Clinical Pharmacology & Biopharmaceutics

Research Article Open Access

Rare Diseases in Spain and Argentina - We Share the Same Reality

Alvaro Lavandeira Hermoso[1]*, Maria Carolina Regis[2], Alvaro Lavandeira Dalama[3] and Alberto De La Montana[3]

[1]*Lawyer, Juris Doctor by the San Pablo-CEU University, Spain*
[2]*Diploma in Right to Health by the Austral University of Buenos Aires, Specialist in Disability and Rare Diseases, Spain*
[3]*Institutional and international relations of the Institute for Health Research and Training, Spain*

Keywords: Rare diseases; Uncommon diseases; Orphanet; Comparative law; Constitutional rights and Guarantees; Legal regulation; Epof; Health; Rare diseases; Health; Right to life

Introduction

Don Quixote also speaks in *lunfardo* [1].

Like Cervantes and his *Don Quixote*, who does not lose faith? Doubts accompany him, but also hope.

"To live in perplexed life; already hoping, already fearing, is death very well known, and it is much better dying, to look for a way out of pain" [2].

Synopsis

Law is becoming increasingly dynamic as it must respond to people's new needs, which in an increasingly globalised world means considering international solutions. In recent years, new technologies, the collapse of health systems, the progress of science and genetics, the pharmaceutical industry, quality clinical trials and the contribution of knowledge from the Associations of patients with Rare or Uncommon Diseases, have generated new factual assumptions that are the object of study, debate, proposal, and solution. This is how the law of people with rare or infrequent diseases has been mutating, and it is extremely interesting and beneficial to venture into comparative law between Argentina and Spain, which invites us to rethink old paradigms and the legislative, doctrinal and jurisprudential evolution of this special area within the right to health.

This is how the Law of patients with Rare or Infrequent Diseases has achieved an active role in both countries, as well as in the European Union. And in this quixotic way, making an analogy, we invite you to get to know the paths of the ingenious nobleman; the barriers and the windmills; the unreachable castles and the unconditional accompaniment of all the Sancho Panza who understand how patients feel. So, as in Spain and in Argentina. They bark, Sancho, the sign that we ride. And it doesn't matter how strange or giant the windmill is, it matters how to continue riding.

In this opportunity, a brief analysis of the legislative and conceptual evolution of the notion of Rare or Uncommon Diseases is presented. It then considers the national regulations - in Argentina and Spain and, therefore, in the European Union - and international regulations governing R.D. or R.O.F.D., which indicate the need to adapt the laws to social needs and, above all, to the time required to implement them and guarantee the quality of life of patients. And finally, it details the different resources and solutions, both public and private, that comparative law has given to R.D. or R.O.F.D.

General considerations on rare diseases

Millions of people in the world suffer from low prevalence diseases, most of which have no treatment: these are the so-called "rare diseases", "infrequent diseases" or even "orphan diseases" [3].

The latter term refers to the limited interest among basic and clinical researchers in the study of the pathogenesis, diagnosis and treatment of these diseases, as it is very difficult to find public or private sources of funding.

Rare, minority or infrequent diseases group together a heterogeneous set of life-threatening or chronically debilitating diseases, affecting, according to EU regulations, a maximum of 5 out of every 10,000 inhabitants in Europe. It is estimated that there are between 5,000 and 8,000 different rare diseases affecting 6-8% of the world's population. In case the disease affects less than 1 in 50,000 people, we are talking about an ultra-rare disease.

It is estimated that in Spain the number of people suffering from a rare disease is more than 3 million people.

In Argentina, a rare disease (RCD) is considered to be those pathologies whose prevalence in the population is equal to or less than 1 person per 2,000 inhabitants, as established by National Act No. 26,689 on Comprehensive Health Care for People with Rare Diseases and their Families.

Eighty per cent of rare or minority diseases are of genetic origin and affect both children and adults. In general, they are progressive, debilitating and degenerative, and often cause chronic pain and consequent deterioration in quality of life for sufferers. In fact, 65% of these pathologies are serious, disabling and highly complex and, in half of the cases, they produce motor, sensory or intellectual deficits that lead to a disability in the autonomy of the sufferer. Furthermore, the morbi-mortality rate is very high, so much so that in 50% of cases the life of the affected person is at stake. Rare or minority diseases are also a serious social problem, the consequences of which not only affect patients but also their families and their immediate environment, as they are highly disabling and disabling pathologies. In Spain, according to studies by patient organisations, 81.25% of those affected suffer from inactivity due to the disease and, in general, there are not enough resources for the social, school and work integration of sufferers.

As we said, not all FPOIDs are genetic in origin. There are others such as rare infections, rare allergic reactions and rare cancers. Other rare diseases debut in young adulthood or adulthood, and it is the patient himself who is devastated by the diagnosis. Rare, minority

***Corresponding author:** Alvaro Lavandeira Hermoso, Lawyer, Juris Doctor by the San Pablo-CEU University, Spain, E-mail: alvaro.lavandeira@yahoo.es

Received: 3-Apr-2023, Manuscript No: cpb-23-95773; **Editor assigned:** 5-Apr-2023, Pre-QC No: cpb-23-95773 (PQ); **Reviewed:** 19-Apr-2023, QC No: cpb-23-95773; **Revised:** 21-Apr-2023, Manuscript No: cpb-23-95773 (R); **Published:** 28-Apr-2023, DOI: 10.4172/2167-065X.1000322

Citation: Hermoso AL, Regis MC, Dalama AL, Montana ADL (2023) Rare Diseases in Spain and Argentina - We Share the Same Reality. Clin Pharmacol Biopharm, 12: 322.

or low-prevalence diseases represent a real challenge in terms of public health due to the various factors that make their diagnosis and treatment difficult.

On the one hand, the lack of sufficient information and experts makes obtaining a diagnosis an excessively long and complicated process, as it often takes years from the appearance of the first symptoms to the definitive diagnosis of the disease.

The average time it takes for a person affected by a rare disease to obtain a diagnosis is almost 5 years, and in some cases, it can even take up to 10 years.

The lack of scientific knowledge and specialised professionals, and therefore of effective treatments for most rare diseases, means that the quality of health care for these patients is not the most adequate.

In 2000, with the aim of alleviating this lack of scientific knowledge and boosting research in the field of rare diseases, the European Parliament and the Council of the European Union approved Regulation 141/2000 [**4**], which states that "Patients affected by rare diseases should be entitled to the same quality of treatment as other patients [...]" and establishes incentives to promote research, development and marketing of medicines by the pharmaceutical industry.

While it is true that the legislation promoted by the European Union and in Spain (with the creation of the Rare Diseases Strategy of the National Health System [**5**]) has sought to lay the foundations to facilitate the development and availability of medicines, there are still few effective treatments and, in any case, only for a small number of pathologies. There are still more than 5000 rare diseases for which there is no pharmacological option. It is therefore necessary to continue to support research from all sectors, public and private.

According to the European Union, an orphan drug is a drug that is intended for the diagnosis, prevention or treatment of a life-threatening or seriously and chronically debilitating disease and that does not affect more than 5 out of 10,000 people. It must also be intended for a disease for which there is no alternative treatment, or it must be a new medicine that provides additional benefits to patients compared to available treatments.

In May 2022, the Argentinean Federation of Rare Diseases (FADEPOF), together with the Ibero-American Alliance for Rare Diseases (ALIBER), presented the results of the **ENSERio LATAM Argentinian Chapter study**, which provides information on nearly 400 patients living with one of these conditions.

According to the Argentina chapter of the Study on the Situation of Social and Health Care Needs of People with Rare Diseases in Latin America [**6**], the delay in diagnosis results in 35% of people with FPOIDs not receiving support or treatment, 31% having their disease or symptoms aggravated and 23% accessing inadequate treatment.

The Right to health protection

Health protection is one of the fundamental principles of modern states. It is a principle that is nowadays a right of every citizen to demand a number of health benefits in accordance with human dignity and the level of social and economic development of each state.

The benefit of enjoying a high level of health is one of the fundamental rights of every human being, according to the World Health Organisation, and the notion of health is not only identified with the absence of illness, but fundamentally with a complete state of well-being in which economic, cultural, social, and not exclusively health factors are involved.

In Spain, Article 43(1) of the Constitution proclaims that "the right to health protection is recognised"; a recognition of protection that is a directly binding norm, given that the Constitution is a legal norm, and all its precepts have this dimension and efficacy. Therefore, it is up to the legislator to make this right effective through laws, and the public administration must execute and comply with such laws.

The Spanish Constitution enshrined the right to health protection in a concise formula that is undoubtedly open to gradual or progressive interpretation and adaptable to the changing circumstances of each historical moment.

In Argentina, the right to health arises from Art. 42 of the National Constitution which refers to the right to the protection of the health and physical integrity of consumers and users; and it is also recognised by the International Treaties with constitutional hierarchy incorporated from the Constitutional Reform of 1994 by means of art. 75 inc. 22 (International Covenant on Economic, Social and Cultural Rights, art. 12; American Declaration of the Rights and Duties of Man, art. XI; Additional Protocol to the American Declaration of the Rights and Duties of Man, art. 10; and Universal Declaration of Human Rights, art. 25). through this Article 75, paragraph 22, the international human rights treaties acquire constitutional status, and the right to health is recognised as a fundamental human right and value.

The right to health protection, as the social right that it is, has to do with ensuring that the entire population has the conditions and means indispensable for a dignified life and, to this end, it inevitably requires the creation and operation of health structures at the service of citizens, which necessarily absorb a large volume of public resources.

It is a right to benefits, the effectiveness of which requires the creation, organisation and financial support of a public service. A major consequence of this is that its effectiveness no longer depends only on political will and legal articulation, but also on the economic possibility of creating and financing the service and on the determination of financial sources and public spending priorities, which are basically political functions.

In the practical organisation, this right to health protection is equated with individual, civil and political rights, and is given the character of universal, i.e., equal rights for all.

This social right considers expectations or claims to resources and goods aimed at satisfying people's basic needs. Consequently, it is of interest to all people, but especially to the most vulnerable members of society, whose access to these resources is often scarce and sometimes non-existent or non-existent.

For this reason, the right to health protection, after its specific development by law, is an immediately effective right that will be enjoyed by all citizens who find themselves in need of health care or assistance.

The right to health, then, implies that every human being has the right to proper professional care to look after their health, to prevent illness, to find a place to be treated and to receive the necessary treatment for their recovery, etc.

All of this requires a series of resources and infrastructures that provide health services to those who demand them and without a doubt that these services be accessible and in optimal conditions for the population. The State has to deploy appropriate active policies and organise efficient facilities and services available to the public.

Consequently, the right to health includes the ability of every

human being to maintain functional organic normality, both physical and mental, and to be restored when a disturbance occurs, within the degree of development reached by medical science, in order to recover the quality of life, while prolonging its life cycle, if treated, according to the provisions of the treating physicians**.**

Legal regulation of rare diseases in Argentina and Spain

In Argentina, Act No. 26.689 was passed in 2011, which aims to promote comprehensive health care for people with rare diseases. This law promotes the right to access and health care for patients with this type of pathology, regulates the creation of an organisation specialised in rare diseases and establishes the obligation to draw up a list of rare diseases in accordance with the prevalence of pathologies in the country.

The regulatory articles extend to other responsibilities, among which it is specified that clinical care for these people must be covered by social security and prepaid medicine companies.

This norm was regulated only four (4) years later, by Decree of the National Executive Power N° 974/2015 dated 11 May 2015. In its second article, it specifies such diseases as those whose prevalence in the population is equal to or less than 1 in 2000 people according to the national epidemiological situation.

What is the National programme for rare diseases?

The goals to be achieved by the Authority of Application are given within the framework of the National Programme for Rare Diseases created by Decree 974/15 regulating the EPoF act (art. 3°) and which is within the orbit of the Undersecretariat of Medicines and Strategic Information dependent on the Secretariat of Access to Health (Res. 1892/20 of the National Ministry of Health), of which the Honorary Advisory Council is a member. Its purpose is to promote comprehensive access to health care for people living with an EPoF, with the elaboration of the List of Rare Diseases (which in February 2021 was officially approved by Res. 641/51 of the Ministry of Health) and the National Registry of Patients with EPOF, which is part of the Argentine Integrated Health Information System; both objectives are set by Act No. 26.689.

What happens in Spain and in the European Union?

In Spain, competences in health management are transferred to the Autonomous Communities, although the bases and general coordination of health care, as well as legislation on pharmaceutical products, depend on the central government. This means that the care of R.D., which requires a high degree of specialisation, is an important area of coordination within the health competences between the Autonomous Communities.

In the world, R.D. began to occupy a place on the public agenda as such at the end of the 1990s. And Spain began to take steps to address RD in 2000, starting with research, in parallel to the first regulatory efforts at European level. It should be recalled that Spain joined the European Economic Community - now the European Union - by signing the accession treaty in 1985, which came into force on 1 January 1986.

The role of the European Union in the field of health is to promote cooperation between Member States and, where necessary, to support their action. The objective has always been to establish a comprehensive Community strategy to support Member States in providing effective and efficient recognition, prevention, diagnosis, treatment, care and research for rare diseases in Europe.

Depending on the Member State or region in which they live, EU citizens have unequal access to specialised services and available treatments. A few Member States have successfully addressed some of the issues raised by the rarity of these diseases, while others have not yet explored possible solutions.

Under the responsibility of the Commission and the EMA (European Medicines Agency), a policy is already being implemented in the field of orphan drugs, for example.

Prior to the Orphan Medicinal Products Regulation, therefore, the European Community understood that the problem of rare diseases required a special concerted effort to avoid significant morbidity or mortality or a significant reduction in the quality of life or socio-economic potential of the people suffering from them. The Community authorities believed that the Community could provide added value to Member States' actions on rare diseases.

Prior to the adoption of the regulation, only eight drugs for rare diseases had been authorised. As of today, there are around 200 medicines available for almost a hundred different pathologies, along with more than 2,000 orphan designations.

What is the EU's UEPROSALUD PROGRAMME?

On 24 March 2021, the European Union published Regulation (EU) 2021/522 of the European Parliament and of the Council establishing a programme of Union action in the field of health (EU ProHealth programme) for the period 2021-2027 and repealing Regulation (EU) No 282/2014107.

This EU Regulation became applicable on 1 January 2021 and is binding in its entirety and directly applicable in all Member States. This Regulation sets out the objectives of the EU ProHealth Programme for the period of the multiannual financial framework 2021-2027, the budget for that period, the forms of Union funding and the rules for the granting of such funding.

Euproshealth Programme in the field of rare diseases

The programme refers to European reference networks, created under Directive 2011/24/EU of the European Parliament and of the Council, as those virtual networks of healthcare providers across Europe. They are intended to facilitate discussion on complex or rare conditions and diseases that require highly specialised treatment and a concentration of expertise and resources. It is considered in the Regulation that European reference networks can improve access to diagnosis and the provision of quality healthcare for patients with rare diseases, and can be focal points for medical training and research and dissemination of information: it is therefore considered that the Programme should contribute to increased networking through European reference networks and other transnational networks.

In this respect, one of the objectives of the Programme is to support integrated work between Member States, and in particular between their health systems, including the implementation of high-impact prevention practices, to support the work of health technology assessments and to strengthen and extend networking through European reference and other transnational networks, including in the area of low prevalence diseases.

In addition, the Regulation identifies a number of activities as eligible for support, including the following activities related to rare diseases. Namely:

Support preventive actions to protect vulnerable groups from health threats and actions to adapt health crisis response and management to

the needs of these vulnerable groups, such as actions aimed at ensuring basic health care for patients with chronic or rare diseases.

Support the creation of new European reference networks for rare, complex and low prevalence diseases, where appropriate, and support collaboration between European reference networks to address multisystemic needs arising from low prevalence and rare diseases and facilitate the creation of cross-specialty and cross-disciplinary networks.

The Regulation considers, as one of the indicators for the evaluation of the programme, access to centrally authorised medicinal products, including authorisations of orphan medicinal products, whether new or existing, for unmet needs.

While interest in orphan therapies is growing in Europe, and the industry maintains its firm commitment to innovation in the field of rare diseases, in Spain access to innovation for patients in all areas is slowing down. And we are not very different in Argentina. Recently, for example, it was announced in January of this year 2023 that the National Ministry of Health reached an agreement with a laboratory to start providing a high-cost gene therapy for the treatment of Spinal Muscular Atrophy (SMA) type 1. The drug Onasemnogen Abeparvovec (Zolgensma), which is used for the gene therapy, has a commercial value of more than 2 million dollars and is one of the most expensive in the region and in the world. As part of the agreement, the State will acquire it for 1.3 million dollars (plus VAT) and with an investment of more than 15 million dollars because an open purchase order will be approved for that amount, with the intention of being able to cover the treatment of 12 patients.

The cost-benefit ratio for this type of disease is inequitable. The commitment and efficiency of the entire health system is important to ensure that the right treatments reach the right patients.

In the European Union, Member States share a common commitment to ensure universal access to high quality healthcare in a fair and supportive manner [**7**]. But when diseases are rare, specialization is also scarce.

From our side, we have always insisted on the implementation of risk-sharing agreements, linking the price, and financing of certain health innovations to their economic-financial and health outcomes. These agreements ensure that both the state and the provider have to monitor compliance with quality standards, helping to mitigate existing health financing problems. Thus, everyone stands to gain from the application of such agreements in the introduction of a particular health technology (win-win strategy).

Social, ethical and legal considerations for rare and rare diseases

Conclusions

Preliminary considerations - Importance of comparative law

According to the RAE [**8**], Comparative Law is the *"Method for the study of law based on the comparison of the different solutions offered by the various legal systems for the same cases"*.

It includes the methodological process of *comparison* itself as those of *analysis*, of the aspects and legal nature compared, as a given problem and the successes and shortcomings in the international understanding of state norms and international conventions, advancing in the search for solutions.

It is therefore important to know the history and legal nature of other world experiences and thus enrich us in order to protect health and guarantee the quality of life and dignity of people.

The last day of February - R.D. or R.P.O.D. Day is commemorated worldwide, with the aim of raising the visibility of individuals and families suffering from an unusual pathology. Since its creation in 2008, World Rare Disease Day has been celebrated every 28 February (or 29 February in leap years), promoted by the European Organisation for Rare Diseases (EURORDIS), together with numerous patient organisations.

We are united in working for equal opportunities, care, and medical coverage, as well as access to diagnostics and therapies for people living with a R.D. or R.P.O.D.

R.P.O.D. or P.O.F.D. has received increasing attention both within the scientific community and in society at large [**9**]. For many years they were considered as orphan diseases because these diseases were neglected from any kind of study. These diseases are a health problem and of necessary social interest.

In spite of their low prevalence and even in spite of the wide variability in frequency that can be observed among them, these diseases associate relevant aspects in the life of the patients and in the natural history of the process they present with their minority character, such as the fact that, in most cases, they are chronic, serious, disabling and sometimes fatal disorders [**10**] that appear early in life [**11**] and also affect adults [**12**].

The real scenario we face, in the field of rare diseases, is that diagnosis is not always possible and, when it is, it is not always established within a reasonable period. Moreover, in most cases, it does not entail any modification of the therapeutic approach, as there is no curative or palliative treatment available, nor is it foreseen that there will be in the medium term. But this does not mean that this group of sufferers should be forgotten. The possible solutions to their problems are complex and require the collaboration of researchers, institutions, pharmaceutical companies, health professionals and patient associations.

Rare diseases have a direct impact both on the family, which in many cases becomes their caregivers, and on society, which must develop specific socio-health and educational programmes to support these patients. Thus, these illnesses affect the entire family environment and require a global approach in this area, i.e., for life.

A family is a life project, and when a rare disease appears within this environment, this project changes radically. From a sociological point of view, rare diseases are usually serious, chronic, and incapacitating, and often appear in childhood, so they have their own sociological profile that requires an appropriate response.

This response must be of a specific nature, with the design of long-term resources and often with a specialised content. In this way, these diseases require society to develop specific socio-health and educational programmes to support these patients.

The concept of rare diseases was coined as an "umbrella" term to facilitate action on a very heterogeneous group of diseases, which includes diseases whose prevalence is always low, but in a spectrum that encompasses very disparate prevalences, of diverse aetiology and difficult to classify. They appear in very different age groups and often without curative or palliative therapeutic options. Most rare diseases are chronic diseases that cause high morbidity and premature mortality, as well as a high degree of disability and, therefore, a significant deterioration in the quality of life of those affected and, therefore, of their immediate environment.

The low prevalence of these diseases confers common characteristics on the people who suffer from them, which mean that they are thought of as a single social group, even though the conditions and characteristics of the different diseases may be very different from one another.

The nature of pathological processes varies from diseases affecting a single organ system to diseases that are multisystemic.

The heterogeneity of these diseases is manifested in different profiles of their natural history, which conditions the clinical and preventive action of health services. These profiles refer to the causes of the disease (aetiology), the age of onset and temporal development of the disease (chronobiology), the clinical expression (semiology and pathophysiology) and the degree of involvement (severity and prognosis).

Obviously, the profiles of the natural history are very diverse and vary from one disease to another and even from one patient to another.

Preventive medicine

Preventive medicine understood in a restricted sense has little impact on each of the rare diseases because the affected population is small, and it is difficult to determine the risk factors that allow for primary prevention. On the contrary, preventive medicine in a broad sense, acting not only on the individual but also on the population or groups of individuals, must consider all rare diseases as a field of action in the aspects they share. In addition, if reference is made to rare diseases with a genetic component, it is possible to speak of a field of action for public health at three levels of population action: the family and close kinship level, the target population, and the group of individuals as belonging to the same species.

Thus, genetic counselling and screening tests are particularly important for the prevention of this type of disease.

The term genetic diagnosis refers to the clinical process by which the presence of a genetic or hereditary disease or the risk of suffering from it is determined through genetic analysis or genetic testing.

Screening can be defined as a public health programme aimed at identifying genetic determinants in individuals for which early medical intervention could lead to the elimination or reduction of mortality, morbidity or disability associated with such determinants.

In this sense, newborn screening programmes are essential for the early detection of certain rare diseases and for the establishment of effective treatment to prevent the development of serious complications. They are conceived as a public health service, offered to all newborns, in which the benefits and risks of the programme and ethical considerations must always be weighed.

In recent years, there have been important advances in screening technology for certain diseases, and there is a national and international debate on the desirability of expanding the diseases that are studied in neonatal screening **[13]**

It is vitally important that R.I. and F.O.P.E., as a group with common and shared problems, are introduced into the curriculum of undergraduate university training, not only in medicine, but also in other health areas such as nursing or psychology.

Specialised training and continuing education must also consider this global and comprehensive approach to rare and rare diseases. Medical education is a field of intervention as essential as the implementation of new health policies **[14]**.

The sensitivity acquired during the residency period must be continued in the centres where the professional activity is carried out. Awareness of the problem of these types of pathologies and syndromes, the availability of structures, resources and circuits must lead to a clear improvement in the care received by these patients.

One of the areas in which there has been most interest in recent years has been the promotion and development of biomedical research, whether basic, clinical, or epidemiological, into these diseases. There are a variety of reasons why research in R.D. and F.O.P.D. makes sense.

These reasons include social rationales since research is about knowledge and offering hope and realities to sufferers. There are also medical justifications, given that research opens new opportunities and offers new instruments to improve clinical practice, especially in the field of diagnosis, but also in relation to the development of new treatments and the recognition of biomarkers that are useful in monitoring the natural history and therapeutic response of patients. And, obviously, there is scientific interest in understanding the mechanisms of disease production and the physiopathology of the process, the definition of new molecular targets and the development of drugs directed towards these targets.

Conclusion

The right to life or health protection is not possible without necessarily involving access to medicines. The right to access to medicines requires the implementation of complex mechanisms in which the State takes precedence as guarantor of collective health.

A patient who is not treated, because it is decided that the treatment is ineffective or too expensive, is abandoned.

Those who suffer from R.E. or P.O.F.S. in the world find themselves with the unexpected adventure of the odyssey to travel a long road of quixotic struggle for the recognition of the rights that should be guaranteed to them.

References

1. The RAE defines it as the “Slang originally used by the lower class people of Buenos Aires, part of whose words and locutions were later introduced into the popular Spanish of Argentina and Uruguay.
2. Cervantes S, Miguel (2022) El ingenioso hidalgo Don Quijote de la Mancha / Miguel de Cervantes Saavedra (formato EPUB) 1547-1616; Alicante : Biblioteca Virtual Miguel de Cervantes.
3. M Chalendar, Daniel M (2014) ORPHANET classification of rare diseases.
4. https://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2000R0141:20090807:ES:PDF
5. https://www.sanidad.gob.es/organizacion/sns/planCalidadSNS/docs/RareDiseases.pdf
6. Solves AJA, Arcos UJM (2016) Estudio Sobre Situación De Necesidades Socio-Sanitarias De Las Personas Con Enfermedades Raras En Latinoamérica. Estudio ENSERio LATAM, Capítulo Argentina.
7. Conclusiones del Consejo sobre los valores y principios comunes de los sistemas sanitarios de la Unión Europea.
8. https://dpej.rae.es/lema/derecho-comparado
9. Remuzzi GSA (2011) Why rare diseases? Annali dellÍstituto Superiore di Sanitá.
10. Posada M, Izquierdo MM, Ferrari AMJ, Avellaneda FA, Copa AP, et al. (2002) Action Plan of the EU and the Spanish State on low-prevalence diseases. Bulletin of the Royal Board on Disability 53: 25-9.
11. González LD, García FM (2008) Rare diseases in pediatrics. Annals of the Health System of Navarrra 31: 21-2.

12. García-Ribes M, Ejarque I, Arenas E, Martín V (2006) New challenges: the family doctor in the face of rare diseases. Primary Care 37: 369-70.

13. Astigarraga AI (2011) Challenges, opportunities and difficulties of research in rare diseases and orphan drugs. Peculiarities, action plans and current situation of research in rare diseases. Extracted from “Rare diseases: lights and shadows of a reality that requires public attention”. Collection Days on human rights. XXIII European Courses UPV/EHE.

14. Benavides GME (2011) Role of the physician in rare diseases. Journal of Biomedical Sciences. Ethics, Bioethics and Humanism 2: 327-330.