Special issue

How Spanish biobanks have adapted the informed consent process during the Covid-19 pandemic

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ABSTRACT: Due to the situation caused by the Covid-19 pandemic, biobanks have adapted, among other processes, the obtaining of informed consents (IC). This paper details the most relevant elements of the applicable regulations, describes the adaptations done by some of the biobanks of the Spanish Biobank Network to manage the IC process, which have been approved by their Ethics Committees, and draws some conclusions from the results obtained from the survey carried out on these biobanks.

KEYWORDS: Biobanks; bioethics; Covid-19; informed consent; Spain

SUMMARY: 1. Introduction – 1.1. The context of biobanks in Spain – 1.2. Key concepts relating to informed consent – 1.3. The management of informed consent according to Spanish legislation – 1.4. The position of the main international and national organizations on the informed consent process during the Covid-19 pandemic – 1.5. The importance of Ethics Committees for the approval of protocol changes – 2. Methodology – 3. Results and discussion – 4. Conclusions.

1. Introduction

On January 31, 2020, the World Health Organization (WHO) declared the outbreak of Covid-19 infection as a public health emergency of international importance, which they raised to an international pandemic on March 11, 2020. In Spain, this circumstance led to the establishment of a state of national alarm on two occasions, in accordance with the measures provided for in two Royal Decrees[1,2].

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[1] Real Decreto 463/2020, de 14 de marzo, por el que se declara el estado de alarma para la gestión de la situación de crisis sanitaria ocasionada por la infección Covid-19 (BOE no. 67, of March 14, 2020).

[2] Real Decreto 926/2020, de 25 de octubre, por el que se declara el estado de alarma para contener la propagación de infecciones causadas por el SARS-CoV-2 (BOE no. 282, of October 25, 2020).

The pandemic has generated a major health crisis due to the high number of infected people, who pose a risk to the health of the population as a whole, and due to the high number of people who need health care, and with relative frequency, hospitalization and critical care, leading to a saturation situation of hospital emergencies and Intensive Care Units. In order to mitigate this situation and reduce the risk of contagion of the disease, when the first state of alarm was decreed, extraordinary measures of different kinds were adopted and applied to the entire population and, in particular, to those affected. On the other hand, emergency measures were also established to face the economic and social impact of Covid-19, including measures to support research on the infection. Thus, the activity of biobanks has been intensified due to an increase in the number of requests for samples, specifically from Covid-19 infected subjects, for use in research projects on the disease. The adaptation of biobanks to this new reality depends, among other factors, on the following ones[3]:

- Human resources (on-site or remote work) and material resources (facilities, equipment and security measures) available.
- The biosecurity guidelines established by the institution to which they are attached.
- The degree of difficulty of obtaining informed consent (IC) by a healthcare staff swamped with a lot of work, taking into account that the usual procedure for obtaining IC involves the signature of the patient (or legal representative, if applicable) and the reporting staff (health professionals).
- The different sources of the samples (surplus / expressly collected samples).
- The quantity, variety and time of collection of the samples to be stored.

Under these circumstances, biobanks are facing, when managing samples from patients with Covid-19, with situations that require a rethinking of the system to be used for the inclusion of samples and obtaining the IC.

1.1. The context of biobanks in Spain

Before addressing this issue, it is worth explaining what biobanks are like in Spain, since their governance, organizational characteristics and sources of funding are different in each European country[4]. In the case of Spain, biobanks for biomedical research purposes are regulated by the *Ley 14/2007, de 4 de julio de investigación biomédica* and the *Real Decreto 1716/2011, de 18 de noviembre*, which develops the mentioned Law. Biobanks are part of the strategic agendas of the National Health System for the promotion and improvement of public and universal healthcare. In fact, the rules that regulate them highlight their "vocation of public service", although it also defines them as "public or private, non-profit establishments that host a collection of biological samples (of human origin) conceived for diagnostic or biomedical research purposes, and organized as a technical unit with quality, order and destination criteria"[5,6]. Thus, a biobank must have a defined structure, a

[3] Spanish Biobank Network, *Gestión por los biobancos de la Red Nacional de Biobancos de la obtención de los consentimientos informados ante la pandemia para investigación sobre el SARS-CoV-2 y la enfermedad Covid-19* (Comité Asesor Ético-Legal, April 2020).

[4] I. MEIJER, J. MOLAS-GALLART, P. MATTSSON, *Networked research infrastructures and their governance: The case of biobanking*, in *Science and Public Policy*, 39 (4), 2012, 491-499.

[5] Ley 14/2007, de 3 de julio, de Investigación biomédica (BOE no. 159, of July 4, 2007).

[6] Real 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

scientific direction and a written operating regulation. As is logical, its main function is to provide quality samples to the scientific community.

These rules establish the authorization system for the constitution and operation of biobanks, which must be authorized by the Autonomous Communities and registered in the Spanish Biobank Register of the *Instituto de Salud Carlos III* (ISCIII). There are currently 75 biobanks authorized in Spain for biomedical research purposes.

The ISCIII, a Spanish organization of international reference in the field of Public Health and Biomedical Research, created, in 2009, the Spanish Biobank Network with the aim of providing high-level scientific, technical and technological support to R+D+i projects in science and health technologies, as well as encouraging innovation in health technologies, by supplying high-quality human biological samples and associated data.

During the last years, the efforts of this network, formed by 39 members, have focused on working in a coordinated but decentralized way, and on creating a catalogue of samples and a single window for sample requests. Although Spain is not a member of the European research infrastructure for biobanks BBMRI-ERIC (https://www.bbmri-eric.eu/), this organization has served as a model to define the work of Spanish biobanks and reconfigure their practices[7]. This fact confirms that, in the case of biobanks, governance tends to be based on guidelines and international collaboration, rather than on state or government action[8].

Since the beginning of the pandemic, the Spanish Biobank Network has played a key role in the coordination of national biobanks, by holding weekly informative meetings, preparing guides and recommendations for the management, collection and conservation of biobank samples from patients affected by Covid-19, to ensure their later usefulness both in terms of quality and integrity as well as the ethical-legal guarantee with respect to current regulations[3,9], and creating a national repository of clinical information associated with samples from patients affected by Covid-19 admitted at different stages of the disease. This information includes epidemiological and clinical aspects, biological markers, treatments and comorbidities, in short, data of interest for detailed knowledge of the characteristics of the patients.

Similar experiences are happening at the European and international level. The International Society for Biological and Environmental Repositories (ISBER) has fostered collaboration between countries to analyze the impact of the pandemic on biobanks globally, while the BBMRI-ERIC has organized two webinars that have helped to continuously monitor the evolution of the pandemic at the international level.

1.2. Key concepts relating to informed consent

The world is living in a reality in which it is necessary to establish a balance between reducing obstacles that appear during the conduct of an investigation, in search of efficiency in terms of time

biológicas de origen humano, y se regula el funcionamiento y organización del Registro Nacional de Biobancos para investigación biomédica (BOE no. 290, of December 2, 2011).

[7] V. ARGUDO-PORTAL, M. DOMÈNECH, *The reconfiguration of biobanks in Europe under the BBMRI-ERIC framework: towards global sharing nodes?*, in *Life Sciences, Society and Policy,* 16:9, 2020.

[8] A.C. DA ROCHA, *Biobancos, cultura científica y ética de la investigación*, in *Dilemata*, 4, 2010, 1-14.

[9] Spanish Biobank Network, *Guía de la Red Nacional de Biobancos para el manejo de muestras humanas en investigación biomédica. Recomendaciones ante la pandemia de Covid-19* (April 2020).

and needs, and the guarantee of its methodological rigor. Depending on whether one or the other of these aspects is given more importance, four types of IC can be considered[10]:

- Specific/closed consent. The donor gives consent for a specific research project. Therefore, it is not possible to carry out secondary research derived from samples stored in biobanks, since at the time of donation there is no information on the future research in which the sample will be used. The solution would be to ask donors for new consent to use the sample previously stored in the biobank, although this can be annoying for them and ineffective for research, and end up causing a reduction in the number of available participants.
- Broad consent. The donor gives consent not only for specific studies, but also extends the acceptance to any class or line of research that the biobank deems appropriate. In this way, advances in research are facilitated.
- Blanket/open consent. The donor gives consent, without restrictions regarding the scope and duration of the research, for any future use of his biological sample and its associated clinical data, including forensic and commercial uses. This type of consent requires minimal administrative and organizational effort. It is used by most genetic data biobanks.
- Dynamic consent. This consent is based on the use of modern communication strategies (computer tools) to inform, involve, offer options and obtain consent for each of the research projects that may be derived from a biological sample. This is a model of continuous two-way communication between donors and researchers, thus overcoming the ethical problem that passive participation implies. It generates greater trust on the part of donors in the research, since participants have control over the use of their biological samples and associated clinical data.

Given these possibilities, it should be noted that there are two different approaches that guarantee the privacy of personal data associated with biological samples and with other relevant data from a public health point of view:

- Anonymization, or irreversible disassociation, which is defined as the "process by which it is no longer possible to establish by reasonable means the link between a piece of data (or a biological sample) and the subject to whom it refers" (art. 3.c) of the *Ley de Investigación biomédica*). This same law also defines, in art. 3.i), the anonymised or irreversibly disassociated data as that "data that cannot be associated to an identified or identifiable person as the nexus with all information that identified the subject has been destroyed or because such association demands a non-reasonable effort, understood as the use of disproportionate amounts of time, expense and work"[5].
- Pseudonymisation, or reversible disassociation, which is defined as that "processing of personal data in such a way that it can no longer be attributed to an interested party without using additional information, provided that said additional information appears separately and is subject to technical and organizational measures designed to guarantee that the personal data is not attributed to an identified or identifiable natural person" (art. 4.5 of Regulation (EU)

[10] N. SERRANO-DÍAZ, E. GUÍO-MAHECHA, M.C. PÁEZ-LEAL, *Consentimiento informado para Biobancos: Un debate abierto*, in *Revista de la Universidad Industrial de Santander. Salud*, 48(2), 2016, 246-256.

2016/679)[11]. This concept also appears in the *Ley de Investigación biomédica,* although with different terminology, since art. 3.k) defines the codified or reversibly disassociated data as that "data that is not associated to an identified or identifiable person as the information that identified that person has been substituted or detached using a code that allows the reverse operation"[5]. In simpler terms, pseudonymising consists of substituting one attribute for another in a record.

Thus, the anonymization can be considered absolute, since it is not possible to know, by reasonable means, the personal data that were originally processed. On the contrary, in the case of the pseudonymisation, the person responsible for the data could reverse the process in order to access the information subject to protection.
For all the above, it is recommended that the less restrictive the type of consent granted by donors is regarding the possible uses of the sample or the data, the greater security measures are used to preserve their identity.

1.3. The management of informed consent according to Spanish legislation

In Spain, the use of biological samples of human origin and associated data in biomedical research is currently regulated by three legal instruments[5,6,12] that include exceptional cases and special regimes that contemplate the adaptation of obtaining IC to the clinical situation of the subject, the pandemic situation and the need for research for public health reasons, and which have been taken into account to assess the situation in each biobank and decide how to proceed in this regard.
It is established that the "obtaining of biological samples for biomedical research shall be undertaken solely when the previous written consent has been obtained from the source subject". The requirements established by Spanish legislation for the generic IC model tallies with broad consent. This consent will also be essential when "the aim is to use biological samples for biological research that have already been obtained for a different purpose, irrespective of whether there is an anonymization"[5].
However, there are some exceptions to this obligation. "Codified or identified samples for biomedical research may be used without the consent of the source subject in situations of exceptional relevance and gravity for public health or when the obtaining of this consent is not possible or it entails a non-reasonable effort. In these cases, the favourable verdict of the corresponding Research Ethics Committee (REC) shall be necessary, which must take into account, at least, the following requisites[5,6]:

a) That the research is of general interest.
b) That the research is undertaken by the same institution that requested the consent for the obtaining of samples, if such consent is necessary.

[11] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (Official Journal of the European Union L 119, 4.5.2016).
[12] Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales (BOE no. 294, of December 6, 2018).

c) That the research is less effective or not possible without the identifying data of the source subject.
d) That there is no record of an express objection of the source subject.
e) That personal data is guaranteed confidentiality.
f) That there is no viable alternative to carry out the project with another group of samples for which consent is available."

Moreover, the *Ley Orgánica 3/2018, de Protección de Datos* adds that "health authorities and public institutions with powers in public health surveillance may carry out scientific studies without the consent of those affected in situations of exceptional relevance and severity for the public health". On the other hand, if the study is carried out by a research group, the consent of the subject for the secondary use of the data (study related to the initial research) can be dispensed with when the following conditions are met[12]:

- The data is pseudonymised.
- There is express authorization from the corresponding REC.

The Spanish legislation also regulates other aspects related to the management of IC by biobanks:

- Time of signing the consent (art. 60.1 and 60.2 of the *Ley de investigación biomédica* and art. 23.4 of the *Real Decreto 1716/2011*)
- Information prior to consent (art. 59 of the *Ley de investigación biomédica* and art. 23.2 and 23.3 of the *Real Decreto 1716/2011*)
- Confidentiality of the source subject (art. 59.1.h) of the *Ley de investigación biomédica*, additional provision 17.2.d) of the *Ley Orgánica 3/2018, de Protección de Datos* and art. 34.3 of the *Real Decreto 1716/2011*)
- Possible purposes of obtaining samples (art. 22.2 of the *Real Decreto 1716/2011*)
- Final destination of non-biobank samples (arts. 59.1.f) and 61.1 of the *Ley de investigación biomédica* and art. 27 of the *Real Decreto 1716/2011*)
- Use of samples from certain groups (art. 58.5 of the *Ley de investigación biomédica* and arts. 23.2.n) and 26.1 of the *Real Decreto 1716/2011*)
- Use of samples from other countries (art. 31 of the *Real Decreto 1716/2011*)

1.4. The position of the main international and national organizations on the informed consent process during the COVID-19 pandemic

In clinical practice, there may be situations in which it is not possible to obtain IC by the usual means and it must be requested by other means, such as orally, or even the need for the exemption of obtaining it should be considered. In fact, as early as 1964, the Declaration of Helsinki of the World Medical Association provided that, in the case of exceptional situations in which it is impossible or impractical to obtain consent for a research, it can only be carried out after being considered and approved by a REC[13].

[13] WMA, Declaration of Helsinki – Ethical Principles for Medical Research involving Human Subjects. Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964.

The International Bioethics Committee (IBC) has indicated that, although the secondary use of health data requires a new specific consent, such rule finds an exception when procedures such as pseudonymisation are implemented, which prevents researchers or third parties from accessing personal data[14]. Another four requirements are added to this one (apparent public interest in the research; difficulty in obtaining a new consent; legal origin of the data; and evaluation by a REC).

The pandemic has highlighted the need to find choices to the usual ethical review procedures. In the current context, the Pan American Health Organization and the World Health Organization itself encourage the practice of broad consent for the use of samples and data in future research that is not planned yet but will probably be designed as new information emerges[15].

Along the same lines, the Bioethics Committee of Spain, in an emergency such as the current one, recommends authorizing the secondary use of health data and biological samples without requiring a new express consent from the source subjects or, in the case of deceased people, their legal representatives. It also emphasizes that the data and samples from health centers that have taken part in the treatment of patients infected with the SARS-CoV-2 virus should be considered, in general, of legal origin, as it is understood that the patients have given their consent to the treatment or any of the exceptions to consent provided by law has occurred[16]. In addition, it indicates that, for this secondary use without express consent to be reasonable, it must have a very relevant interest for the health of the community and enough guarantees must be implemented to prevent non-legitimized third parties from accessing the individual's identity through the data. As expressed above, this can be achieved through two different approaches: anonymization and pseudonymisation. The authorization of the corresponding REC is also necessary, as established in the additional provision 17.2 of the *Ley Orgánica 3/2018, de Protección de Datos*. The Bioethics Committee of Spain makes all these recommendations based on the legal regime applicable to these cases, which it explains in depth in section 3 of its report.

On the other hand, and although it does not directly affect the field of biobanks, the approach of the European Medicines Agency regarding the management of ICs for clinical trials during the pandemic is also relevant. This body has stated that "unless linked to the implementation of urgent safety measures, changes in IC procedures will need to be reviewed and approved by the relevant ethics committee in advance", and that "in case a sponsor plans to initiate a trial aiming to test new treatments for Covid-19, advice should be sought on alternative procedures to obtain IC, in case the physical consent cannot leave the isolation room, and therefore is not appropriate as trial documentation"[17]. And it adds that "if re-consent is necessary for the implementation of new urgent changes in trial conduct, alternative ways of obtaining such re-consent should be considered during the pandemic. These could comprise contacting the trial participants via phone or video-calls and

[14] International Bioethics Committee, UNESCO, *Report Of The IBC On Big Data And Health* (Paris, 15 September 2017).

[15] Pan American Health Organization (World Health Organization, Regional Office For The Americas), *Ethics guidance on issues raised by the novel coronavirus disease (Covid-19) pandemic* (Washington, D.C., March 16, 2020).

[16] *Informe del Comité de Bioética de España sobre los requisitos ético-legales en la investigación con datos de salud y muestras biológicas en el marco de la pandemia de Covid-19* (Madrid. April 28, 2020).

[17] European Medicines Agency, *Guidance on the management of clinical trials during the Covid-19 (coronavirus) pandemic* (Version 3, 28/04/2020).

obtaining oral consents, to be documented in the trial participants' medical records, supplemented with e-mail confirmation. Any consent obtained this way should be documented and confirmed by way of normal consent procedures at the earliest opportunity when the trial participants are back at the regular sites".

1.5. The importance of Ethics Committees for the approval of protocol changes

There is no single method that all Spanish biobanks can apply, it is difficult to establish a harmonized procedure for all of them. In any case, changes in the management of obtaining ICs must be endorsed by the opinion of the Ethics Committee to which the biobanks are attached (REC), which makes an assessment, taking into account the following aspects[3]:

- The implementing legislation. Apart from the three previously mentioned legal texts of state scope, it should be noted that, during the first state of alarm caused by Covid-19, only one of the seventeen autonomous communities that make up the country (Galicia) has specifically regulated the management of IC by biobanks during the health emergency period[18].
- The urgency of availability of samples for projects on Covid-19.
- The circumstances of each biobank.
- The inability of obtaining IC in a hospital by non-health staff.
- The infectious capacity of the physical IC document.
- The isolation of the admitted subjects and the severity of their condition, which affects their ability to consent.

Taking into account all these factors, RECs can choose from different decisions, ranging from authorizing total exemption from obtaining the IC to forcing consent to be obtained through the usual procedure, including intermediate options such as obtaining the IC in the near future or authorization of oral consent or in electronic format.
The role of the RECs is also essential in evaluating the requests for samples received by biobanks and the methodological, ethical and legal quality of research projects. This process is a new point of control and verification of compliance with the procedure that had been established to obtain ICs, always trying to guarantee respect for the fundamental rights of people, also and, specially, in times of health emergency[19].

2. Methodology

In order to better understand how the management of ICs by Spanish biobanks has worked since the Covid-19 pandemic began, an online survey (Annex) was carried out, the preparation of which was based, among other sources, in a report published by the Spanish Biobank Network in April 2020. The survey was sent to 43 biobanks from the coordination office of the network itself, a large majority of

[18] Orden de 2 de abril de 2020 por la que se aprueban medidas en materia de investigación sanitaria en los centros del Sistema público de salud de Galicia durante el período que dure la emergencia sanitaria por el COVID-19 (Diario Oficial de Galicia no. 68, of April 7, 2020).
[19] A. Cervera Barajas, M. Saldaña Valderas, *Investigación clínica y consentimiento informado en época de pandemia COVID-19. Una visión desde la ética de la investigación*, in *Medicina Clínica*, 2020.

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them being members of it. According to the Spanish Biobank Register, there are 75 biobanks authorized to act as such in Spain[20], so the number of biobanks to be surveyed represents a sufficiently representative sample to draw conclusions.
Although participation in the survey was voluntary, a thank you message was sent to all those biobanks that offered their collaboration. Biobanks had 9 calendar days (from March 8 to March 16, 2021) to answer the 13 questions posed in the survey.
At the beginning of the survey, the identification of the biobank that responded was requested. This request was made to check that a single answer had been obtained for each biobank. The scientific directors of the biobanks were informed of this point and warned that the data obtained would be published, in any case, anonymously and in an aggregate manner. The survey contained two filter questions (see survey in Annex):

- Question 2. If "No" was answered, the survey ended at that point;
- Question 7. If the answer was "Yes", then another question included in question 7 itself would appear. If the answer was "No", you would advance directly to question 8.

3. Results and discussion

Finally, the survey was answered by 36 of the 43 biobanks to which it was sent, which represents a participation rate of 84%. Considering that there are 75 authorized biobanks in Spain, the study includes information on almost 50% of the authorized Spanish biobanks. The biobanks that have participated in the survey come from the following autonomous communities: Aragón, Asturias, Balearic Islands, Basque Country, Cantabria, Castilla y León, Catalonia, Community of Madrid, Galicia, Murcia, Navarra and Valencian Community.
91.7% of the total number of biobanks that responded to the survey have managed samples for projects or created a collection of patients affected by Covid-19 in the course of the pandemic, and 75% have modified the procedure of obtaining IC, which involves its signature by the patient (or the legal representative) and the reporting staff.
Considering that the rest of the questions in the survey have focused on the modifications carried out in the way of managing IC, the results presented below correspond to a total of 27 biobanks. The remaining 25% did not answer any more questions in the survey.
It is especially striking that, among the 25% of the biobanks that did not modify the usual procedure for obtaining IC, there are several biobanks from hospitals in the Community of Madrid, the autonomous region most affected by the pandemic during the first of the two states of alarm.

Statistical analysis of the biobanks that were forced to modify the procedure for obtaining IC

One aspect that has been asked about has been the dates during which biobanks have been affected in obtaining the IC of Covid-19 patients, considering two different periods:

[20] https://biobancos.isciii.es/ListadoBiobancos.aspx (last visited 11/03/2021).

- First state of alarm caused by the Covid-19 disease (from March 14 to June 21, 2020). During this period, 17 of the 27 biobanks whose way of obtaining IC was affected did so from the week following the declaration of the state of alarm, which reflects the speed of action. This situation lasted until June 21 in 26 of the 27 biobanks.
- From the end of the first state of alarm to the start date of the survey. During this period, almost 90% of these 27 biobanks had their way of obtaining IC affected. This situation began on the same day as the end of the first state of alarm (June 22, 2020) for 75% of them. On the other hand, for 66% of biobanks, this situation lasted until the start date of the survey, that is, it was still in force at that time.

Regarding the Covid-19 patient samples managed by the biobanks, 25.9% of them have worked only with surplus healthcare samples, 11.1% have worked only with expressly collected samples, and the remaining 63% have worked with both types of sample.
In Figure 1, you can see how the management of IC has changed in biobanks for the case of patients diagnosed with Covid-19. These data are closely related to those obtained in question 12, which can be seen in Figure 2. The alternatives to the standard obtaining of the IC have been based mainly on allowing the exemption of its obtaining or the verbal consent.

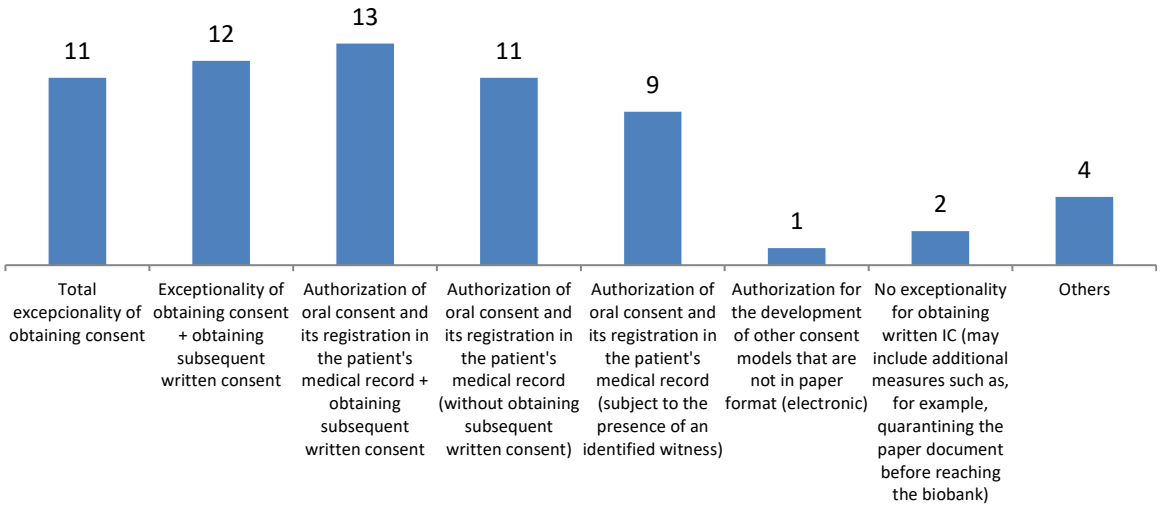

Figure 1. Measurement of the frequency in the application of several action choices regarding obtaining the IC of COVID-19 patients in Spanish biobanks (The same biobank may have applied more than one option)

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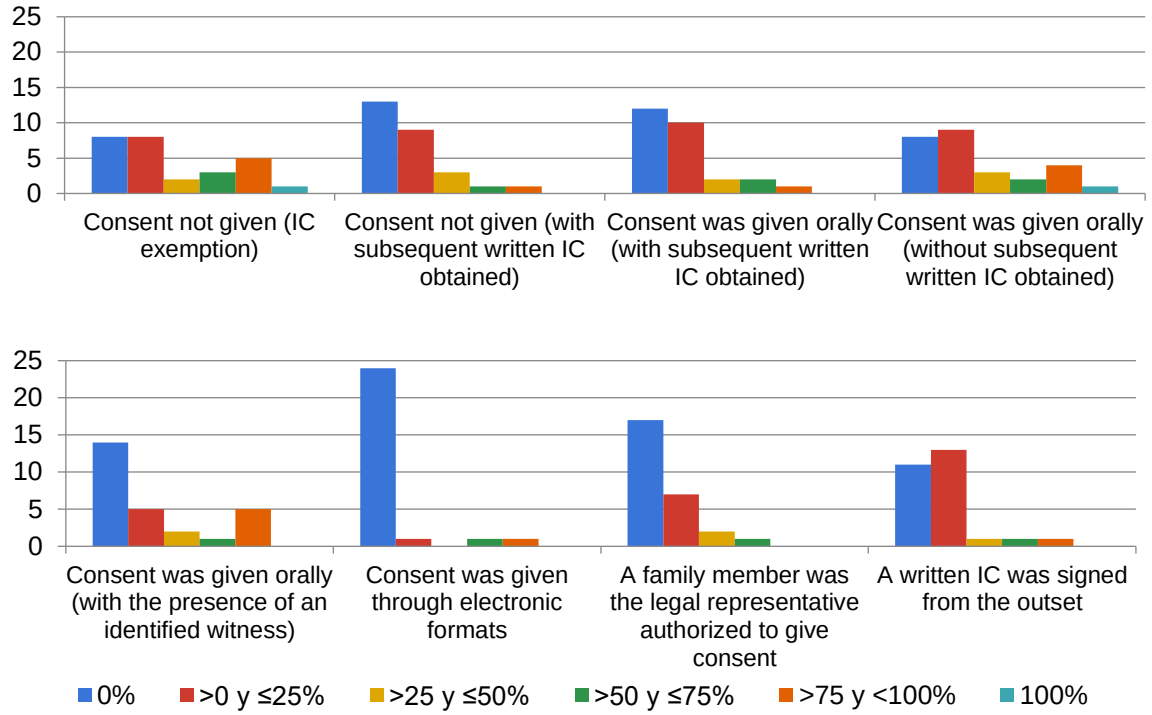

Figure 2. Estimation of the percentage of people who are in different situations related to IC with respect to the total number of people from whom a COVID-19 sample was obtained for biobank (The ordinate axis represents the number of biobanks that chose each percentage section as a response)

Regarding the people who did not sign the written IC from the outset, the process to collect that document in paper format is active in 44.4% of the biobanks (dated March 8, 2021), while in the rest is not active because it has not started (25.9%), has already finished (3.7%) or is not applicable (25.9%). In the cases in which the process is underway, the average percentage of people from whom the document has already been obtained is 45.7%.

For 51.9% of biobanks, the new way of IC management has undergone a modification again. Table 1 shows which have been both the most common previous and later options with respect to this modification. In this case, modification should be understood as the verdict of a REC. Therefore, the previous options are those allowed by the REC before the verdict, and the later options are those allowed by the REC after the verdict. It should be noted that neither the previous nor the later options contemplate obtaining IC through the usual procedure as the only possibility allowed.

	Previous option	Later option
Total exceptionality of obtaining consent	9	3
Exceptionality of obtaining consent + obtaining subsequent written consent	9	9
Authorization of oral consent and its registration in the patient's medical record + obtaining subsequent written consent	9	8
Authorization of oral consent and its registration in the patient's medical record (without obtaining subsequent written consent)	8	6

Authorization of oral consent and its registration in the patient's medical record (subject to the presence of an identified witness)	3	4
Authorization for the development of other consent models that are not in paper format (electronic)	1	2
Authorization of the consent given by the patient's relatives + subsequent consent of the patient	2	2
No exceptionality for obtaining written IC (may include additional measures such as, for example, quarantining the paper document before reaching the biobank)	1	2
Others	1	0

Table 1. Number of biobanks whose RECs chose different choices in terms of obtaining the IC of COVID-19 patients as previous and/or later options regarding a change in the way of proceeding during the time in which the obtaining was not carried out by the usual method (14 biobanks have participated in these statistics)

Regarding the verdict of exceptionality, without being the options raised in question 8 mutually exclusive, 70.4% of the biobanks have affirmed that it was requested by themselves, while 22.2% recognized that it was requested by research groups of their center whose samples were prepared in the biobank. On the other hand, 29.6% of the biobanks admit that the verdict was issued by their REC without previous request.

These verdicts could have been motivated by the existence of other previous documents. Table 2 shows the influence of several reports or legislation on the verdicts of the RECs:

Autonomous (regional) legislation (decree, order ...)	6
Verdict/recommendation of a Reference Committee	8
AEPD (Spanish Agency for Data Protection) report on data processing in relation to COVID-19	8
Bioethics Committee of Spain report on the ethical-legal requirements in research with health data and biological samples in the framework of the COVID-19 pandemic	8
Document prepared by the Spanish Biobank Network "Management of obtaining ICs by the biobanks of the Spanish Biobank Network in the face of the pandemic for research on SARS-CoV-2 and the COVID-19 disease"	11
None of these options	6

Table 2. Measurement of the influence that the publication of different documents has had on the REC's verdicts of exceptionality (The numbers indicate how many biobank RECs relied on each document for the preparation of the verdict. Each biobank has been able to choose more than one option)

It should be noted that two of the responses that marked the option "None of these options" (Table 2) did so because the information for which it is asked was unknown in the biobank, referring to the REC to which they are assigned as responsible of the decision. In only 3.7% of the biobanks, the verdict of exceptionality was applied to all their active collections, while in 85.2% it was applied to the collections of patients affected by Covid-19. In addition, in 25.9% of the biobanks the verdict was applied to the Covid-19 patient samples prepared in the biobank and linked to research projects.

On the other hand, it should be noted that, in at least one in three centers, the verdict of exceptionality has not been applied equally to biobank samples than to samples linked to research projects on Covid-19 (however, it is necessary to indicate that half of the respondents do not know if it has been applied equally or not, so it is possible that the real data is much higher than that which

has been reviewed). Some of the differences that have been recorded in the survey in this regard are:

- "Total exceptionality of consent in research projects, although with anonymization obligation";
- "Absence of verdict for samples destined to projects";
- "Absence of written consent in the case of the biobank, and written consent signed by a witness in the case of the project";
- "Samples of non-Covid-19 patients collected with the usual consent".

4. Conclusions

Different conclusions can be drawn from the results obtained in the survey. First of all, it is evident that a large majority of Spanish biobanks have managed Covid-19 patient samples. Thus, it is clear that the activity of these research facilities has been altered by the pandemic, as has happened in all areas of the Spanish health system.

It has also been reflected in the results that this management of Covid-19 patient samples has caused an alteration in the usual way of obtaining IC in the case of most biobanks. Although this alteration was very frequent during the first state of alarm, it has continued to be present, albeit with a slightly lower frequency, in subsequent months. So much so that, in March 2021, approximately half of the biobanks that have managed Covid-19 patient samples (17 out of 33 biobanks) have not yet recovered the usual procedure for obtaining consent.

About 90% of the biobanks that have managed this type of sample have received surplus healthcare samples, which confirms that they have faced difficulties in obtaining IC through the usual course. The vast majority of RECs have made decisions so that biobanks could adapt to this situation. The most widespread response among RECs has been to allow exemption in obtaining consent or authorization of oral consent, subject, in both cases, to obtaining written consent at a future time when conditions are more favourable. For this reason, 70% of biobanks are currently collecting these documents or pending to start collecting them. On the contrary, the authorizations of electronic formats of consent or of relatives as legal representatives have been little-explored options.

It should be remembered that obtaining the IC in a future time under more favourable conditions is not compulsory when the use of the samples and data has been carried out in the framework of a public health emergency, as explained above. However, it can be a guideline made by a REC, which should not be understood as a legal obligation, but a moral one. Therefore, a refusal by the patient to consent to this retrospective use would not imply a legal problem, and it would even be possible to continue using said data if it is considered essential, usually on the condition that they are subjected to an anonymization process (or, in other words, an irreversible disassociation).

Notwithstanding the above, for half of the biobanks, the verdicts of the RECs for the transfer of samples from biobanks to research projects have undergone modifications during the course of the pandemic. In this sense, it should be noted that the total exceptionality of consent (that is, without the obligation to obtain it in the future) was an option that was frequently allowed at the beginning of the pandemic but that has no longer been allowed so assiduously in later months, perhaps because the health emergency (volume of work in hospitals, need for research samples) decreased

its level of severity. This is a clear indication of the fair balance that has been attempted to be maintained between the rights of the individual and the benefit of the collective.

In one out of every three cases, the verdict of exceptionality was issued by the REC by its own initiative. This means that, in most cases, it was the hospital's own biobank or research groups who asked the RECs for an exceptionality. It is worth highlighting the uniformity of action in those Autonomous Communities that have a Reference Ethics Committee or a single REC compared to those in which each center has its own.

Furthermore, the report that most influenced the verdicts of the RECs was the one prepared by the Spanish Biobank Network[3], which is a symptom of the importance of this Research Platform as a benchmark for the biobanks of the country. However, this document already included, at the time of its publication, the verdicts available from some RECs in relation to the management of Covid-19 patient samples by biobanks. Although only one Autonomous Community urgently published specific legislation, it can be said that it was the fastest and most effective action.

In general terms, the data show that the use of samples in research projects on Covid-19 has suffered more restrictions than the inclusion of this type of samples in biobanks. This circumstance is in line with Spanish legislation, which establishes that, while health authorities can carry out studies without IC of those affected in particularly serious situations, IC can only be dispensed with for secondary use of these data and samples by a research group when they have been pseudonymised and there is a favourable verdict of a REC[12].

It is also important to note that, in only one of the 27 biobanks, the verdict of exceptionality was applied for all types of active collections, in addition to the Covid-19 collection. This fact implies a high degree of compliance with the law, which indicates that written IC can only be dispensed with in cases of "general interest" or for public health reasons. In other words, the health emergency was not a sufficient reason for the exceptionality to become a generalized method. Thus, in most biobanks, the IC for sample types already collected before the onset of the pandemic continued to be obtained by the standard procedure. This is a significant fact of the legal and ethical rigor with which the RECs acted and that the exceptions to the general rule should be well justified.

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ANNEX

SURVEY ON INFORMED CONSENT (IC) MANAGEMENT DURING THE PANDEMIC

***Mandatory**

Biobank name (The biobank name is a field that will be kept confidential and is only collected to ensure that only one survey per biobank is answered)*:

Autonomous Community to which the biobank belongs*:

1. Has your biobank managed samples for projects or created any collections of patients affected by COVID-19 during the pandemic?*
   - ☐ Yes
   - ☐ No

2. Has the obtaining of IC been affected at any time and cannot be carried out by the usual procedure that involves signing it by the patient/legal representative and the reporting staff?*
   - ☐ Yes
   - ☐ No

(If you answer "No" in question 2, the survey ends and is sent. If you answer "Yes", you continue to answer the following questions)

3. Taking into account only the period that includes the initial state of alarm (from March 14 to June 21, 2020), could you indicate the dates between which obtaining the IC of COVID-19 patients has been affected? (Please answer this question only if applicable to you)

   From _____ to _____
   (Dates are chosen from a drop-down calendar)

4. Taking into account only the period from the end of the initial state of alarm (June 21, 2020) to the present, could you indicate the dates between which obtaining the IC of COVID-19 patients has been affected? (Please answer this question only if applicable to you)

   From _____ to _____
   (Dates are chosen from a drop-down calendar)

5. The COVID-19 patient samples managed by the biobank are (You can indicate more than one option)*:
   - ☐ Surplus of healthcare samples
   - ☐ Expressly collected samples

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6. In what terms has obtaining the IC of COVID-19 patients been affected? (You can indicate more than one option)*
   - ☐ Total exceptionality of obtaining consent
   - ☐ Exceptionality of obtaining consent + obtaining subsequent written consent
   - ☐ Authorization of oral consent and its registration in the patient's medical record + obtaining subsequent written consent
   - ☐ Authorization of oral consent and its registration in the patient's medical record (without obtaining subsequent written consent)
   - ☐ Authorization of oral consent and its registration in the patient's medical record (subject to the presence of an identified witness)
   - ☐ Authorization for the development of other consent models that are not in paper format (electronic)
   - ☐ No exceptionality for obtaining written IC (may include additional measures such as, for example, quarantining the paper document before reaching the biobank)
   - ☐ Others. Indicate: _____

7. Has the way of obtaining consent undergone changes during the time that it has not been carried out by the usual procedure?*
   - ☐ Yes
   - ☐ No

(If you answer "Yes" in question 7, you continue to answer what is asked in this same question. If you answer "No", you go directly to question 8)

Indicate from which previous option to which later option the biobank has switched to (You can indicate more than one option):

Previous options:

- ☐ Total exceptionality of obtaining consent
- ☐ Exceptionality of obtaining consent + obtaining subsequent written consent
- ☐ Authorization of oral consent and its registration in the patient's medical record + obtaining subsequent written consent
- ☐ Authorization of oral consent and its registration in the patient's medical record (without obtaining subsequent written consent)
- ☐ Authorization of oral consent and its registration in the patient's medical record (subject to the presence of an identified witness)
- ☐ Authorization for the development of other consent models that are not in paper format (electronic)
- ☐ Authorization of the consent given by the patient's relatives + consent of the subsequent patient
- ☐ No exceptionality for obtaining written IC (may include additional measures such as, for example, quarantining the paper document before reaching the biobank)
- ☐ Others. Indicate: _____

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Later options:

- ☐ Total exceptionality of obtaining consent
- ☐ Exceptionality of obtaining consent + obtaining subsequent written consent
- ☐ Authorization of oral consent and its registration in the patient's medical record + obtaining subsequent written consent
- ☐ Authorization of oral consent and its registration in the patient's medical record (without obtaining subsequent written consent)
- ☐ Authorization of oral consent and its registration in the patient's medical record (subject to the presence of an identified witness)
- ☐ Authorization for the development of other consent models that are not in paper format (electronic)
- ☐ Authorization of the consent given by the patient's relatives + consent of the subsequent patient
- ☐ No exceptionality for obtaining written IC (may include additional measures such as, for example, quarantining the paper document before reaching the biobank)
- ☐ Others. Indicate: _____

8. The verdict of exceptionality ... (You can indicate more than one option)*:
   - ☐ was requested from the biobank itself.
   - ☐ was requested by research groups of my center whose samples were prepared in the biobank
   - ☐ was issued by the Research Ethics Committee (REC) to which the biobank is attached, without previous request.

9. The verdict of exceptionality was supported… (You can indicate more than one option)*:
   - ☐ by the publication of autonomous (regional) legislation (decree, order...).
   - ☐ by a verdict/recommendation of a Reference Committee
   - ☐ by the AEPD (Spanish Agency for Data Protection) report on data processing in relation to COVID-19 (https://www.aepd.es/es/documento/2020-0017.pdf)
   - ☐ by the Bioethics Committee of Spain report on the ethical-legal requirements in research with health data and biological samples in the framework of the COVID-19 pandemic (http://assets.comitedebioetica.es/files/documentacion/Informe%20CBE%20investigacion%20COVID-19.pdf)
   - ☐ by the document prepared by the Spanish Biobank Network "Management of obtaining ICs by the biobanks of the Spanish Biobank Network in the face of the pandemic for research on SARS-CoV-2 and the COVID-19 disease" (https://redbiobancos.es/wp-content/uploads/DT-PS-0002-Informe-Gestion-Consentimiento-Informado-COVID-19.pdf)
   - ☐ It was not motivated by any of these options

10. The verdict of exceptionality was applied… (You can indicate more than one option)*:
    - ☐ to all the active collections of the biobank
    - ☐ to the biobank's COVID-19 patient collections
    - ☐ to COVID-19 patient samples prepared in biobank and linked to research projects
    - ☐ Others. Indicate: _____

11. Has the verdict of exceptionality in your center been applied equally to biobank samples as to samples linked to research projects on COVID-19?*
    - ☐ Yes
    - ☐ No
    - ☐ I don't know

    If not, could you explain the differences? _____

12. During the states of exceptionality adopted by your REC and up to the present time, taking into account the people from whom a COVID-19 sample was obtained for your biobank, what percentage of them do you think...* (Mark only one percentage for each question)

	0%	>0 and ≤25%	>25 and ≤50%	>50 and ≤75%	>75 and <100%	100%
…did not give their consent (IC exemption)?						
…did not give their consent (with obtaining subsequent written IC)?						
…gave their consent orally (with subsequent obtaining of written IC)?						
…gave their consent orally (without subsequent obtaining of written IC)?						
…gave their consent orally (with the presence of an identified witness)?						
…gave their consent through electronic formats?						
…had a relative who was the legal representative authorized to give consent?						
…signed a written IC from the outset?						

13. Regarding the people considered in the previous question who did not sign the written IC from the outset, is the process to collect their IC on paper active?*
    - ☐ Yes
    - ☐ No, it hasn't started
    - ☐ No, since it's already over
    - ☐ No, it does not apply to the particular case of my biobank

    If the answer is affirmative, indicate the approximate percentage of people from whom this document has already been obtained: _____

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