Special issue

Newborn screening and informed consent in a constitutional perspective. The Italian "model" and some knots still to be untied

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ABSTRACT: Starting from variability analyses in newborn screening systems at international, European and regional levels, this paper focuses on the Italian "model" highlighting some critical issues in a constitutional perspective. The law n. 167 of 2016 and the ministerial decree of 13 October 2016 allowed to achieve uniformity in the national diagnostic offer but their mutual inconsistencies contributed to a regional variability in the management of informed consent/dissent and in the management of the biological material collected. The protection of fundamental rights at stake still requires a constitutionally oriented harmonisation and development of the rules governing the newborn screening national system.

KEYWORDS: Newborn screening; informed consent; informed dissent; constitutional principles; regional variability

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1. Introduction

Neonatal screening is one of the most important secondary public preventive medicine programmes.

It falls within the secondary type of prevention which, unlike vaccines which are of the primary type and include all interventions intended to hinder the onset of diseases in the population and are aimed at so-called herd immunity, has the primary purpose of protecting the health of the newborn; the objectives of such screening are the early identification of those who are sick, preventing the onset and progression of the disease.

Screening is not a diagnostic assessment but a generalised diagnostic investigation strategy on a given population. It is therefore a predictive test that constitutes the initial moment of a diagnostic process which, after completing a further "confirmation test" (biochemical, enzymatic and/or molecular), allows the formulation of a certain diagnosis.

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Most of the screening concerns the analysis of the genetic mutations of the newborn.
Diseases subject to newborn screening tests are rare congenital and inherited endocrine and metabolic disorders.[1]
The history of screening as a population test dates back to the early 1960s in the United States of America when biologist Robert Guthrie developed a simple and inexpensive bacterial inhibition test capable of identifying the most common aminoacid disease: phenylketonuria.
During the following decade, neonatal screening for congenital hypothyroidism and subsequently for cystic fibrosis (implemented with different methods) began both in the USA and in Europe, including Italy.[2]
In Italy, neonatal screening for phenylketonuria was first introduced in Italian Region Liguria in 1973 and afterwards was gradually widened to include the entire nation.
In another Italian Region, Tuscany, screening for phenylketonuria, hypothyroidism and cystic fibrosis was established in 1983, and this then became mandatory nationally in 1992, with law n. 104 of 5 February 1992 and the subsequent regulations for implementation.
In the 1990s, the development of analytical technology – tandem mass spectrometry – allowed the development of versatile, specific and sensitive analytical methods that made it possible to measure many biomarkers in a single and very rapid analysis.
This technology has made it possible to move from the concept of "one test – one disease" to that of "one test – many diseases", effectively revolutionizing the approach to newborn screening tests.
The criteria used date back to the 1960s, and these aim to identify the panel of diseases to be controlled.
The best known, defined by the World Health Organization, date back to 1968 and are known as the Wilson and Jungner criteria; these refer to both the characteristics of the disease (severity, frequency, possibility of dietary and/or pharmacological treatment able to improve quality and life expectancy) and the characteristics of the screening test (appropriateness, costs, acceptability by the population).[3]
Neonatal screening is normally carried out between 48 and 72 hours after birth and involves the collection of a few drops of blood. The main problems regarding newborn screening tests are not related to the invasiveness, which is very low, nor with the balance between risks and benefits of the

[1] Inherited Metabolic Disorders (IMDs), also called inborn errors of metabolism, constitute an important category of rare genetic diseases caused by the altered functioning of a specific metabolic pathway. They represent a heterogeneous group of over 700 different pathologies which, taken individually, are rare but together have a cumulative incidence ranging from 1 in 500 to 1 in 4,000 live births. From the point of view of public health, IMDs represent a group of pathologies with a considerable impact on the health of the person, the family and on society as a whole, as they are multi-systemic diseases that can cause irreversible damage to many organs and systems, responsible for early neonatal mortality and permanent psychic and neuromotor delays since childhood.

[2] See J.G. LOEBER, P. BURGARD, M.C. CORNEL, T. RIGTER, S.S. WEINREICH, K. RUPP, G.F. HOFFMANN, L. VITTOZZI, *Newborn screening programmes in Europe; arguments and efforts regarding harmonization. Part 1 - From blood spot to screening result*, in *Journal of inherited metabolic disease*, 35, 2012, 603-611; D.B. JR. BAILEY, *Early intervention and newborn screening parallel roads or divergent highways?*, in *Infants & young children*, January-March 2021.

[3] See J.M.G. WILSON, G. JUNGNER, *Principles and practice of screening for disease*, WHO, 1968.

act itself, since there are no risks to the physical well-being of the newborn; rather, the issues for concern are around the management of the autonomy profile and the self-determination of the legal representatives of the newborn in relation above all to the information that can be derived from the screening and future management of the data of the newborn.

2. Remarks about variability in the use of existing screening tests

There is extreme variability in this area at international, European, national and regional levels, since there is no international consensus on what should be included in the panel of diseases to be controlled; this is in spite of increased attempts to coordinate the screening programmes.[4] The fundamental question that emerges, having observed this divergence, is whether some countries or regions overdiagnose while others register a diagnostic supply deficit.

2.1. The variability of screening tests at international and European level

At international and European level, the diversity of the health systems is a relevant issue in reference to financing, insurance or the public system; in the identification of the primary recipients of the screening system (the newborn, the parents, the society); and in the interpretation of the concept of clinical utility (referring to possible treatment and cure of the disease or as a possibility for treatment and improvement of the quality of life and prognosis).[5]

Political decision makers in various European countries give different weight to the various factors involved in the screening processes, and the consideration given to the different evaluation possibilities of the screening systems is notably different.

A lack of harmonisation among European countries emerge in the provision of information about newborn screening to parents and emphasised the need for more comprehensive guidelines at the European level.[6]

The practices of access to screening are also differentiated,[7] including systems that refer to an opt-out clause, whereby the test is considered mandatory and presumes consent, on the basis that it provides protection in the best interests of the child, but nevertheless leaves open the possibility for parents or legal representatives to disagree and refuse it; to an opt-in model, which requires

[4] Cfr. the initiatives of the International society for neonatal screening (ISNS), https://isns-neoscreening.org/.

[5] The extensive screening is discussed and questioned in literature, because of the massive collection of data not necessarily related to immediate or actual clinical utility, so to the individual health of the patient. See M.S. Househ, B. Aldosari, A. Alanazi, A.W. Kushniruk, E.M. Borycki, *Big data, big problems: a healthcare perspective*, in *Studies in Health Technology and Informatics*, 238, 2017; Q.K. Fatt, A. Ramadas, *The usefulness and challenges of big data in healthcare*, in *Journal of Healthcare Communications*, 3, 2018.

[6] V. Franková, R.O. Driscoll, M.E. Jansen, J.G. Loeber, V. Kožich, J. Bonham, P. Borde, I. Brincat, D. Cheillan, E. Dekkers, R. Fingerhut, I.B. Kuš, P. Girginoudis, U. Groselj, D. Hougaard, M. Knapková, G. la Marca, I. Malniece, M.I. Nanu, U. Nennstiel, N. Olkhovych, M. Oltarzewski, R.D. Pettersen, G. Racz; K. Reinson, D. Salimbayeva, J. Songailiene, L. Vilarinho, M. Vogazianos, R.H. Zetterström, M. Zeyda, *Regulatory landscape of providing information on newborn screening to parents across Europe*, in *European Journal of Human Genetics*, 2020, 1-10.

[7] About this aspect see R. Brownsword, J. Wale, *In ordinary times, in extraordinary times: consent, newborn screening, genetics and pandemics*, in this issue.

informed consent to the procedure; and to hybrid models. Other discrepancies exist regarding the regulations around the retention of biological material beyond the time strictly necessary for carrying out the tests, and the possible uses to which the profiles can be put, including research not specifically linked to the screening.[8]

In addition to the number and type of diseases to be controlled, the profile relating to consideration of the clinical validity and clinical usefulness of the test, in particular the latter, is recorded and evaluated differently in the various countries.

Internationally, newborn screening programmes are active in more than 64 countries.[9] At European level, the wide variability in the use of screening has been highlighted starting from the final report of the survey on newborn screening[10] launched following the approval of the Council Recommendation on rare diseases of 2009,[11] and this has been outlined even more recently.[12]

The systems are significantly different in each country, and this difference affects the number and types of diseases to be controlled: for example, in Great Britain, the disease panel includes 9 pathologies; in Italy 47; in the Netherlands 34; in the Czech Republic 20; in Spain 7; in Ireland 6; and in France 5.[13]

It is evident that at European level, Italy offers the widest diagnostic in the screening sector.

2.2. The variability of screening tests at Italian regional level

At Italian regional level, analysing the experiences of three Italian Regions, such as Liguria, Emilia Romagna and Tuscany, some interesting insights emerge on the extent of variation in the screening offer.

As mentioned, Liguria was the first Region in Italy to introduce the screening test for phenylketonuria, in August 1973, with the regional law n. 31.[14]

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[8] Cfr. P. Burgard, M. Cornel, F. Di Filippo, G. Haege, G.F. Hoffmann, M. Lindner, J.G. Loeber, T. Rigter, K. Rupp, D. Taruscio, L. Vittozzi, S. Weinreich, *Short executive summary of the report on the practices of newborn screening for rare disorders implemented in Member States of the European Union, candidate, potential candidate and EFTA Countries*, October 2011; J. Kraszewski, T. Burke, S. Rosenbaum, *Legal issues in newborn screening: implications for public health practice and policy,* in *Public health reports*, 2006; B.M. Knoppers, D. Avard, K. Sénécal, *Newborn screening programmes: emerging biobanks?*, in *Norsk Epidemiologi*, 21, 2, 2012, 163-168.

[9] B.L. Therrel, C.D. Padilla, J.G. Loeber et al., *Current status of newborn screening worldwide: 2015*, in *Seminars in perinatology*, 39, 3, 2015, 171-187.

[10] P. Burgard, M. Cornell, F. Di Filippo et al., *Report on the practices of newborn screening for rare disorders implemented in Member States of the European Union, Candidate, Potential Candidate and EFTA Countries*, 2012, http://ec.europa.eu/chafea /documents/news/Report_NBS_Current_Practices_20120108_FINAL.pdf.

[11] European Council, *Council Recommendation of 8 June 2009 on an action in the field of rare diseases*, 2009.

[12] J.G. Loeber, *The European Union should actively stimulate and harmonise neonatal screening initiatives*, in *International journal of neonatal screening*, 4, 2018; B.L. Therrell, C.D. Padilla, J.G. Loeber, I. Khneisser, A. Saadallah, G.J.C. Borrajo, J. Adams, *Current status of newborn screening worldwide 2015*, cit.

[13] N. Meade, J. Spink, *Let's grasp this opportunity to examine the potential future of screening*, in *BioNews*, November 2019, https://www.bionews.org.uk/page_146203. For the Italian system see Servizio Studi della Camera dei Deputati, *I nuovi livelli essenziali di assistenza*, 12 January 2021, 7.

[14] Cfr. regional law n. 31 of 17 August 1973, *Regulations for the identification and treatment of phenylketonuric disease*.

Subsequently, with the implementation of regional law n. 26 of 8 September 1986, regional law n. 31 was abrogated, and screening for hypothyroidism was also introduced.[15]

The Ligurian system appears complex, because although there are no regional regulations, the screening tests have been carried out as a pilot project since 2005 as part of the regional newborn screening programme, ensuring coverage of all newborns in the Region.

The panel of controlled diseases with screening starting from 2005 was very large and was equivalent to that implemented in Tuscany. Indeed, about thirty diseases were screened as part of the mentioned pilot project coordinated by the Gaslini teaching hospital based in Genoa.

The screening system in Emilia Romagna was launched only in 2010.

With the regional regulation n. 107 of 1 February 2010, *Enlargement of screening for inherited metabolic disorders*, the number of diseases to be controlled was extended to 19 pathologies in addition to the three provided for as mandatory by the national law n. 104.[16]

In relation to this regional regulation a trial occurred before the administrative judge.

The decision of the Regional Administrative Court of Emilia Romagna of 17 December 2010 n. 8138 and the decision of the Council of State, the Italian Supreme Administrative Court, of 19 January 2012 n. 247 concerned the challenge of regulation n. 107 which determined the progression of the regional screening system.

The complaint to the Regional Administrative Court was promoted by a Patients' Association against the Emilia Romagna Region.

The main object of the plea was the annulment of the disputed part of the regulation in which the screening of hereditary metabolic diseases does not include all diagnosable diseases processed through the technology of tandem mass spectrometry; or, subordinately, in the part in which the early mass screening excludes a series of pathologies that are listed by the claimants.

The plea has been declared inadmissible because it required an integration of the regional provision through an action for annulment that could not lead to this effect.

Anyway, the Regional Administrative Court goes partially through the matter and states that the regional regulations did not violate, as alleged by claimants, the right to health of Emilian citizens because the provisions extended the execution of newborn screening well beyond the three pathologies provided nationally (to 19 pathologies in addition to the three declared mandatory by national law n. 104).

[15] Cfr. regional law n. 26 of 8 September 1986, *Regulations for the identification and treatment of hypothyroidism and phenylketonuria diseases*.

[16] The regional regulation n. 1898 of December 19, 2011, *Establishment of the hub and spoke network for hereditary metabolic diseases subject to newborn screening and organization of the path of global care of the pediatric patient*, and the regional regulation n. 365 of 27 March 2017, *First implementing measure in the context of territorial care of the Prime Minister's Decree of 12 January 2017 on the definition and updating of the essential levels of care pursuant to art. 1, paragraph 7, of the legislative decree 30 December 1992, n. 502* published in the Official Gazette n. 65 of 18 March 2017, constitute regulations with organizational functions of the regional screening system. The regional regulation n. 2260 of 27 December 2018 was approved in implementation of the law of 19 August 2016 n. 167 and the ministerial decree of 13 October 2016 relating to newborn screening for the early diagnosis of hereditary metabolic diseases and regional provisions on the subject.

The ruling of the Council of State two years later confirmed the first stage decision of the Regional Administrative Court, rejected the appeal, and focused on interesting aspects: the criteria for including and excluding diseases from the screening test.

The Council of State affirmed that in the absence of "universally shared international scientific criteria", the choice of diseases to be controlled is inspired by the fundamental principle of "diagnostic opportunity/usefulness" or, if preferred, "costs/benefits". In fact, it was not possible to manage an excessive number of false positives with the possible consequence of subjecting "clinically healthy subjects" to "inappropriate and continuous therapies" or of causing "anxiety for a long time to families". Even more difficult to manage was the risk of a single false negative.

The administrative judge concluded that "the choice whether or not to include certain pathologies in the mass screening (which are very rare by definition) involves very delicate profiles (for example because, for some of them, the intrinsic margin of error could cause more harm than good); hence the high degree of discretion removes the decision from judicial review competence, once it has been ascertained that it was adopted with reasonableness and thoughtfulness".[17]

Finally, Tuscany, more than other Regions, has a deep-rooted tradition of developing screening.

In Tuscany, from 1983, screening for phenylketonuria, congenital hypothyroidism, and subsequently for cystic fibrosis, was introduced; these screenings were subsequently made mandatory throughout the nation with article 6 of the law of February 5, 1992 n. 104.

The extended screening system began as a pilot project in 2002, and in 2004 it was launched throughout the Region with the specific regional regulation of 2 August, 2004.

Since 1 November 2004 with regional regulation n. 800 of 2004, screening in Tuscany has been extended to about 30 other metabolic diseases besides phenylketonuria, by means of mass tandem analysis.

The regional regulation n. 420 of 2018 concerning the *Tuscan Extended Neonatal Screening System: Update on the basis of the Decree of the Ministry of Health of 13/10/2016 and Law n. 167/2016 on the subject of diagnostic tests for the prevention and treatment of hereditary metabolic diseases* reaffirmed the function of the University Hospital Meyer, based in Florence, in coordinating the screening system, with the task of governing and monitoring the activities of the regional neonatal screening system as a whole. It confirmed that with the introduction of galactosemia following the ministerial decree of 13/10/2016, the panel of pathologies that in the Tuscany Region, currently subject to extended and mandatory neonatal screening, corresponds to the list in Annex A of the ministerial decree of 13/10/2016.[18]

[17] See ruling of the Council of State of 19 January 2012 n. 247.

[18] A further development occurs with the regional regulation n. 909 of 6 August 2018 *Extended neonatal screening for the early diagnosis of metabolic diseases and hereditary immunodeficiencies. Further development of the regional screening programme*. The Tuscan system also included other diseases that were not initially fostered in National rules and then inserted following by the 2019 budget law. It should be noted that from 1 January 2006 the Healthcare Authority n. 1 of the Umbria Region carries out the extended screening at the University Hospital Meyer and from 1 January 2010, according to the Memorandum of Understanding referred to in regional regulation n. 1277/2009, concerning *Regulation n. 236/2004 "Interregional framework agreement between the Tuscany Region and the Umbria Region for the management of healthcare mobility*", the neonatal screening activities have been extended to the entire territory of the Umbria Region according to a renewable three-year agreement.

3. The Italian "model" and the rules on newborn screening in a constitutional perspective

The Italian newborn screening "model" is the most developed system among those in Europe, considering that it currently has as its object a panel of 47 diseases to be controlled. The Italian system has developed since the 1990s and with the 2016 legislation – law n. 167 of 2016 and ministerial decree of 13 October 2016 – has substantially implemented the Tuscan diagnostic proposal that has represented the more developed regional model since the 1990s-2000s.

As mentioned, screenings for phenylketonuria, hypothyroidism and cystic fibrosis have been made mandatory at the national level starting from article 6, letter g, of the law 5 February 1992, n. 104 – *Framework law for assistance, social integration and the rights of disabled people* and subsequent implementing acts.[19]

Starting from the law n. 244 of 24 December 2007 (2008 Finance Law) important funding has been allocated (about 3 million euros) for the purchase of new analytical methods, based on "tandem mass spectrometry", to carry out expanded newborn screening for hereditary metabolic diseases, where there is scientific evidence that therapy is effective.

Law n. 147 of 2013, *Provisions for the preparation of the annual and multi-year budget of the State* (Stability Law 2014), in paragraph 229 of article 1 establishes: "[...] the experimental launch throughout the national territory, within the limit of 5 million euros, of neonatal screening for the early diagnosis of hereditary metabolic diseases, for whose therapy, pharmacological or dietary, there is scientific evidence of therapeutic efficacy or for which there is scientific evidence that an early diagnosis, in neonatal age, entails an advantage in terms of access to therapies in an advanced state of experimentation, including dietary ones".[20]

The same provision states that the Minister of Health should approve a ministerial decree, after consulting the Higher Institute of Health and the Permanent Conference for relations between the State, the Regions and the Autonomous Provinces of Trento and Bolzano, to define the list of pathologies on which the screening should be carried out and the procedures for its implementation.

A relevant change is undoubtedly marked by law n. 167 of 2016, *Provisions on mandatory neonatal diagnostic tests for the prevention and treatment of hereditary metabolic diseases*, which came into force on 15 September 2016, as it provides for the inclusion of extended neonatal screening (ENS) in the new Essential Levels of Care (ELC) so as to be able to guarantee access to ENS for all newborns nationwide.[21]

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[19] See the Prime Minister Decree of July 9, 1999 *Act of guidance and coordination for the regions and autonomous provinces of Trento and Bolzano in the matter of investigations for the early diagnosis of malformations and mandatory control for the identification and timely treatment of congenital hypothyroidism, phenylketonuria and cystic fibrosis*. See also the law n. 548 of 23 December 1993 *Rules for the prevention and treatment of cystic fibrosis*.

[20] Law n. 190 of 2014 (2015 stability law), in paragraph 167 of art. 1, then increased the National Health Fund by a further 5 million euros, starting from 2015, thus increasing the funds for extended neonatal screening (ENS) to 10 million euros a year.

[21] Law n. 167 of 2016 provides for the inclusion in the Essential Levels of Care (ELC) of mandatory neonatal screenings for the early diagnosis of hereditary metabolic diseases; it establishes the Coordination Center on neonatal screening at the Higher Institute of Health; it establishes that the Ministry of Health should prepare an operational protocol for the management of screening and for taking care of the sick; it assigns to the

On March 19, 2017, the date of enforcement of the Prime Ministerial Decree of January 12, 2017 which updated the ELC, the ENS passed from the experimental phase to full operation. In fact, in the provision of the new ELC, in article 38 paragraph 2 of the Prime Ministerial Decree of 12 January 2017, the inclusion of ENS was envisaged, referring to a ministerial decree for the list of diseases and the methods of implementation.

The decree of the Ministry of Health of 13 October 2016, *Provisions for the start of newborn screening for the early diagnosis of hereditary metabolic diseases* contains a series of indications concerning the list of pathologies covered by ENS: the information and consent procedures; the methods of collecting, sending and storing the blood spot; the organization of the newborn screening system, whether regional or interregional, to ensure the continuity of the entire ENS path from the first-level test, to the second-level test, to diagnostic confirmation; and taking charge of the confirmed positive cases in newborns.

However, there are important inconsistencies between law n. 167 of 2016 and the ministerial decree of 13 October 2016 which must be highlighted.

Law n. 167 establishes the inclusion in the ELC of neonatal screenings which are qualified as mandatory and therefore the tests become the responsibility of the National Health Service.[22]

While law n. 167 qualifies the screening as mandatory, the ministerial decree of 13 October 2016 contains in article 2 rules about information and consent for non-mandatory screenings[23], and Annex

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National Agency for Regional Health Services the evaluation of the Health Technology Assessment (HTA) on newborn screening; and finally it provides for the method of financing the activity in question and establishes that from the entry into force of the Prime Minister's Decree that updates the ELC, the experimentation, started with law n. 147/2013, art. 1 paragraph 229, ceased. Subsequently, the 2019 budget law made important changes, extending the screening to genetic neuromuscular diseases, severe congenital immunodeficiencies, and lysosomal storage diseases.

[22] See art. 1 and art. 2 of law n. 167: art. 1 (Purpose): "This law aims to ensure the prevention of hereditary metabolic diseases, by including mandatory neonatal screening in the essential levels of care (ELC) [...]"; art. 2 (Scope of application): "The diagnostic tests as part of the mandatory screening referred to in art. 1 are carried out for hereditary metabolic diseases for which there is scientific evidence of therapeutic efficacy, pharmacological or dietary, or for which there is scientific evidence that an early diagnosis, in neonatal age, involves an advantage in terms of access to therapies in advanced state of experimentation, including dietary ones".

[23] Art. 2, titled "Information and consent", of the ministerial decree of 13 October 2016 is particularly interesting for our purposes and it reads as follows: "1. The ENS is carried out, after suitable information referred to in paragraph 2, provided to the interested parties by the professionals of the birth point. Where national or regional acts do not establish the obligation for the execution of the ENS, informed consent must be obtained for the execution of the ENS and for the processing of the personal data of the newborn, pursuant to art. 13 of the legislative decree 30 June 2003, n. 196, issued by natural parents or by the person exercising parental responsibility over the newborn. 2. The information, drawn up by the regions and autonomous provinces in an easily understandable language and translated into the languages most widely used in the area, must briefly and colloquially specify what the purposes and methods of the ENS are; the optional or mandatory nature of the screening procedure; the specific aims pursued (treatment and, if the ENS gives a positive result, genetic counselling); the methods of carrying out the test and the diseases tested; the achievable results, including any unexpected news known as a result of the differential diagnostics of the diseases referred to in attached table 3, which share the primary markers with those listed in table 1; the methods and times of storage of the samples; the scope of data communication, especially with reference to neonatal screening laboratories, clinical reference centres and the National Register of rare diseases, to which the data are

A to the ministerial decree presents a model of informed consent to be given to parents and legal representatives.[24]

Actually, the two fundamental acts of the Italian legislation on newborn screening seem to be mutually inconsistent.

From a strictly formal point of view, the ministerial decree of October 13 2016 refers in its foreword to law n. 167 but appears to be implementing paragraph 229 of article 1 of the Stability Law of 2014.[25]

From a substantial point of view, a series of critical issues emerge from a constitutional perspective.

First of all, by article 2 paragraph 1 of the ministerial decree of 2016, which reads: "[...] Where national or regional acts do not establish the obligation to execute the ENS, informed consent must be acquired for the execution of the ENS and the processing of personal data of the newborn […]", it could be understood that at the regional level, before the 2016 legislation, the screening tests provided could be considered mandatory. The first problem therefore concerns the possibility of qualifying a test as mandatory at regional level.

As known, art. 32, paragraph 2, of the Italian Constitution places a State law reserve when it requires a State law for the imposition of a mandatory health treatment that does not violate the limits of respect for the person.

On this point, a clear response comes from constitutional case law issued on the basis of the State legislation reserve contained in article 32, second paragraph, of the Italian Constitution on mandatory health treatments and on the basis of the division of legislative competences between the State and the Regions in the exclusive and concurrent matter of health guarantee contained respectively in second paragraph, letter m, of article 117 (determination of essential levels of care) and in third paragraph of article 117 (health protection), of the Italian Constitution. In decision n. 5 of 2018, the Italian Constitutional Court affirms that it is up to the State "to qualify a certain health treatment as mandatory, on the basis of the medical and scientific knowledge available".[26]

The discipline of mandatory treatments is straightforwardly assigned to the State legislative competence as it belongs to the determination of the fundamental principles concerning the matter of health protection.[27]

Since the criterion of the voluntary or mandatory nature of the treatments affects fundamental rights, such as the right to self-determination and the right to health that belong to the State

communicated through the regional registers. 3. The collection of informed consent, referred to in paragraph 1, must be carried out before carrying out the screening test, according to the contents of the model in Annex A to this decree, which is an example. It must contain the consent to carry out the screening, to the processing of data and to the storage of samples".

[24] As mentioned, in the first annex to the ministerial decree, a list of about 40 metabolic diseases is drawn up, which constitutes the most complete panel of diseases at European level, while in annex A of the decree an informed consent model is prepared which raises some issues.

[25] Art. 1, paragraph 229, of the law n. 147 of 27 December 2013 (Stability Law of 2014) referred to a ministerial regulation the definition of the list of diseases on which to carry out newborn screening.

[26] See the ruling of the Italian Constitutional Court n. 5 of 2018, paragraph n. 7.2.2 of the decision.

[27] With reference to vaccinations see the decision of the Italian Constitutional Court n. 137 of 2019 and n. 5 of 2018.

legislative competence, it can be assumed that a regional act cannot decide whether a treatment is mandatory.[28]

A second, relevant problem concerns the normative qualification of screening as mandatory or voluntary. While in article 1 of the law n. 167 of 2016 it is stated that neonatal screenings have become mandatory, in article 2 of the ministerial decree of 2016, a series of rules on information and informed consent are provided for *tamquam non esset*, except from a strictly formal point of view, the law n. 167. Looking at Annex A of the ministerial decree of 2016 and reading the model of informed consent reported there, it could be understood that the mandatory nature refers only to the three diseases provided for by the old law n. 104 of 1992, while everything else is framed as voluntary neonatal screening.

Leaving aside here the overview issue of the reserve contained in article 32 of the Italian Constitution as an absolute reserve of law, also reinforced by the provision of the respect for the human person,[29] or a relative reserve,[30] the contrast substantially existing between the law n. 167 of 2016 and the ministerial decree of October 13 2016 poses, *de facto*, some questions about the respect for the hierarchy of sources and highlights significant interpretative problems that have led to a great variability in clinical practice in the screening sector at regional level.

These problems require an in-depth study on the mandatory and voluntary nature of a test or a treatment.

As required by the Italian Constitution in article 32, second paragraph, only a State law, i.e. a primary source, can declare a treatment voluntary, even by not specifying anything on the point of obligation and therefore enhancing the constitutional principle of self-determination, or mandatory, when this is aimed not only at improving or preserving the conditions of health of those subjected to it, but also at guaranteeing the collective interest to health, since it is precisely this further proposal that justifies the suppression of individual self-determination.[31]

The definition of a treatment or a test as mandatory/voluntary is assigned to a State primary source as it belongs to the determination of the fundamental principles concerning the right to health.

In addition, the Italian Constitution provided for a reinforced legal reservation when it established that "The law cannot in any case violate the limits imposed by respect for the human person"[32] and

[28] See the decision of the Italian Constitutional Court n. 438 of 2008.

[29] On this position see P. BARILE, *Diritti dell'uomo e libertà fondamentali*, Bologna, 1984, p. 385; A. PACE, *La libertà di riunione nella Costituzione italiana*, Milano, 1967, 87 ff.; B. PEZZINI, *Il diritto alla salute: profili costituzionali*, in *Diritto e Società*, 1983, 28 ff.

[30] On this position see M. LUCIANI, *Il diritto costituzionale alla salute*, in *Diritto e Società*, 1980, 10; F. MODUGNO, *Trattamenti sanitari «non obbligatori» e Costituzione*, in *Diritto e Società*, 1982, 309; V. CRISAFULLI, *In tema di emotrasfusioni obbligatorie*, in *Diritto e Società*, 1984, 558; S.P. PANUNZIO, *Trattamenti sanitari obbligatori e Costituzione*, in *Diritto e Società*, 1979, 900; E. CAVASINO, *La flessibilità del diritto alla salute*, Napoli, 2012, 181.

[31] See the decisions of the Italian Constitutional Court n. 268 of 2017, n. 107 of 2012, n. 226 of 2000, n. 118 of 1996, n. 258 of 1994 and n. 307 of 1990.

[32] The Court affirmed in judgment n. 194 of 1996 that "blood sampling – now of ordinary administration in medical practice – does not harm the dignity or psyche of the person, just as it does not normally endanger his life, safety and health in any way (see decision n. 54 of 1986)". The limits of respect for the human person can be identified with the very low degree of invasiveness and its effects on the psycho-physical integrity of the person. The assessment also concerns the incisiveness that the test has on the freedom and self-determination of the person. With respect to this it is necessary to verify the possible provision of a compulsory treatment,

prevents such a qualification, related to the mandatory or voluntary nature of a test, being made from a secondary source, including, therefore by a ministerial decree.[33]

The constitutional case law on the matter is extensive and the relevant constitutional principles ensue from articles 2, 13, 32 of the Italian Constitution. The Italian Constitutional Court affirms that the balance between the individual's right to health and the interest of the community must take place in such a way that the right of the individual is not excessively affected except for temporary, minor and in any case tolerable consequences.

Over the years, the Court's case law has clarified the requisites necessary for the purposes of a legislative provision of an obligation of test or treatment. First of all, a justification of reasonable scientific efficacy at an epidemiological level is needed for the prevention of the disease in the subject undergoing test and for the management of a significant risk to public health and the legislative provision of measures to contain as much as possible the risks of adverse events.

Furthermore, on the basis of the solidarity duty that presides over the subject of the mandatory tests and treatments, compensation must be provided to compensate for any damage, even if not of a purely financial nature, suffered by the person who has undergone the treatment or test.[34]

In the case of newborns, there is a need for balance between the protection of the best interests of the child,[35] the exercise of parental responsibility, and the collective interest in preventing serious diseases whose management impacts on the community.

As stated, screening does not strictly represent a health treatment but constitutes an investigation strategy carried out in the context of secondary prevention.

We need to specify that the collective interest protected in the case of neonatal screening is of a different nature from the collective interest protected in the case of vaccines. While in the case of vaccines the collective interest is directly related to health, aimed at protecting both individuals and public health, in the case of screening the collective interest is not directly linked to protection of public health, but it does have an impact on health and social costs, considering the very high impact that metabolic diseases have on the person, the family, and the community because they are multi-systemic diseases that can cause irreversible damage to several organs and systems and are responsible for early neonatal mortality as well as permanent psychic and neuromotor delays from childhood.[36]

As we said before, massive screening program are disputed, but the possibility of preventing these inherited disorders or stopping their progression may undoubtedly correspond to an important collective interest of a socio-economic nature.

Similar examples that can be referenced in defining the contours of this collective interest and which also have an indirect impact on health, are the obligation to wear a helmet or seatbelt when riding or

which would require further, pursuant to art. 13 of the Italian Constitution, the legislative discipline of cases and methods of coercion and a provision of the judicial authority.

[33] It is necessary to specify here that once a national law has established that a treatment or a test is mandatory, a ministerial decree cannot decide otherwise as if the State law did not exist.

[34] See the decisions of the Italian Constitutional Court nn. 5 of 2018, 258 of 94, 307 of 90.

[35] On the relevance of protection of the best interests of the child for mandatory screening, see M. TOMASI, *Genetica e Costituzione. Esercizi di uguaglianza, solidarietà e responsabilità*, Napoli, 2019, 294 ff.

[36] See supra footnote n. 1.

driving vehicles. The obligation to use these safety measures does not have an immediate health purpose. Its function is to protect the individual and, from the collective point of view, is not aimed at protecting public health but at containing a risk, which can be statistically highlighted, and which is linked to significant economic and social effects on the national system and on the National Health Service.

As in the case of newborn screening, there is therefore an economic-functional link with respect to public health that is the basis of the imposition of the obligation that protects the collective interest and the health of the individual.[37] In this sense, it is possible to state that only a primary source, i. e. a State law, can define the boundaries of what should be mandatory and establish its effects.

4. Regional practices after the rules of 2016

As we mentioned before, paragraph 2 of article 117 of the Italian Constitution establishes that the "determination of essential levels of care" constitutes an exclusive legislative competence of the State, while paragraph 3 of art. 117 of the Italian Constitution includes the "health protection" competence among the concurrent competences. As part of this latter competence, it should be specified that the fundamental principles are provided for by the law of the State while the organizational rules are established at the regional level.[38]

On the basis of these constitutional norms, while the law of the State establishes which are the essential levels of care that must be guaranteed throughout the national territory (see the Prime Ministerial Decree of January 12, 2017), the Regions establish the procedures and organizational practices aimed at meeting the essential levels established. Within this constitutional framework of division of legislative powers between State and Regions, regional practices often differ and lead to very different organizational models.

In this context, the aforementioned inconsistency between the two 2016 acts on newborn screening has led to an increase in regional divergences in the ways of carrying out screening, managing informed consent and dissent, and managing the storage and the use of the biological material collected.

About the mentioned inconsistency of the two 2016 acts, we could deduce that according to law n. 167 extended newborn screening is mandatory and included in the ELC, while on the basis of the ministerial decree of 13 October 2016 the expression of consent concerns only the extended newborn screening which concerns diseases listed in the annex to the ministerial decree, while the three mandatory screenings remain those established by law n. 104 of 1992.

It must be said that there would be a need for a specific implementation of law n. 167 in order to overcome the critical issues envisaged. However, on the basis of the principle of conservation of legal acts, the interpreters carried out some operations of mutual adjustment and adaptation between the two acts. These operations were successful in some respects and not in others, as emerges from the analysis of regional practices subsequent to the 2016 rules. In fact, while on the one hand these norms, together with the decree updating the essential levels of care, made it possible to obtain

[37] See the decisions of the Italian Constitutional Court n. 180 del 1994 and ordinance n. 49 del 2009.

[38] Cfr. decisions of the Italian Constitutional Court n. 510 of 2002, n. 329 of 2003, n. 338 of 2003.

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uniformity in the provision of the screening offer, the same uniformity cannot be traced in the management of informed consent and dissent. In addition, it seems evident that some aspects, such as the management of the conservation of the biological material collected and the use of the same for research purposes, require further analysis.

4.1. Regional practices with reference to development of screening programmes and to management of informed consent and dissent to the procedure

In order to highlight some features of regional practices on the subject, we will refer to the three reports, so far prepared by the Italian Higher Institute of Health and the Coordination Center on Neonatal Screening (CCSN), established by article 3 of the law n. 167 of 2016[39], in collaboration with the National Center for Rare Diseases, on monitoring the state of implementation of law n. 167 of 2106 and of the ministerial decree of 13 October 2016.[40]

In the first monitoring report on the state of implementation of law n. 167/2016 and the ministerial decree of 13 October 2016 on Extended Neonatal Screening (ENS) in Italy[41], the state of the art of the individual regional programmes of the ENS as of 30 June 2017 is described. The data highlighted that 18 Regions/Autonomous Provinces out of 20 Regions and two Autonomous Provinces on that date had started the ENS programme, while in 3 Regions the ENS system was still in the activation phase at the indicated date.[42]

The second monitoring report on the state of implementation of the 2016 rules provides an update on the evolution of the ENS system in the Regions, and documents the changes introduced on 30 September 2018 through a fact-finding survey conducted by the Coordination Center on Neonatal Screening (CCSN), with the aim of highlighting the new regional actions and strategies introduced between 30 June 2017 and 30 September 2018.[43] The state of the art on 30 September 2018 indicates that all the Regions/Autonomous Provinces, except Calabria, had started the ENS programmes. The ENS regional system in Calabria was, in fact, in the activation phase. Of the other Regions/Autonomous Provinces which had started the system, almost all covered the entire panel of metabolic diseases provided for in the ministerial decree of 13 October 2016.

[39] One of the tasks assigned to the CCSN (Article 3 of Law 167/2016) is to monitor and promote the maximum uniformity of application of newborn screening in Italy.

[40] We refer to, in chronological order, Higher Institute of Health, *Screening neonatale esteso nelle Regioni: monitoraggio dell'attuazione della Legge 167/2016 e del decreto ministeriale del 13 ottobre 2016. Stato dell'arte al 30 giugno 2017*, Rapporto Istisan 18/11; Higher Institute of Health, *Screening neonatale esteso in Italia: stato dell'arte al 30 settembre 2018*, 2019; Higher Institute of Health, *Programmi di screening neonatale esteso nelle Regioni e Province autonome in Italia. Stato dell'arte al 30 giugno 2019*, Rapporto Istisan, 20/18.

[41] Higher Institute of Health, *Screening neonatale esteso nelle Regioni: monitoraggio dell'attuazione della Legge 167/2016 e del decreto ministeriale del 13 ottobre 2016. Stato dell'arte al 30 giugno 2017*, Rapporto Istisan, 18/11.

[42] Not all Regions have defined the various levels of articulation of the ENS system, based on art. 4 of the ministerial decree of 13 October 2016. Furthermore, only 50% of the Regions have full coverage of the pathologies covered by the ENS.

[43] See Higher Institute of Health, *Screening neonatale esteso in Italia: stato dell'arte al 30 settembre 2018*, 2019.

In the Regions of Abruzzo, Campania, Friuli Venezia Giulia, Lombardy, and the Autonomous Provinces of Bolzano and Tuscany, new information sheets have been created to make parents and legal representatives aware of the purposes of ENS.

The Regions of Basilicata, Friuli Venezia Giulia, Molise, Umbria and Valle d'Aosta and the Autonomous Provinces of Bolzano and Trento have activated the ENS system in agreement with other Regions. Moreover, 10 Regions have issued new specific administrative acts for the ENS Regional System (Abruzzo, Basilicata, Campania, Emilia Romagna, Lazio, Lombardy, Piedmont, Valle d'Aosta, Tuscany and Veneto).[44]

In conclusion, in Italy, the ENS for the prevention, early diagnosis and treatment of Inherited Metabolic Disorders (IMDs), despite the inconsistencies existing between the law n. 167 of 2016 and the ministerial decree of 13 October 2016, passed from an experimental phase to a mandatory offer phase on all newborns in the national territory.

The third report of the Higher Institute of Health on screening concerns a survey that specifically provides information on regional practices relating to the management of informed consent and dissent to the procedure.[45]

As part of the fact-finding survey, the Regions/Autonomous Provinces were asked whether, for the execution of the ENS, informed consent was required from parents and legal representatives of the newborn.[46]

The results are interesting: 7 Regions and Autonomous Provinces (Campania, Lombardy, and the Autonomous Provinces of Trento, Puglia, Tuscany, Umbria, Valle d'Aosta) declared that they did not require informed consent; among the remaining Regions and Autonomous Provinces, the request for informed consent takes place in 4 Regions only for diseases not provided for in Annex A of the ministerial decree of 13 October 2016;[47] in 7 Regions the collection of informed consent occurs for provided and not provided diseases in Annex A of the ministerial decree of 13 October 2016;[48] and in 3 Regions only for the diseases listed in Annex A of the ministerial decree of 13 October 2016.[49]

Regarding the consent and dissent to the execution of ENS, the answers provided by the Regions/Autonomous Provinces seem to highlight a situation of chaos relating to the issue. In fact, half of the respondents require informed consent for "provided" or "not provided" diseases in Annex A of the ministerial decree of 13 October 2016 and do not require the systematic collection of dissent to the execution of ENS.

In conclusion, the rules of 2016 have essentially made it possible to move from a hybrid model – in which, with respect to three diseases at national level, on the basis of law n. 104 of 1992, a

[44] See Higher Institute of Health, *Screening neonatale esteso in Italia: stato dell'arte al 30 settembre 2018*, 2019, 4 ff.

[45] See Higher Institute of Health, *Programmi di screening neonatale esteso nelle Regioni e Province autonome in Italia. Stato dell'arte al 30 giugno 2019*, 4-9.

[46] See Rapporto Istisan, 20/18, *Programmi di screening neonatale esteso nelle Regioni e Province autonome in Italia. Stato dell'arte al 30 giugno 2019*, 7 ff.

[47] They are Friuli Venezia Giulia, Autonomous Province of Bolzano, Sicily, Veneto (Laboratory of Verona).

[48] They are Abruzzo, Emilia-Romagna, Lazio, Molise, Piemonte, Sardegna, Veneto (Laboratory of Padua).

[49] They are Basilicata, Liguria e Marche. It is useful to specify that Calabria did not provide the requested information. See Higher Institute of Health, *Programmi di screening neonatale esteso nelle Regioni e Province autonome in Italia. Stato dell'arte al 30 giugno 2019*, 7.

mandatory nature was envisaged, while at the regional level the wider diagnostic offer was based on a voluntary basis of the investigations – to an opting out model allowing for the implementation of uniformity of practice in the field of tests and procedures.

This uniformity achieved in terms of the diagnostic offer does not correspond to a similar uniformity in terms of regional practices as regards the awareness of the effects of the mandatory tests and the organizational management of informed consent and dissent, and in terms of the collection of informed consent for aspects not envisaged as mandatory by the rules of 2016.

The information that emerges from the fact-finding survey on the organizational management of consent and dissent highlights some unresolved issues.

Given the absence of uniform management at regional level, the Higher Institute of Health provides some recommendations on how to manage informed consent and dissent.[50]

On the basis of the analyses developed before in paragraph n. 3, and considered the inconsistencies between the two normative acts of 2016, we can affirm that the recommendations of the Higher Institute of Health are consistent with the constitutional oriented reading of the rules on the mandatory/voluntary nature of treatments and tests and on informed consent/dissent that we have tried to outline *supra*.

In fact, the Higher Institute of Health specifies that it should be necessary to ensure that informed consent would be acquired in the case of the execution of ENS for diseases not provided for by the ministerial decree of 13/10/2016 or for diseases other than those mentioned by other laws that make screening mandatory.

In this way, the principles established by the Italian Constitution in article 32, second paragraph, according to which only a State law, i.e. a primary source, can declare a treatment or a test voluntary or mandatory, are fully respected.

About the dissent, the Higher Institute of Health clarifies that the parental couple can express their objection to the execution of the mandatory ENS. However, it is necessary that the Birth Center transcribes this dissent on the information form, affixing the date and simultaneously acquiring the signature of those exercising parental responsibility and the signature of the healthcare professionals involved. The information form containing the dissent must be included in the medical record of the newborn and in the case of a home birth in the obstetric record.

4.2. Regional practices on storage and use of biological material

From another point of view, the Higher Institute of Health checked also the uniformity of regional storage and use practices. Since the cardboard containing the blood spot collected for the extended neonatal screening of metabolic diseases contains biological material of significant value, both in terms of public health and research, it must be stored in ways that allow respect for the fundamental rights at stake (e.g. family autonomy and self-determination, privacy, etc.)

From the data reported in the third report of the Higher Institute of Health and related to regional practices, we see that there is extreme variability in terms of time and methods of storage of the

[50] See Higher Institute of Health, *Programmi di screening neonatale esteso nelle Regioni e Province autonome in Italia. Stato dell'arte al 30 giugno 2019*, 8-9.

card containing the blood spot.[51] From these data it is clear that there is a lack of process norms to regulate the methods of conservation and use of the residual material on the cardboard containing the blood spot, not only for diagnostic and medical legal purposes but also for research purposes, to ensure uniformity of the storage conditions and the methods of use at national level.

In the absence of any explicit regulatory provision on this point, it can be assumed that the biological material of the newborn, the drops of blood on the card, can be stored only for the time strictly necessary for carrying out the tests related to screening.

Beyond this time, the biological material should be removed or, if possible, the data of the newborn should be anonymised.[52]

If the biological material is kept for research reasons beyond the time necessary to carry out the tests, it can be concluded that these aspects could be the subject of informed consent, both regarding the conservation profile and the research uses, and for concerns about the processing of data and its codification and pseudonymisation.

The point has an obvious relevance and it is necessary to distinguish the uses that are made of the biological material in relation to the screening tests and the uses that can be made in relation to future research not related to the screening tests. The management models for conservation and future research on biological material, based on a minimisation of data processing (codification/pseudonymisation/anonymisation), and the authorisation of the competent ethics committee, may be various and may require adequate information to be given to the parents and legal representatives; the collection of the parents' informed consent may, in turn, have a variable scope and could *in abstracto* include alternatives, ranging widely from specific consent to partially restricted consent, tiered consent up to broad consent.[53]

5. Some conclusive reflections

There is no doubt that the newborn screening programme developed in Italy represents the most advanced "model" in Europe – from a specific viewpoint, i.e. the panel of the diseases to be checked – and that the research has achieved significant objectives in this area. The constant scientific research work on the subject portends a progressive expansion of screening programmes. The

[51] See Higher Institute of Health, *Programmi di screening neonatale esteso nelle Regioni e Province autonome in Italia. Stato dell'arte al 30 giugno 2019*, 31-32.

[52] The real possibility of anomymization is questioned in literature. See F.K. Dankar, A. Ptitsyn, S.K. Dankar, *The development of large-scale de-identified biomedical databases in the age of genomics-principles and challenges*, in *Human Genomics*, 10 April 2018.

[53] On the possible modelling of informed consent for scientific research cfr. C. Grady, L. Eckstein, B. Berkman, D. Brock, R. Cook-Deegan, S.M. Fullerton, H. Greely, M.G. Hansson, S. Hull, S. Kim, B. Lo, R. Pentz, L. Rodriguez, C. Weil, B.S. Wilfond, D. Wendler, *Broad consent for research with biological samples: workshop conclusions*, in *American journal of bioethics*, 15, 9, 2015, 34-42; R.B. Mikkelsen, M. Gjerris, G. Waldemar et al., *Broad consent for biobanks is best – provided it is also deep*, in *BMC Medical Ethics*, 20, 2019; J. Murphy, J. Scott, D. Kaufman, G. Geller, L. LeRoy, K. Hudson, *Public perspectives on informed consent for biobanking*, in *American journal of public health*, 99, 12, 2009, 2128-2134; E. Salvaterra, L. Lecchi, S. Giovanelli, B. Butti, M.T. Bardella, P.A. Bertazzi, S. Bosari, G. Coggi, D.A. Coviello, F. Lalatta, M. Moggio, M. Nosotti, A. Zanella, P. Rebulla, *Banking together. A unified model of informed consent for biobanking*, in *EMBO Reports*, 9, 4, 2008 April, 307-313.

development of prevention in this area is undoubtedly a noteworthy factor in the development of the entire health and social system of the country. The greater the relevance of the screening programme to the overall system, the more urgent will become the management of the problematic aspects concerning the coordination of screening programmes at international and European level, both as regards the clinical usefulness of the tests and, consequently, the panel of the diseases to be checked and with regard to the management of the procedures for accessing the investigations. In addition, the issue of a general harmonisation of the Italian rules of 2016 must be urgently addressed in order to overcome the critical issues highlighted in the discussion and to respect the Italian constitutional principles ruling the health sector. In particular, in the Italian context, in the face of research and medical science that have developed scientifically valid screening programmes, we have traced some problems relating to the management of informed consent and dissent to the procedure deriving from some inconsistencies existing in the rules established in 2016 at national level. These inconsistencies have generated evident confusion at regional level about the voluntary or mandatory nature of the proposed screening tests with repercussions for the management of informed consent and dissent.

In this paper we have tried to outline a proposal for a constitutionally oriented reading of the rules of 2016 starting from the constitutional principles and the constitutional case law in the field of health protection.

As we observed, the constitutional principles enshrined in the Italian Constitution and the constitutional case law are clear to declare that only a State law, i.e. a primary source, can declare a treatment or a test voluntary, even by not specifying anything on the point of obligation and therefore enhancing the constitutional principle of self-determination, or mandatory, when there is the need for balancing individual right to health and collective interests to health.

In the case of newborns, there is a need for balance between the protection of the best interests of the child, the exercise of parental responsibility, and the collective interest in preventing serious diseases whose management strongly impacts, from a socio-economic viewpoint, on the community.

Collectively, the Italian rules of 2016 have essentially made it possible to move from a hybrid model – in which, with respect to three diseases at national level, on the basis of law n. 104 of 1992, the mandatory nature of tests was envisaged, while at regional level the broader diagnostic offer was based on the voluntary nature of the investigations – to an opting out model allowing for the implementation of uniformity of practice regarding tests and procedures.

The uniformity achieved in terms of the diagnostic offer through the rules of 2016 is still lacking regarding the awareness of the effects of the mandatory test and the organizational management of informed consent and dissent, and in terms of the collection of informed consent for the aspects not envisaged by the legislation of 2016.

Finally, on this latter aspect with regard to the issues of conservation of the biological material collected and its use for research purposes, there is a need to develop further regulatory guidelines that will make it possible to standardise regional practices on the subject and to guarantee the widest protection of fundamental rights of newborns and their families.