hecho, a principios del siglo XXI, la legislación española ha respondido rápidamente a los retos planteados por los avances de la biotecnología y la genómica en el campo de la investigación biomédica mediante la promulgación en 2007 de la Ley de Investigación Biomédica para mantenerse al día con el cambio de paradigma. Durante los últimos 10 años, este marco español junto con el Real Decreto 1716/2011 ha tenido el mérito de abordar las cuestiones éticas más controvertidas relacionadas con los biobancos. Sin embargo, hoy la regulación de la investigación biomédica y los biobancos tiene que lidiar con la inteligencia artificial e investigaciones con gran cantidad de datos que han planteado una serie de desafíos y controversias. El objetivo de este artículo es doble. En primer lugar, analizaré desde un punto de vista ético los méritos de la regulación española sobre biobancos con el fin de extraer algunas lecciones de la situación aún no regulada en otros Estados miembros. En segundo lugar, trataré el cambio de paradigma en la investigación biomédica y me preguntaré si el marco ético y legal que introdujo la ley española a principios de siglo todavía es capaz de mantenerse firme ante los nuevos desafíos contextuales y sociales. En este sentido, identificaré algunas oportunidades de implementación y sugeriré estrategias para lograrlas en el contexto específico de los biobancos.

Palabras clave: biobancos; regulación; principios; bioética; investigación biomédica basada en datos; España.

Resum

En el panorama europeu, Espanya representa un punt de referència positiu pel que fa a la regulació dels biobancs. De fet, a principis del segle XXI, la legislació espanyola ha respost ràpidament als reptes plantejats pels avanços de la biotecnologia i la genòmica en el camp de la recerca biomèdica mitjançant la promulgació en 2007 de la Llei de Recerca Biomèdica per a mantenir-se al dia amb el canvi de paradigma. Durant els últims 10 anys, aquest marc espanyol juntament amb el Reial Decret 1716/2011 ha tingut el mèrit d'abordar les qüestions ètiques més controvertides relacionades amb els biobancs. No obstant això, avui la regulació de la recerca biomèdica i els biobancs ha de bregar amb la intel·ligència artificial i recerques amb gran quantitat de dades que han plantejat una sèrie de desafiaments i controvèrsies. L'objectiu d'aquest article és doble. En primer lloc, analitzaré des d'un punt de vista ètic els mèrits de la regulació espanyola sobre biobancs amb la finalitat d'extreure algunes lliçons de la situació encara no regulada en altres Estats membres. En segon lloc, tractaré el canvi de paradigma en la recerca biomèdica i em preguntaré si el marc ètic i legal que va introduir la llei espanyola a principis de segle encara és capaç de mantenir-se ferm davant els nous desafiaments contextuals i socials. En aquest sentit, identificaré algunes oportunitats d'implementació i suggeriré estratègies per a aconseguir-les en el context específic dels biobancs.

Paraules clau: biobancs; regulació; principis; boètica; recerca biomèdica basada en dades; Espanya.

1. Introduction

The increasingly important role of biobanks is worldwide recognised. Undeniably, today biobanks are fundamental infrastructures and resources for precision medicine and translational research since they have the capacity to provide for the huge amount of biospecimens and related data required by the advancement of those fields (Price II 2019). However, challenges and obstacles to an efficient use of biobanks persist almost everywhere. In particular, critical points are the lack of international common criteria on sample collection and sharing, and a lack of harmony among legal requirements (Beier & Lenk 2015).

To date, the European landscape of biobank regulation is characterised by an amalgam of differing, and often conflicting, laws and policies.

Despite some common legal and ethical references[1], the legal frameworks that apply to biobanks vary from country to country and are in constant evolution. Particularly, we can distinguish between three different regulatory cases (Beier& Lenk 2015; Ducato 2010; Penasa et al 2018): i) countries with a specific law on biobanking, e.g. Spain, Portugal, Belgium, Latvia; ii) countries with composite regulations for biobanks and which also resort to soft law tools, e.g. Italy, France, Germany; iii) countries with no domestic regulation which rely on international guidelines on sample and data collection and sharing.

Among the first group, Spain stands up because of the originality of its regulation on biomedical research and biobanking. Indeed, in 2007 with the entry in force of the *Ley 14/2007 de Investigación Biomédica* (LIB), Spain has introduced in the European scenario an innovative framework and legal tool to facilitate the development and regulation of the most cutting-edge fields of biomedical research (Romeo Casanova 2009). Over the past 10 years, this normative framework was supplemented first by the *Real Decreto 1716/2011* on the basic requirements for biobanks and the treatment of human biological samples. All together, they hold the merit to have tackled the most urgent controversial ethical and legal issues related to use of human samples and

1Those common references include both binding or soft law tools: Recommendation Rec(2006)4 on research on biological materials of human origins;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, Spain,1997; Regulation EU 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data; WMA Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, Helsinki, Finland, 1964 (last revision 2013); European Commission. Biobanks for Europe. A Challenge for Governance: Report of the Expert Group on Dealing with Ethical and Regulatory Challenges of International Biobank Research, Brussels, 2012; OECD - Guidelines on Human Biobanks and Genetic Research Databases, 2009; ISBER (International Society for Biological and Environmental Repositories), Best Practices for repositories: collection, storage, retrieval, and distribution of biological materials for research, 2012.

personal data in biomedical research and biobanking such as informed consent, secondary uses of data and samples and data confidentiality (Nicolás Jiménez 2015).

Nevertheless, as time and society progress, today the regulation of biomedical research and biobanking has to deal with the emergence of a complex and transformative phenomenon such as the convergence of biomedicine and big data (Costa 2014; De Lecuona & Villalobos-Quesada 2018). Despite its undoubted benefits, it bears a number of ethical and legal challenges which must be taken into account by European regulations and guidelines.

On the basis of the above considerations, the aim of this paper is two-fold. First, in a comparative perspective, I will analyse the merits of the Spanish regulation on biobanks in order to draw some lessons for the still blurred or unregulated situation in other European countries.

Secondly, I will reflect on the capability of biobank regulation to accommodate data-driven biomedical research and, in particular, I will question whether the ethical and legal framework introduced by the Spanish law at the beginning of this century is still able to hold the ground with the new contextual and societal challenges.

In this respect, I will suggest that there is space for implementation, at national and international level, if we look at implementing transparency, accountability and participation mechanisms while raising awareness on specific risks and challenges among the general public, participants and biobank stakeholders.

2. The first paradigm shift: Spanish regulation on biomedical research at the beginning of XXI century

The enactment of the Spanish law on biomedical research[2] (LIB) in 2007 responded to the urgent need of regulations in emerging areas that were previously unregulated or partially regulated such as genetic analysis, research with human biological samples and biobanks. It aimed to facilitate the advancements of the most innovative fields of biomedicine and, at the same time, it attempted to take advantage of research results for the collective health and wellbeing of citizens while ensuring the respect of individual rights and freedoms (Romeo Casabona 2009).

One of the most appreciated novelties introduced by this law is the regulation of the collection, use, storage and transfer of biological samples for diagnostic and research purposes in biomedical research. In this regard, the Spanish framework seeks to facilitate researchers the

2Ley 14/2007, de 3 de julio, de Investigación biomédica.

access to the largest number of samples and data on the basis of the values of transparency, quality and non-profit. Such an approach intended to promote the development of research projects of high quality together with a suitable respect for the wishes and rights of patients and participants (Arias-Diaz et al 2012).

In 2012 the LIB has found its reinforcement in the *Real Decreto 1716/2011*[3] on what concerns the basic requirements for authorization and operation of Biobanks for biomedical research purposes, the process of human biological samples and, finally, the creation of a National Registry of Biobanks.

In order to complete this overview on Spanish biobank regulation, we should also mention the *Ley Orgánica 3/2018*[4] on data protection and guarantee of digital rights which was enacted in 2018 as a national implementation of the European General Data Protection Regulation (GDPR). Although the latter does not directly refer to the biobank databases, it regulates the collection, treatment and processing of personal data in biomedical research which is very closely related to the everyday biobanking practice. In particular, its *disposición adicional decimoséptima* gives precise indications on informed consent procedures, secondary uses of data, the supervision of Ethics Committees, pseudonymisation and what technical and organizational measures have to be put in place when processing personal data.

Back in its days, the LIB was received with enthusiasm by legal and bioethical scholars for many reasons (Sánchez-Caro & Abellan-García Sánchez 2007).

First of all, it is worth noting that this regulation has responded promptly to the change of paradigm occurred in biomedicine at the turn of last century. Indeed, it has faced this sudden shift triggered by the convergence of new biotechnologies, discoveries in genetics and advances in information technologies, by ensuring the freedom of research and scientific production to keep the country up to date. At the same time, as stated in the preamble of the law, the regulation and the development of advanced research in the field of biomedicine tried to take into account the human and social context in which it develops in its daily practice.

Furthermore, what stands out is the valuable systematic work of the Spanish framework. In particular, it is appreciated the way in which the law identifies seven specific areas of biomedical research (i.e. research related to human health that uses invasive procedures, the donation and use of human germ cells, tissues and organs for research purposes, the storage and

3Real Decreto 1716/2011, de 18 de noviembre, por el que se establecen los requisitos básicos de autorización y funcionamiento de los biobancos con fines de investigación biomédica y del tratamiento de las muestras biológicas de origen humano, y se regula el funcionamiento y organización del Registro Nacional de Biobancos para investigación biomédica.

4Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales.

handling of human biological samples, biobanks, Spanish Committee on Bioethics) delimiting for each of them concrete aspects and priorities. For instance, the way in which biobanks are set up and structured facilitates the efficiency and the utility of these infrastructures for biomedical research (García-Merino 2015).

Another special mention has to be made to the way in which the regulation has shaped its founded principles and their application in each specific area. In line with the Oviedo convention, the regulation promotes the development of biomedical research and innovation in the respect of fundamental rights and freedoms. In the next section, I will explore deeper the merits of the Spanish regulation concerning research biobanks as well as the ethical principles that underpin it.

3. Remarkable points of Spanish Regulation on Biobanking

In this paragraph I shall present what I have identified as four remarkable points of the Spanish regulation applied to biobanking, namely the broad consent, the role of Research Ethics Committees, the emphasis on non-profit and the focus on the dual identity of human biological samples.

The analysis that has led me to extract the aforementioned points has been conducted through a comparison with the main scientific literature on the topic, international documents on biobanking such as OECD Guidelines on Human Biobanks and Genetic Research Databases (2009) and ISBER Best Practice for Repositories (2012), and other national specific regulations on biobank (Portugal, Belgium, etc.).

The aim here is to point out some lessons of good regulation and practice for those European countries that still lack specific laws and policies for biobanking. As often happens, the numerous positive points of the Spanish regulation that I will highlight below may present in parallel some criticism and incompleteness. However, I believe that they can provide important lessons likewise.

The first merit of Spanish regulation on biobanks is represented by its conceptualisation of informed consent. Indeed, the LIB represents one of the first cases in Europe where a more flexible approach towards the principle of informed consent in biomedical research and biobanking has made its way into legislation. Therefore, in order to facilitate the advancements in research, the traditional requirements of informed consent (i.e. specific and prior) have been adapted to the scope of biobanks, namely collecting samples and data prospectively (Casado da Rocha & Seoane 2008; Casado da Rocha & Etxeberria 2009).

As stated in art. 60.2, the LIB allows the possibility that "the initial consent may provide for the use of a sample for other lines of research related to those initially proposed". In other words, at the time of collection biobank participants might be asked to agree with a single act of consent to further unspecific uses of their samples and data within the biobank.

However, in opening up towards the open goal nature of biobanking and allowing a more flexible and broader consent (Arias-Diaz et al. 2013), the law subordinates the secondary uses of collected samples and data (i.e. the incorporation to a line of research that is not related to that for which the consent was initially granted) to the approval of the Research Ethics Committee (REC) of the centre (art. 62). Therefore, it is up to a REC supervising the biobank to make the decision on the unspecified research on the participant's behalf.

Against this broadening of the informed consent model entailed by the law, as we will see below, it must remain clear that the RECs' power of making decisions concerning permission to use already collected samples for new research purposes is always conditional on the consent given by the participant in the first place. Indeed, at the level of principles, this commitment of the LIB to balance participants' protection and research flexibility through the role of REC that act as an over-seeing third party can be interpretated as a way to compensate a decreasing degree of autonomy for the individual in decision making associated with biobanks (Casado da Rocha 2015).

The second point of strength of the Spanish regulation regards the role of Ethics Committees in the governance of biobanks. Particularly, in systematizing the organization of biobanks, the art. 66 of the LIB states that "the biobank shall have a scientific director, who is responsible for the files and shall be assigned to two external committees, one scientific and the other ethical, that will assist the director of the biobank in his or her functions". This disposition has been expanded by art. 15 of the *Real Decreto 1716/2011* and, in particular, art. 15.3 clarifies the functions of the external Ethics Committee. The scope of its functions ranges from assessing the requests for the use and transfer of samples and evaluating each research project presented by requestors to drafting and/or assessing consent forms models and ensuring data confidentiality (Jiménez et al. 2018). As such Ethics Committees hold a key role in the decision-making, governance and functioning of biobanks for several reasons (de Lecuona 2009; Garcia-Merino et al. 2015; Alfonso Farnós et al. 2016): first of all, they are the main decision-makers in reviewing and giving permission for any research project with human biological samples to proceed; they act as guarantors of individual rights such as privacy, dignity and freedom of research; thirdly, their oversight role is fundamental to generate trust among the general public and potential biobank participants as they are supposed to ensure the compliance with the ethical principles of biomedical research; finally, they have the function of balancing the importance of national and international sharing of sample and data for the growth of research with the local needs of each

institution, and for this reason a certain degree of criteria variation in their evaluations is expected and accepted.

In sum, the exercise of the function of approving exemptions to the informed consent principle – that we have discussed above – along with the task of assessing every single sample request and research project has resulted in making the Ethics Committee a powerful and principal body in the Spanish biobank governance.

This "Governance-by-Committee" approach, although it has the merit of ensuring adequate ethical oversight to biobanking services, lacks a set of uniform criteria of decision-making which would make the evaluation more homogeneous across the country (Garcia-Merino et al. 2015; Alfonso Farnós et al. 2016).

The third remarkable point that stands out from the analysis of the Spanish regulation from a more strictly ethical point of view is the strong reference to the principle of altruism and the emphasis on no-profit. Specifically, in line with the Council of Europe Convention for the Protection of Human Rights[5], in its art. 7 the LIB states that "the donation and use of human biological samples shall be gratuitous, whatever its specific origin, and the compensation that is provided for in this Law can in no way be of lucrative or commercial nature". In other words, the Spanish law allows biobanks to charge for obtaining, handling, shipping and distribution of samples for the sake of its own sustainability (Garcia-Merino et al 2015) but, at the same time, it respects the principle of no commercialization of the human body which is considered the bulwark of the protection of the human dignity (Gómez Sánchez 2007).

This emphasis that the Spanish regulation put on no-profit and no commercialization appears increasingly appropriate with the course of this century and the primary role taken by the market (Casado 2017). As brilliantly claimed by Sandel, it is now a fact that the logic and the values of the market have reached into spheres of life traditionally governed by non-markets norms (i.e. biomedicine) and, as such, it has fostered the commodification of everything (Sandel 2012): human biological samples and associated data included. Thus, while is true that the core mission of biobanks lies in collecting, organizing and providing high-quality biospecimens for the scientific community on the basis of an altruistic-based model, they are not immune to the logic and influence of the economic and cultural contexts in which they operate and, in particular, to the trends set by our market and information society (de Lecuona 2017).

5Council of Europe, European Convention for the Protection of Human Rights and Fundamental Freedoms, as amended by Protocols Nos. 11 and 14, 4 November 1950, ETS 5, available at: https://www.refworld.org/docid/3ae6b3b04.html [accessed 12 October 2020].

Finally, it is worth noting how the dual identity of human biological samples is repeatedly emphasized by the Spanish regulation. Starting from how it defines biological samples (art. 3) as "any biological material of human origin capable of conservation and that can hold information on the genetic endowment that is characteristic of a person", the LIB acknowledges the dual nature of human biological samples: along with their material value, samples are also data because they are sources of information of a personal nature (Gil 2012).

From this definition, we can derive the important conclusion that the Spanish framework on biomedical research and biobanking appreciates that the same general principles applied to personal data protection must be implemented when using human biological samples (Romeo Casabona 2007). The strength of this assumption, which represents an exception in the European legal frameworks, lies in the fact that the Spanish law has foreseen that samples and data should be treated in the same way in a context characterised more and more by data-driven research. However, we still have to assess if the Spanish model is able to keep up with the current change of paradigm in biomedical research triggered by the use of health-related big data.

4. The second paradigm shift: toward data-driven biomedical research and new challenges for biobank regulation

The Spanish regulation as we have discussed so far certainly presents an innovative approach in dealing with the crucial ethical and legal issues related to biomedical research and, back in the times it was enacted, represented a virtuous example of how the legislation should promptly respond to societal and contextual changes.

However, as technology and society progress ever more rapidly in the last few years, existing regulations and governance of biomedical research are facing the emergence of a complex and transformative phenomenon that is the convergence of biomedicine and big data. Undoubtedly, compared to the beginning of the XXI century when the previous paradigm shift occurred, biomedicine has undergone an accelerated push towards big data health research which is currently questioning both the sustainability of the existing regulations and the preparedness of biomedical research and biobanks to handle the increasingly data-intensive research model (Blasimme & Vayena 2019).

Within the context of the rise of the European data market[6], big data has also become highly valuable for health-related activities and, for this reason, biobanks draw more and more attention

6See the Commission's communication to the European Parliament, the Council, the European Economic and Social Committee and

to them. Indeed, as the material contained in biobanks generates a great amount of data (e.g. medical records, omics data, biomedical and biometric data, info about lifestyle), this information is organized in databases and can be proceeded in the context of big data.

Accordingly, the relationship between data-intensive health research (i.e. precision medicine) and biobanks gets tighter while the complexity of ethical and legal issues increases. On the one hand, precision medicine relies on larger cohorts of research participants for his advancement and, on the other one, biobank viability depends on the willingness of participants to donate their samples and data and ability to earn and maintain public's trust (De Lecuona & Villalobos-Quesada 2018). For these reasons, the way in which biobanks are regulated and structured is fundamental for both the advancement of biomedical research and their own sustainability.

In what follows, I will present some of the crucial challenges and risks that biobank regulation has to face since biomedical research has adopted the big data paradigm.

In the first place, the enormous value given to health and personal data in fostering biomedical research and innovation is forcing a reconsideration of the mechanisms of data confidentiality (Cohen 2012). Anonymisation and pseudonymisation which until now represented a guarantee of privacy and compliance with regulations in biomedical research and biobanking (e.g. GDPR) have been recently questioned (Casado et al. 2015). It is known, in fact, that computer engineering techniques make it possible to re-connect previously anonymised or codified personal data to the individual it belongs to.

Therefore, anonymity is increasingly becoming a relative concept and its role of confidentiality's keeper should be reconsidered in biomedical research and biobank regulation. In addition, even if biobanks adopt various strategies to protect personal data, it is a fact that the recourse to anonymity and pseudonymity both limits the research performance and does not ensure an adequate confidentiality (Garcia-Merino et al 2015).

Even with the enactment of the new GDPR in 2018 which was supposed to shed some light on the treatment of personal data for scientific research purposes (art. 9) and regulate research-related derogations from a set of participants' rights (art. 89), the regulation does not seem to have found a solution for participant data confidentiality and other individual rights that goes

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the Committee of the Regions "Towards a thriving data-driven economy" (com/2014/0442 final), available on EUR-Lex database, retrieved from <http://eur- lex.europa.eu/legal-content/ES/TXT/HTML/?uri=CELEX:52014DC0442&from=EN>, consulted on 12 October 2020.

beyond pseudonymisation and no better specified technical and organisational measures (Dove 2018; Stauton et al 2019).

To sum up, it is worth noting that the emergence of big data-driven biomedical research and its impact on biobanks was not adequately followed by a public comprehensive understanding of the business behind the extraction of value from health data or by a general acknowledgement of the importance of protecting personal data against discrimination or exploitation (Casado et al. 2015).

Besides, another important feature of the rise of data-driven health research is its proximity to values and logic coming from the market society. In particular, the data-driven economy pursued almost worldwide stimulates new health and wellness business models that are fed by personal data (e.g. health, genetic, lifestyle, behavioural information) without a proper understanding and control of their owners (de Lecuona 2017). Unsurprisingly, those business models are making their way in biomedical research by pursuing a financial gain over the commercialisation and exploitation of human biological samples and associated health data.

This growing trend is also affecting biobanks undermining the role of the aforementioned no-commercialization principle. In particular, biobanks are commonly approached by companies hired by researchers as intermediates whose job is to seek out and collect biobank materials and data for financial gain in place of their customers.

As such, it is very clear that this trend toward the transfer of property on body material and health data in exchange of financial rewards is controversial at least for two reasons: first, the morally problematic exploitation of materials and data donated within a solidarity-based framework (de Lecuona 2017); secondly, the harm and difficulties this may bring to patients' and participants' control over how their samples and data are used and with whom they are shared (Beier & Lenk 2015).

5. The preparedness of biobank governance for big data-driven biomedical research and the impact on Spanish regulation

In view of the challenges posed by the big data paradigm applied to biomedical research, in this section I shall question the preparedness of biobanks for this revolution and, in particular, its impact on Spanish regulation.

The following discussion is carried out on two levels: an ethical reflection on the role of bioethics as an effective support and guidance in the transition of biobank governance towards

the new paradigm will be followed by some practical considerations on the shortcomings of the Spanish regulation on biobanking.

Over the last decade, the rise of new features and issues brought by the intersection of biomedicine and big data has forced to acknowledge the shortage of the traditional biomedical ethics framework[7] based on a human rights and paternalistic approach as it was conceived starting from the 1950s. Indeed, those ethical principles that were the basis of the old framework (i.e. autonomy, dignity, beneficence, justice) are no longer sufficient to cope with new problems faced by research infrastructures ground in a digital society. This is because, so far, bioethics has been unable to adapt to the new scenarios in research and innovation since it seems to continue to use old patterns for dealing with new and very complex problems such as discrimination, risks of breaches of data confidentiality and market interests in place of common good and public interest (de Lecuona 2017).

In this scenario, however, a new remarkable trend was opened by the Declaration of Taipei on Ethical Considerations Regarding Health Databases and Biobanks[8] issued by the World Medical Association in 2016.

What stands out here is that this document, in accordance with the Declaration of Helsinki[9], recognised that in order to respect the dignity, autonomy, privacy and confidentiality of individuals, database and biobank governance must be governed by internal and external mechanisms based on the principles of protection of individuals, transparency, participation and inclusion, accountability.

Although today it is recognised that good biobank governance implies at a minimum transparency, accountability, public engagement strategies and the implementation of oversight mechanisms, the document suggests that much work must be done in order to clarify those new principles and to understand how to apply them in the specific context of biobanking.

Accordingly, bioethicists, legislators and biobank stakeholders should question what is the information that the public and participants actually need to interact in a proper and signified way; what it is the scope and the effectiveness accountability mechanisms; what are the adequate measures to protect participants and their data in research biobanks; what are the concrete risks in the everyday biobanking practice that the public and participants should be aware of (Gille et

7The Nuremberg Code (1946); the Belmont Report (1979); European Convention on Human Rights and Biomedicine (1997); Charter of Fundamental Rights of the European Union (2000); UNESCO Universal Declaration on Bioethics and Human Rights (2005).

8 WMA Declaration of Tapei on Ethical Considerations Regarding Health Databases and Biobanks, Tapei, Tiwan, 2016.

9 WMA Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, Helsinki, Finland, 1964 (last revision 2013).

al. 2020). Only by clarifying those points and translating the aforementioned new principles in the practice we will be able to go further in the bioethical and legal guidance of biobanks.

Another important point that is worth highlighting here is the gap between legal and ethical compliance that can occur after having applied the regulation in the context of biomedical research and biobanks. As recently raised by Floridi (2018), legal «compliance is necessary but insufficient to steer society in the right direction». For this reason, we should continue to engage in ethical evaluation also when legal compliance is already available.

If we apply this framework to the context of biobank governance and data protection regulation, it seems clear that while art. 9 and 89 of the GDPR provides clear guidance in terms of collecting and processing personal data for research purposes, the ethical assessment *ex-post* of the technical and organizational measures in place (i.e. pseudonymisation) might still detect some ethical limitations experienced by data subjects on their right to control the use of their personal data and biological material in research. Therefore, from the moment that in a data-intensive context anonymity becomes uncertain, it becomes urgent to establish a much clearer legal and ethical ground for legitimizing the suspension of individual rights such as the right to consent, to withdraw, to access and, in turn, enhancing ethical standards in the everyday biobanking practice (Staunton et al. 2019).

Moving to the consequences of the big data paradigm on the Spanish regulation on biobanking, it can be interesting to assess some of the points of our previous analysis in the light of the challenges that we have just considered.

Starting from the so-called Governance-by-Committee approach, we have seen that in the context of biobanks the law grants to RECs an extensive power when it comes to deliberate over secondary uses of samples and data, research projects and resources allocation. Furthermore, we highlighted the Spanish solution to accommodate the open-goal nature of biobanks by including in the legislation an opening up towards a broader and flexible consent.

However, many scholars have critically pointed out that while this model holds the merit of balancing protection and flexibility, it should not prevent from investing on participant empowerment and public engagement in the field of biobanks (Nicolás Jiménez & Romeo Casabona 2009; Casado da Rocha & Etxeberria 2009).

In other words, it is worth noting that the Spanish law has determined expert self-regulation (Casado da Rocha & Soane 2008) which, while it does act as ethical guarantee, it might not represent the best approach in dealing with the new data-driven paradigm. Indeed, the necessary loss of control over their samples and data experienced by biobank participants with the recourse to broad consent should be balanced with an effort of opening up toward a more inclusive and

participatory approach fostered by the new principles of transparency and trust which is growing in other domains of biomedical research (Casado da Rocha 2015).

Secondly, the emphasis on no-profit and the paramount position of the no-commercialization principle in the Spanish regulation may be undermined by the trend towards commodification and commercialization of biobank's resources brought by the big-data paradigm. In order to avoid that, the legislators and the RECs should be aware of the risks and ready to identify commercial interest where there should only be research purposes and preventing a scenario where a price is placed on human beings and personal data.

Finally, what we have emphasised as the acknowledgement of Spanish regulation on the dual identity of samples seems to well accommodate the shift towards a data-driven research. Therefore, the fact that the Spanish law has placed on the same level samples and data can be considered a good starting point in facing the new paradigm. But, what has been foreseen by the law should now be followed by a widespread acknowledgement in the general public, research participants and biobank stakeholders. That is, more information and education should be put in place in order to promote the concept that biobanks deal with resource that at the end of the day is all reduced to data. Therefore, in times where the research and the personal data are threatened by the risk of commodification and breaches in participant confidentiality, new strategies should be implemented to better communicate practical risks related to biobank practice and what accountability and protection mechanisms are put in place by each biobank.

To conclude and to advance some concrete solutions, the assessment of the preparedness of the Spanish model of biobank regulation and governance reveals some important opportunities of improvement in response to the big data revolution in biomedical research. First, the role of RECs as ethical safeguards should be balanced by the enforcement of participant-centred initiatives (Kaye et al 2012) and public engagement initiatives in order to educate participants and the general public regarding the benefit that they can bring to biomedical research and innovation when their values and expectations are adequately listened. Further, regulation and ethical guidelines should promote a change in education focused in bringing an appropriate understanding of the change of paradigm to all the stakeholders involved in biobanking. In particular, participants and the general public should be educated regarding values and risks associated with their health and personal data (Hood & Auffrey 2013) whereas biobank actors should be made aware that often there are markets hidden behind the free status and civic altruism of samples and data sharing (de Lecuona 2017).

Those implementations are in prospective the best ways to promote a biobank governance model in which a true participant and society empowerment springs as a spontaneous consequence of transparent and trustworthy procedures.

6. Conclusion

The Spanish regulation on biomedical research provides a successful example of promptness and originality of the law when it came to face the contextual and societal changes occurred at the beginning of the XXI century such as the advancement of genetic research and the heavy reliance on biotechnologies in biomedical research.

In particular, the part concerning biobanks is commendable for its effort to systematize a field that, at least at the European level, had not many precedents in terms of legal frameworks. Accordingly, in the first section of this paper, I have argued that the ways in which the Spanish law has conceived the broad consent, the role of RECs, the no commercialization principle and the focus on informational nature of human biological samples could provide a starting ground for those countries that are approaching now the process of regulating biobanks.

However, the new phenomenon of convergence of big data and biomedicine which has driven progress in research over the last few years along with the establishment of a European data market, is forcing a reconsideration of both the ethical and legal standards on which we have relied so far in conceptualizing biobank regulation. In particular, in the second section of this paper, I have maintained that the recourse to health-related big data in biomedical research is going to heavily affect biobank governance and regulation. Hence legislators, participants and biobank stakeholders should be aware of two main risks associated with the new paradigm shift: the vulnerability of confidentiality in a system where the concept of anonymity has become relative and the trend towards the commodification of human biological samples and associated data.

Moving further, in the third section, I have suggested that nowadays the process of thinking and systematizing biobank regulation should include an assessment of the preparedness of biobank governance in facing big data-driven biomedical research. This assessment should include first an understanding and clarification of the new principles of transparency, participation, individual protection and accountability in the everyday practice of biobanking; secondly, it is important to continue the ethical evaluation of biobanking practice beyond the legal compliance in order to implement ethical standards that are able to balance the loss of autonomy experienced by participants.

Finally, coming back to our Spanish case study, I have concluded that the current regulation should come to terms with the new paradigm shift and there is need of a reassessment of those that so far has been the strengths of the Spanish regulation model of biobanks. In that respect, I have argued that there is space for implementation by reducing the power of the experts in favour of effective participatory strategies and public engagement initiatives. Secondly, I believe that

regulations and soft tools should put more emphasis in preventing commercial and market interest in a context characterised by research and solidarity. Finally, the equivalence of biobank samples and data made by the Spanish law should be reinforced by a widespread communication and education on the importance of personal data biomedical research along with the concrete issues related to biobanking practice in order to ensure ethical procedures to empowered participants and general public.

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