Impact and Implementation of Medical Devices Regulation in Spain

Status of the regulatory works undertaken in Spain for the complete implementation of the new legal frame following the 2017 EU regulations

Jorge Robles González. Málaga, Spain*

On May 26, 2021, and May 26, 2022, began the direct application of, respectively, Regulations (EU) 2017/745 and 2017/746 on medical devices and in vitro diagnostic medical devices. The full implementation of this regulatory framework in Spain requires the approval of new internal rules that repeal those in force until now and regulate the aspects that the EU regulations entrust to national regulations. To this end, the Ministry of Health is currently working on the drafting of two sets of regulations, which would be completed with a third set of regulations, of legal rank, on the advertising of medical devices.

General considerations: the need, purpose and function of new regulatory standards on medical devices in Spain

On 26 May 2021, Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices amending Directive 2001/83/EC, Regulation (EC) 178/2002 and Regulation (EC) 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC finally entered into application after a deferral of the date initially set.[1]

One year later, on 26 May 2022, the direct application of Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU started.

These EU regulations represent, from the point of view of the regulatory instrument used, a singular change with respect to the previous situation. Up until this point, EU regulation in this matter had been carried out essentially by means of directives, which required transposition into the domestic law of each Member State by means of the approval of national rules for their application and effectiveness: specifically, the EU directives on medical devices, on active implantable medical devices and on medical devices for in vitro diagnosis were transposed into Spanish law by specific royal decrees[2], with Royal Decree 1591/2009 being in force at the date of entry into force of the Community regulations, of 16 October 2009, which regulates medical devices, Royal Decree 1616/2009, of 26 October 2009, which regulates active implantable medical devices, and Royal Decree 1662/2000, of 29 September 2000, on in vitro diagnostic medical devices[3].

As the Community regulations are directly applicable, the Spanish royal decrees have been displaced (but not repealed) in those aspects that do not conform to them, as a result of the primacy of Community law. This requires an interpretative task that compromises the desirable legal certainty, which, in fact, has led the Court of Justice to declare that the Member State concerned is obliged to purge its legal system of any rules that conflict with Community law.[4]

It should also be taken into account that Regulations (EU) 2017/745 and 2017/746, despite being directly applicable rules, refer or make certain aspects or issues subject to the regulation to be established at national levels.

These circumstances have led the Ministry of Health to initiate works on the processing and drafting of Royal Decrees regulating medical devices and in vitro diagnostic medical devices.

Status of the processing of the new rules

Draft Royal Decree on medical devices

The aforementioned works were initiated by the Ministry of Health by opening a public consultation on 27 February 2020 for input and feedback prior to the drafting of the text of the project, which ended on 7 June 2020.

In the prior public consultation (as well as in the regulatory impact assessment prepared after the drafting of the text), it is noted that this regulation is necessary in order to: (i) establish the requirements and procedures for the regulation of prod-

ucts manufactured and used in a healthcare facility (in house); (ii) establish the requirements and procedures for the regulation of the reprocessing of single-use medical devices; (iii) establish the requirements and procedures for the regulation of the implantation card; (iv) establish the creation of a National Register for the marketing of medical devices; (v) regulate the language regime; (vi) establish the requirements for the conduct of clinical investigations in Spain; (vii) establish that, with regard to Regulation (EU) 2017/745, the competent authority is the Spanish Agency for Medicines and Medical Devices (hereinafter, AEMPS), regardless of the competences of other health authorities.
Accordingly, the Spanish Agency of Medicines and Medical Products (AEMPS) undertook the preparation of the text of the draft royal decree, which, as indicated in its Report, pursues a threefold objective:

- Revoke Royal Decree 1591/2009 of 16 October 2009 regulating medical devices and Royal Decree 1616/2009 of 26 October 2009 regulating active implantable medical devices in view of the direct application of Regulation (EU) 2017/745.
  This is a laudable objective in terms of legal certainty and security, as it removes possible doubts about the applicable regulatory provisions.
  However, it should be noted that this objective is not fully achieved, as the repeal is not absolute: Articles 21, 38, 39 and 40 of Royal Decree 1591/2009 and Articles 18, 34, 35 and 36 of Royal Decree 1616/2009 remain in force, i. e. the provisions of both regulations relating to advertising, promotion, incentives and sponsorship of scientific meetings, and the procedures of the Notified Body.[5]
  The justification for the continuation of these rules lies in the fact that work is currently underway on new legal provisions that will specifically regulate the advertising of medical devices, as well as the procedures of the Notified Body.
- To develop the necessary regulatory measures for those aspects where the EU regulation has determined that it will be the Member States that will establish the regulation at national level.
- Adapt, adopt or maintain measures required by national legislation.

Once the drafted royal decree had been drawn up by the AEMPS, it was submitted, during the months of June and July 2021, to public information and a hearing of the associations and organizations representing the interests affected, and reports were also obtained from various government bodies.
At present, the Ministry has already taken a decision on the comments received, so it is expected that in December 2022 or in the first months of 2023 the new Royal Decree will be approved by the Council of Ministers.

Drafted Royal Decree on in vitro diagnostic medical devices

Between 23 July 2021 and 8 August 2021, the Ministry of Health carried out the prior public consultation process, stating that such a regulation is necessary in order to: (i) establish the requirements for genetic information, counselling and informed consent; (ii) establish the requirements and procedures for the regulation of products manufactured and used in a healthcare centers (in house); (iii) establish the requirements for the notification of in vitro diagnostic products to the marketing registry; (iv) regulate the language regime; (v) establish the requirements for the performance evaluations in Spain; (vi) establish that, with regard to Regulation (EU) 2017/746, the competent authority is the AEMPS, regardless of the competences of other health authorities.
It adds that the objectives of this regulation are: a) to repeal Royal Decree 1662/2000 in view of the direct application of Regulation (EU) 2017/746; b) to develop rules for those aspects that the EU regulation refers to national regulations; c) to adapt, adopt or maintain the measures required by national legislation.
The text of this draft royal decree is currently being prepared by the AEMPS. It was expected that the text already drafted would be submitted for public information and hearing of representative organizations in August or September 2022, which has not taken place, so this process should be imminent.

Reference to the draft bill on advertising of medical devices.

In addition to the above, it should be noted that work has also begun on the processing of the amendment of a regulation with the status of law, Royal Legislative Decree 1/2015, of 24 July, which approves the revised text of the Law on Guarantees and Rational Use of Medicines and Medical Devices.
To this end, the Ministry of Health opened, from 6 July 2022 until 31 July 2022, a public consultation prior to the drafting of the text of the preliminary draft law. The scope of the bill would cover both medicinal products and medical devices. With regard to medical devices, the objectives pursued are: (i) to incorporate

the amendments and definitions of Regulation (EU) 2017/745 and Regulation (EU) 2017/746; (ii) to clarify the wording of medical devices subject to prescription; (iii) to incorporate a separate chapter on guarantees for medical devices, cosmetics and personal care products; (iv) to amend the articles relating to the advertising of medical devices.
It should be noted that, in this case, once the text of the preliminary draft law has been drawn up by the Ministry, it would have to be approved as a draft law by the Council of Ministers. And, from that moment on, its parliamentary processing would begin until its eventual approval as a law by the Cortes Generales.

Considerations on the text of the draft royal decree on medical devices.

Scope

At present, the only regulatory project for which we have a drafted text is the draft royal decree on medical devices.
It should be noted that this draft royal decree is not, as the one on in vitro diagnostic medical devices will not be, a translation at national level of the Community regulation (as Royal Decree 1591/2009 and Royal Decree 1616/2009 were with respect to the directives they transposed). The Community regulation and the draft royal decree regulate different matters and issues (related – closely related – but different), and it is no longer possible to rely solely on the national regulation.

Structure and content

As regards its structure, it consists of a preamble, 41 articles (divided into nine chapters), three additional provisions, nine transitional provisions, one repealing provision and three final provisions.
In terms of content, and without being exhaustive, the following issues should be highlighted

Health guarantee and language regime

Chapter I contains the so-called general provisions (purpose, definitions – for the purposes of which it refers *in totum* to the Community regulation –, scope, competent authority – which is the AEMPS –, health guarantees for products and administrative cooperation).
With regard to the health guarantee of products, the regulation (Article 5) is substantially limited to adapting the equivalent provision of the Royal Decrees still in force. And it introduces the reference to the language regime, by establishing that at the time they are put into service in Spain, products must include the data and information contained in section 23 of Annex I of Regulation (EU) 2017/745, i. e. the data and information that must appear on the label and instructions for use, "at least in Spanish".
This is not a minor requirement that merits reflection. The translation of the label, in the case of a product for professional use and for which there is no doubt as to its unequivocal identification, does not seem justified if it is in an official EU language of general knowledge (English), and could be accompanied by graphics that clearly identify the product; however, this possibility has been rejected by the Ministry in its response to the observations raised.
The complexity of this translation requirement is very high: not only because Regulation (EU) 2017/745 has increased the information that must appear on the product label, but also because, in addition, the obligation to translate the description or identification of the product into Spanish, when this type of requirement is not established in other Member States, may mean that importers or distributors have to carry out this modification of the labelling in their facilities with the requirements of Article 16.4 of the Community regulation, which calls into question the proportionality of this measure in the (absolute and unconditional) terms in which it appears in the draft royal decree.
Of particular relevance are computer software for professional use, with regard to which it should be taken into account that the informative circular no. 12/98[6] has established that "they may offer the messages on the screens in English as long as they are accompanied by information in Spanish that guarantees their use in complete safety".
In any case, it should be noted that Annex I of the draft Royal Decree (AEMPS Report on the contributions received in the public consultation process prior to the draft) recalls that electronic instructions are regulated in Commission Regulation (EU) 207/2012 of 9 March 2012, indicating that the new Royal Decree does not establish additional requirements.

Pre-license for the operation and manufacture of products by health care facilities for the exclusive use of the facility itself

Chapter II (Articles 7 to 10), under the heading "Facilities", regulates the prior license for the operation of facilities, the manufacture of products by healthcare facilities for the exclusive use of the facility itself and the manufacture of custom-made products.

The draft royal decree maintains the requirement for a prior license for the operation of facilities, extending its scope of application. Whereas until now this license was required for the manufacture, importation, grouping or sterilization of medical devices, the draft royal decree extends it to the manufacture of devices and instruments used in permanent or semi-permanent make-up or skin tattooing using invasive techniques, to the manufacture of products for non-medical purposes and to reprocessing.
The draft royal decree adds that the import license will be required not only of the importer established in Spain who introduces a product from a third country into the EU market, but also of anyone who, without being an importer in accordance with Regulation (EU) 2017/745, physically imports the product (in the replies to the comments, the Ministry refers to future guides to resolve possible dysfunctions). It also requires a prior operating license from the manufacturer (complete manufacture) for third parties.
In addition, the requirement for a technical manager as a requirement for obtaining a license is maintained, while the admissible qualification requirements for this position are extended to include other types of qualification and experience. It should be borne in mind that the functions corresponding to the technical manager are different from the functions corresponding to the person responsible for regulatory compliance, as defined in Article 15 of Regulation (EU) 2017/745; however, a person who meets the requirements established both in the new royal decree and in the EU regulation could hold both positions.

An important novelty is the regulation of the manufacture of products by healthcare institutions for the exclusive use of the institution itself. This is a possibility provided for in Article 5.5 of Regulation (EU) 2017/745, which is subject to a series of requirements (mandatory requirements which, in order not to reiterate a directly applicable EU regulation, are not included in the draft Royal Decree).[7]
The draft Royal Decree, by virtue of the powers of development that the Community regulation confers on the Member States, restricts this possibility to health centers that have the status of hospital[8] (a decision questioned in the Report of the National Commission for Markets and Competition), excluding from this manufacturing class IIb, class III and implantable products, and prohibiting subcontracting.[9]
In the first text of the draft royal decree, hospitals were required to obtain a prior operating license to carry out this activity, although this requirement has been eliminated and replaced by prior notification to the AEMPS.

Reprocessing of single-use products
Regulation (EU) 2017/745 establishes (Article 17) that reprocessing of single-use devices may be carried out only when permitted by national legislation, and that the requirements it lays down must be observed in all cases; and distinguishes between reprocessing carried out by a natural or legal person (who becomes the manufacturer of the reprocessed products, with the obligations imposed on the manufacturer by the EU regulation) and a health institution (for which national legislation may choose not to subject the manufacturer to all the requirements applicable to the manufacturer, subject to the limits indicated).
On this basis, in exercise of the powers to adopt more restrictive provisions that the regulation attributes to national legislation, the draft royal decree[10] excludes various types of single-use products from the possibility of reprocessing, prohibits the use in Spain of products reprocessed (totally or partially) in a third country and allows reprocessing by three agents:

- Manufacturer (i. e. the natural or legal person who reprocesses the single-use product), who must obtain a prior operating license, may not subcontract any stage of reprocessing and may only distribute directly to hospitals, returning the product after use to the same manufacturer of the reprocessed product.
- Hospitals, which will have to obtain a prior operating license and may either carry out the reprocessing directly or subcontract it to an external reprocessor.
- An external reprocessor, which will not require a prior operating license (it will operate under the license of the subcontracting hospital) and will not be able to subcontract.

In the case of hospitals, a subsequent implementing regulation will have to establish the requirements, conditions and criteria for reprocessing, which is why the entry into force of the project's provisions on reprocessing activities in hospitals will be deferred until such implementing regulation is approved.
This structure determines that the knowledge and analysis of the regulation of reprocessing will require the examination of four bodies of legislation: Regulation (EU) 2017/745, the

Implementing Regulation (EU) 2020/1207[11], the Royal Decree and the subsequent implementing regulations.
The traceability of the product and the division of responsibilities between the manufacturer of the original product and the manufacturer of the reprocessed product (or, as the case may be, the hospital that carries out the reprocessing – directly or by subcontracting – constitute important challenges to be solved.

Notified bodies: responsible authority and language regime
The draft deal decree[12] attributes to the Ministry of Health the status of the authority responsible for notified bodies (and thus for their designation and, where appropriate, their withdrawal).
The rule states that all documents required for the application and assessment of the designation must be written at least in Spanish.
It also establishes that the documentation generated by the notified body corresponding to the conformity assessment procedures, the conformity assessment certificates, as well as the documentation required by the authority in the follow-up actions, must be written at least in Spanish.

Marketing and entry into service: marketing register
The draft Royal Decree, by dealing in Chapter V (Articles 18 to 27) with marketing and putting into service, is limited to merely updating and adapting the rules contained in two chapters of the same title in Royal Decree 1591/2009 and Royal Decree 1616/2009 to the regime of Regulation (EU) 2017/745.
However, it should be noted that the marketing register that it regulates differs substantially from the marketing register of the aforementioned royal decrees and it could even be questioned whether it goes beyond the distributor register that Article 30.2 of Regulation (EU) 2017/745 entrusts to national legislation, whose mandate it would have to fulfil.
As noted in the Report, the draft Royal Decree establishes the creation of a new marketing register for all types of products, regardless of their risk class (the existing register is currently for class IIa, IIb, and III products, and will be extended in the new register to class I products and non-medical products); and it is also noted in the Report that the communication and registration (and, consequently, the obligation to pay a fee) will be per product (i. e. per reference), not per set or category of products.
With this configuration, the question has been raised as to whether it is in fact a register of products, rather than distributors, and whether in such a case it would constitute a redundant duplication of EUDAMED.[13] In this respect, the Ministry has pointed out, when replying to the comments on the text submitted during the hearing and public information procedure, that the main objective of the marketing register is to make available to the general public information on all products marketed in Spain (regardless of their risk class), including their labelling and instructions for use, as well as the companies that market them (i. e. all economic agents that market products in Spain, without exception), complementing the information in EUDAMED (and feeding on EUDAMED with respect to the information already contained in this database).

Intra-Community and external trade: free sales certificates
As a novelty, the draft royal decree empowers the AEMPS to issue, in addition to the certificates of free sale provided for in Regulation (EU) 2017/745 (i. e. in favor of a manufacturer or authorized representative), to other economic agents that have their registered office in Spain.

Clinical evaluation and clinical research
Regulation (EU) 2017/745 regulates this matter extensively. In accordance with the provisions of the EU regulation, the draft royal decree distinguishes between, on the one hand, clinical investigations conducted to demonstrate the conformity of devices and clinical investigations with CE-marked devices outside their intended purpose and, on the other hand, clinical investigations with CE-marked devices within the scope of their intended purpose and clini-


Jorge Robles González

Jorge Robles González is Partner of Cuatrecasas since 2010. He is specialist in medical devices and pharmaceutical law, advises in regulatory matters, public law and tender procedures. He is lecturer in the Pharmaceutical Law Course of the Barcelona Bar Association.

cal investigations under Article 82 of Regulation (EU) 2017/745[14] (hereinafter other clinical investigations).
As regards the former, it makes them subject to authorization by the AEMPS, which incorporates the procedural provisions and deadlines established in the Community regulation, requiring a favorable opinion from the Ethics Committee for Research involving Medicinal Products (CEIm), which must be a single opinion in the case of multi-center research, and establishes the language regime: application, investigator's manual, clinical research plan, informed consent, instructions and labelling and protocol must be submitted at least in Spanish.
In the case of the latter, the regime is of communication to the AEMPS, requiring a favorable opinion from the CEIm (single opinion in the case of multi-center research) and the communication, investigator's manual, clinical research plan, informed consent, instructions and labelling must be submitted at least in Spanish.
In this regard, it should be noted that, until now, for clinical investigations conducted with CE marked devices within the indications included in the conformity assessment procedure, where there was no alteration of the usual clinical practice and no cluster randomization, the approval of the CEIm is sufficient, as permitted by Article 74(1) of Regulation (EU) 2014/745 for Class I or non-invasive Class IIa and IIb investigational devices. However, the Ministry has opted to require communication for these products as well.

Monitoring system: implant card
The draft royal decree devotes Chapter VIII to this matter.
As regards the vigilance system (Article 35), as explained in the AEMPS report, both the obligation to notify (which must be done electronically to the AEMPS) serious incidents is maintained for all healthcare professionals (including, according to the express criteria of the AEMPS, pharmacists), as well as the obligation for healthcare centers to designate a monitoring officer for the procedures arising from the implementation of the monitoring system and for the supervision of compliance with the obligations established with regard to the completion and delivery to the patient of the implant card and the documentation required in Article 18.1 of Regulation (EU) 2017/745.
The designation of the person responsible should continue to be communicated to the health authorities of the Autonomous Community and to the AEMPS, adding the possibility that the Agency establishes an electronic register for such communications, in which case the communication will be made only through this register.
It establishes the obligation of the manufacturer to inform the AEMPS of any corrective action before it is carried out[15], and specifies that the safety note intended for communication to users or customers must be sent to the AEMPS before its dissemination and be provided in Spanish (the language to be used in any other information from an economic operator communicating any corrective action to users or customers).
Regarding implant cards (Article 36), being directly applicable the provisions of Article 18 of Regulation (EU) 2017/745, the draft royal decree: (i) specifies that the information that the manufacturer must provide together with the product and the information on the implant card must be at least in Spanish, (ii) obliges the healthcare center to send a copy of the implant card to patients (adding that, in the event that a National Implant Register has been set up, healthcare centers will be obliged to communicate the required data to the aforementioned registers) and (iii), as regards the minimum information that must be included on the implant card (established in article 18.1.d of the Community regulation), includes the identification of the center and the patient, which must be completed by the center.
The AEMPS warns, in the Report on the contributions received in the public prior consultation process, that there is no physical implant card format established by law, but that the Commission document "MDCG 2019-8 v2 Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices" provides information for its design.

Market surveillance and health protection measures
As this matter is extensively regulated in Regulation (EU) 2017/745 (articles 93 to 100), the draft royal decree devotes its last chapter to it, assigning the AEMPS the coordination of market control activities, regulating inspection in similar terms to those in force until now and entrusting, in the cases authorized by the Community regulation, the adoption of health protection measures (precautionary measures provided for in national legislation or other appropriate measures) to the AEMPS and other competent health authorities, of which the Commission and other Member States must be informed.

It also maintains the power of the AEMPS to adopt special transitional health control measures.

Conclusion

Although Regulations (EU) 2017/745 and 2017/746 are directly applicable from 26 May 2021 and 26 May 2022, respectively, their full implementation in Spain requires the approval of internal rules that regulate aspects that are either complementary or that the EU regulations refer directly to the national rules.

In this regard, two draft regulations are currently being processed in Spain: on the one hand, the draft Royal Decree on medical devices, which has already been drawn up and whose processing has been completed, so that its approval is expected to take place in December 2022 or in the first months of 2023; and, on the other hand, the draft Royal Decree on medical devices for in vitro diagnostics, which the AEMPS is still working on, so that its text is not known and its processing is still to be completed during 2023.

Also with regard to the advertising of medical devices, a legal regulation has been initiated, although it is still at a very early stage.

*Authors' contact data:

Jorge Robles González
Partner of Life Sciences and Public Law departments of Cuatrecasas
Calle Martínez número 11
Planta 3ª, C.P. 29005 (Málaga, Spain)
Phone: +34 952 061 820
E-mail: jorge.robles@cuatrecasas.com
www.cuatrecasas.com

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1 The regulation foresaw its general application as of 26 May 2020. As a consequence of the outbreak of COVID-19 and the public health crisis resulting from it, this provision was amended by Regulation (EU) 2020/561 of the European Parliament and of the Council of 23 April 2020, deferring it by one year.

2 The transposition into Spanish domestic law of EU legislation on medical devices has been carried out by means of regulations approved by the Council of Ministers, without the need for the processing and approval of laws by the Spanish Parliament.

3 Recently amended by Royal Decree 588/2021 of 20 July to regulate the sale to the public and advertising of COVID-19 self-testing products.

4 Judgment of the Court of Justice of 15 October 1986, Case 168/85 (Commission v Italy).

5 On a transitional basis, and until EUDAMED is fully operational, the provisions of those Royal Decrees also remain in force for the purposes of fulfilling the obligations set out in the provisions listed in the first paragraph of Article 123(3)(d) of Regulation (EU) 2017/745 and, in particular, the information concerning the communication of placing on the market and putting into service, registration of persons responsible for placing on the market, clinical investigations, notifications of certificates and notifications of surveillance.

6 Informative Circular No 12/98 of the Directorate General for Pharmacy and Medical Devices, "APPLICATION OF THE LEGISLATION ON MEDICAL DEVICES: DATES AND ACCREDITATIVE DOCUMENTS".

7 For example, the requirement to justify that the specific needs of the intended patient group cannot be satisfied, or cannot be satisfied with the appropriate level of performance, by another equivalent device on the market.

8 In accordance with Royal Decree 1227/2003, of 10 October, which establishes the general bases for the authorisation of health centres, services and establishments.

9 It also adds the possibility of in-house production of products needed in the event of a health crisis.

10 Chapter III, Articles 11 to 14.

11 Commission Implementing Regulation (EU) 2020/1207 of 19 August 2020 laying down detailed rules for the implementation of Regulation (EU) 2017/745 of the European Parliament and of the Council as regards specifications for the reprocessing of single-use products.

12 Chapter IV.

13 European Database on Medical Devices (Article 33 of Regulation (EU) 2017/745).

14 Clinical investigations carried out for purposes other than those listed in Article 62(1) of Regulation (EU) 2017/745.

15 In accordance with the provisions of Articles 87(1) and 87(8) of Regulation (EU) 2017/745.