A GUIDE TO MEDICAL DEVICE REGULATION FOR DENTAL PROFESSIONALS WHO PRESCRIBE AND MANUFACTURE CUSTOM-MADE DEVICES IN THE UNITED KINGDOM

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December 2020

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INTRODUCTION

In 1993, Directive 93/42/EEC (Medical Device Directive, MDD)[1] was published with the aim of harmonising legislation regarding medical devices within the European Union (EU). The Directive came into force on 12 July 1993 and was implemented on 1 July 1994. The MDD was given effect in UK law by the Medical Devices Regulations 2002 (SI 2002/618, UK MDR 2002).[2]

In the years that followed, incidents with sub-standard devices identified weaknesses in the Directive and the need for more robust legislation. This led to the implementation of Regulation (EU) 2017/745 (Medical Device Regulation, EU MDR),[3] which entered into force on 25 May 2017 and was scheduled to be fully implemented, repealing the MDD, on 26 May 2020. On 23 April 2020, Regulation (EU) 2020/561 was adopted as a result of the COVID-19 pandemic, which amended the EU MDR and deferred its full implementation for one year until 26 May 2021.[4]

On 23 June 2016 a UK-wide referendum on the country's membership of the EU took place, in which 52% voted to leave. Whilst the result was non-binding, the UK government said it would respect the result. In anticipation of the UK's departure, the EU MDR was largely transposed into The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 (referred to in this guide as the UK MDR), an amendment of the UK MDR 2002,[5] which was expected to come into effect on exit day.

The UK left the EU on 31 January 2020 but instead entered an 11-month implementation period (IP), during which EU legislation continued to apply in the UK. This transition period ends on 31 December 2020, after which Great Britain (GB) will be required to follow the UK MDR 2002 in the form in which it exists on 1 January 2021; this is expected to be the UK MDR 2019, which was further amended by the Medical Devices (Amendment etc.) (EU Exit) Regulations 2020, which substitutes 'exit day' for 'IP completion day'.[6] The UK MDR only applies in GB; Northern Ireland (NI) is remaining in line with the EU legislation and implementation date under the terms of the Ireland/Northern Ireland Protocol,[7] meaning that this region will need to follow the EU MDR from 26 May 2021.[8]

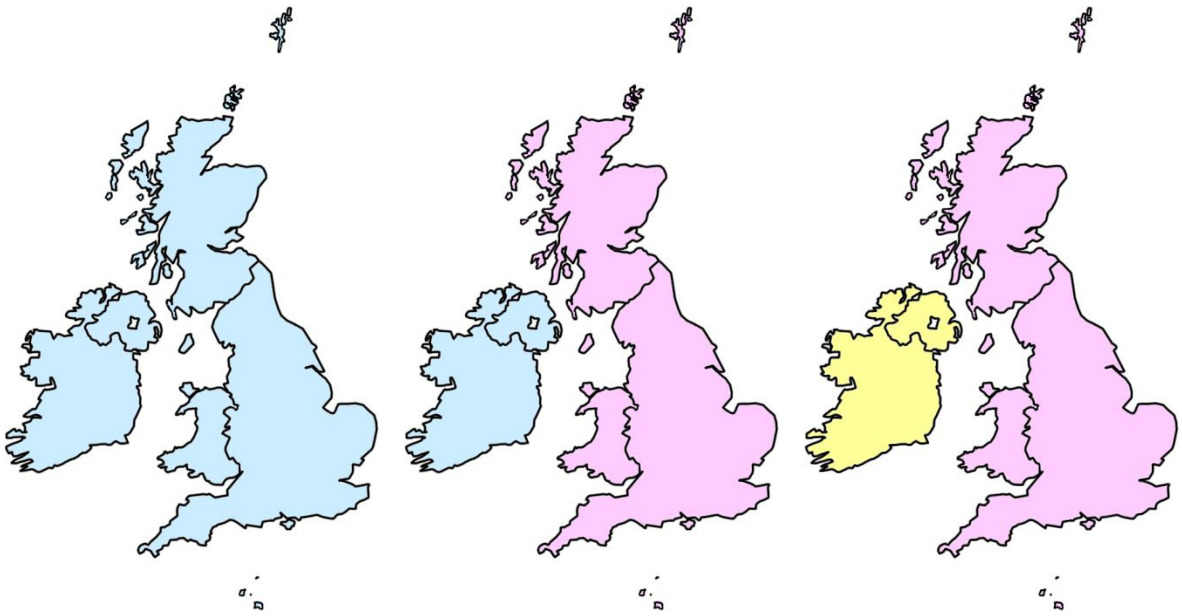
Dental professionals who prescribe and / or manufacture custom-made devices must do so in accordance with the relevant parts of the appropriate legislation. This guide gives an overview of the UK and EU legislative requirements that relate to custom-made devices in a dental context in ten steps and is based on a series of lectures that were held between May 2019 and March 2020 at various locations in the UK.[9-14] It is not intended as a substitute for reading the Regulations directly.

The relevant excerpts from the MDD, EU MDR and UK MDR in this guide are colour coded as follows:

Directive 93/42/EEC (Medical Device Directive, MDD)

Regulation (EU) 2017/745 (Medical Device Regulation, EU MDR)

The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 (UK MDR)



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REGISTER WITH THE MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (MHRA)

The MDD states that:

> Member States may require that the manufacturer shall submit to the competent authority a list of such devices which have been put into service in their territory.

— *MDD Article 11(6)*

This remains the same under the EU MDR and the UK MDR:

> Member States may require that the manufacturer of a custom-made device submit to the competent authority a list of such devices which have been made available in their territory.

— *EU MDR Article 21(2)*

> The Secretary of State may require a manufacturer of a custom-made device to send to the Secretary of State a list of such devices.

— *UK MDR Regulation 86(4)*

The competent authority in the UK is the Medicines and Healthcare products Regulatory Agency (MHRA), who require that manufacturers of custom-made devices submit a list of such devices.

For some manufacturers, such as hospitals, this is a new obligation so there are grace periods for registering, which vary according to the class that the device falls under:

30 April 2021:	Class IIb implantable devices
31 August 2021:	Class IIb non-implantable devices / Class IIa devices
31 December 2021:	Class I devices (unless presently required to register with the MHRA).

This grace period does not apply to devices that are placed on the Northern Ireland market.[8] Begin the process by accessing this website: https://mhrabpm.appiancloud.com/suite/plugins/servlet/registration

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APPOINT A PERSON RESPONSIBLE FOR REGULATORY COMPLIANCE

The Person Responsible for Regulatory Compliance (PRRC) is a new obligation, the requirements of which are given in EU MDR Article 15 and UK MDR Regulation 80:

1. Manufacturers shall have available within their organisation at least one person responsible for regulatory compliance who possesses the requisite expertise in the field of medical devices. The requisite expertise shall be demonstrated by either of the following qualifications: (a) a diploma, certificate or other evidence of formal qualification, awarded on completion of a university degree or of a course of study recognised as equivalent by the Member State concerned, in law, medicine, pharmacy, engineering or another relevant scientific discipline, and at least one year of professional experience in regulatory affairs or in quality management systems relating to medical devices; (b) four years of professional experience in regulatory affairs or in quality management systems relating to medical devices. Without prejudice to national provisions regarding professional qualifications, manufacturers of custom-made devices may demonstrate the requisite expertise referred to in the first subparagraph by having at least two years of professional experience within a relevant field of manufacturing.

2. Micro and small enterprises within the meaning of Commission Recommendation 2003/361/EC (1) shall not be required to have the person responsible for regulatory compliance within their organisation but shall have such person permanently and continuously at their disposal.

3. The person responsible for regulatory compliance shall at least be responsible for ensuring that:
(a) the conformity of the devices is appropriately checked, in accordance with the quality management system under which the devices are manufactured, before a device is released;

(b) the technical documentation and the EU declaration of conformity are drawn up and kept up-to-date;

(c) the post-market surveillance obligations are complied with in accordance with Article 10(10);

(d) the reporting obligations referred to in Articles 87 to 91 are fulfilled;

(e) in the case of investigational devices, the statement referred to in Section 4.1 of Chapter II of Annex XV is issued.

4. If a number of persons are jointly responsible for regulatory compliance in accordance with paragraphs 1, 2 and 3, their respective areas of responsibility shall be stipulated in writing.

5. The person responsible for regulatory compliance shall suffer no disadvantage within the manufacturer's organisation in relation to the proper fulfilment of his or her duties, regardless of whether or not they are employees of the organisation.

6. Authorised representatives shall have permanently and continuously at their disposal at least one person responsible for regulatory compliance who possesses the requisite expertise regarding the regulatory requirements for medical devices in the Union. The requisite expertise shall be demonstrated by either of the following qualifications:

(a) a diploma, certificate or other evidence of formal qualification, awarded on completion of a university degree or of a course of study recognised as equivalent by the Member State concerned, in law, medicine, pharmacy, engineering or another relevant scientific discipline, and at least one year of professional experience in regulatory affairs or in quality management systems relating to medical devices;

(b) four years of professional experience in regulatory affairs or in quality management systems relating to medical devices.

—EU MDR Article 15

(1) Subject to paragraph (4), manufacturers must have available within their organisation at least one person who is responsible for regulatory compliance and who possesses the requisite expertise in the field of medical devices.

(2) Subject to paragraph (3), the requisite expertise in paragraph (1) may be demonstrated by either of the following—
(a) a diploma, certificate or other evidence of formal qualification, awarded on completion of a university degree or of a course of study recognised by the Secretary of State as equivalent in—

(i) law,

(ii) medicine,

(iii) pharmacy,

(iv) engineering, or

(v) another relevant scientific discipline,

and at least one year of professional experience in regulatory affairs management relating to medical devices;

(b) 4 years of professional experience in—

(i) regulatory affairs, or

(ii) in quality management systems relating to medical devices.

(3) Where a manufacturer manufactures custom-made devices the requisite experience may be demonstrated by having at least 2 years of professional expertise within a relevant field of manufacturing.

(4) Micro and small businesses, within the meaning of Commission Recommendation 2003/361/EC of 6 May 2003 concerning the definition of micro, small and medium-sized enterprises(a) (as it has effect in European Union law), are not required to have a person responsible for regulatory compliance within their organisation but must have such a person permanently and continuously at their disposal.

(5) The person responsible for regulatory compliance must at least be responsible for ensuring that—

(a) the conformity of devices is appropriately checked, in accordance with the quality management system under which the devices are manufactured, before the device is released;

(b) the technical documentation and declaration of conformity are drawn up and kept up-to date;

(c) the post market surveillance obligations are complied with in accordance with regulation 76(15);

(d) the reporting obligations referred to in regulations 125 to 128 are fulfilled;

(e) in the case of investigational devices, the statement referred to in paragraph 4(1) of Chapter II of Schedule 15 is issued.

(6) If a number of persons are jointly responsible for regulatory compliance their respective areas of responsibility must be stipulated in writing.

(7) The person responsible for regulatory compliance must not suffer any disadvantage within the manufacturer's organisation in relation to the person's proper fulfilment of their duties, regardless of whether or not they are employees of the organisation.

— UK MDR Regulation 80

The closing sentence of EU MDR Article 15(1) and UK MDR Regulation 80(3) is the most relevant for manufacturers of custom-made devices: that a PRRC must have at least two years of relevant experience/expertise.

EU MDR Article 15(2) and UK MDR Regulation 80(4) state that small and micro enterprises can subcontract the PRRC responsibilities to a third party, within the meaning of Commission Recommendation 2003/361/EC of 6 May 2003.[15] This Recommendation defines a micro enterprise as one that employs fewer than 10 persons and whose annual turnover and/or annual balance sheet total does not exceed €2 million. A small enterprise is defined as one that employs fewer than 50 persons and whose annual turnover and/or annual balance sheet total does not exceed €10 million. This means that an organisation with a staff headcount of more than fifty and a balance sheet total or turnover of ≤ €10 million where a dental professional prescribes or manufactures custom-made devices needs to have at least one person within their laboratory or practice with at least two years of post-GDC registration experience. Organisations that are smaller than this will need to have such a person permanently and continuously at their disposal.

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APPOINT AN AUTHORISED REPRESENTATIVE IN THE EU OR NI (FOR MANUFACTURERS OUTSIDE THE EU OR NI PLACING DEVICES ON THE EU OR NI MARKET) OR A UK RESPONSIBLE PERSON (FOR MANUFACTURERS OUTSIDE GB PLACING DEVICES ON THE GB MARKET)

Under the MDD, manufacturers outside the EU who place medical devices on the EU market are required to appoint an authorised representative in Europe:

> Where a manufacturer who places a device on the market under his own name does not have a registered place of business in a Member State, he shall designate a single authorised representative in the European Union. For devices referred to in the first subparagraph of paragraph 1, the authorised representative shall inform the competent authority of the Member State in which he has his registered place of business of the details referred to in paragraph 1.

— *MDD Article 14(2)*

This requirement remains the same under the EU MDR, but it has been expanded and will now also include devices placed on the NI market by manufacturers outside the EU or NI:

> 1. Where the manufacturer of a device is not established in a Member State, the device may only be placed on the Union market if the manufacturer designates a sole authorised representative.

2. The designation shall constitute the authorised representative's mandate, it shall be valid only when accepted in writing by the authorised representative and shall be effective at least for all devices of the same generic device group.

3. The authorised representative shall perform the tasks specified in the mandate agreed between it and the manufacturer. The authorised representative shall provide a copy of the mandate to the competent authority, upon request. The mandate shall require, and the manufacturer shall enable, the authorised representative to perform at least the following tasks in relation to the devices that it covers:

(a) verify that the EU declaration of conformity and technical documentation have been drawn up and, where applicable, that an appropriate conformity assessment procedure has been carried out by the manufacturer;

(b) keep available a copy of the technical documentation, the EU declaration of conformity and, if applicable, a copy of the relevant certificate, including any amendments and supplements, issued in accordance with Article 56, at the disposal of competent authorities for the period referred to in Article 10(8);

(c) comply with the registration obligations laid down in Article 31 and verify that the manufacturer has complied with the registration obligations laid down in Articles 27 and 29;

(d) in response to a request from a competent authority, provide that competent authority with all the information and documentation necessary to demonstrate the conformity of a device, in an official Union language determined by the Member State concerned;

(e) forward to the manufacturer any request by a competent authority of the Member State in which the authorised representative has its registered place of business for samples, or access to a device and verify that the competent authority receives the samples or is given access to the device;

(f) cooperate with the competent authorities on any preventive or corrective action taken to eliminate or, if that is not possible, mitigate the risks posed by devices;

(g) immediately inform the manufacturer about complaints and reports from healthcare professionals, patients and users about suspected incidents related to a device for which they have been designated;

(h) terminate the mandate if the manufacturer acts contrary to its obligations under this Regulation.

4. The mandate referred to in paragraph 3 of this Article shall not delegate the manufacturer's obligations laid down in Article 10(1), (2), (3), (4), (6), (7), (9), (10), (11) and (12).

5.Without prejudice to paragraph 4 of this Article, where the manufacturer is not established in a Member State and has not complied with the obligations laid down in Article 10, the authorised representative shall be legally liable for defective devices on the same basis as, and jointly and severally with, the manufacturer.

6.An authorised representative who terminates its mandate on the ground referred to in point (h) of paragraph 3 shall immediately inform the competent authority of the Member State in which it is established and, where applicable, the notified body that was involved in the conformity assessment for the device of the termination of the mandate and the reasons therefor.

7.Any reference in this Regulation to the competent authority of the Member State in which the manufacturer has its registered place of business shall be understood as a reference to the competent authority of the Member State in which the authorised representative, designated by a manufacturer referred to in paragraph 1, has its registered place of business.

— EU MDR Article 11

Manufacturers outside GB who place medical devices on the GB market must appoint a UK responsible person, the requirements of which are given in UK MDR Regulation 77:

A person regarded as the UK responsible person must—

(a) ensure that the declaration of conformity and technical documentation have been drawn up and, where applicable, that an appropriate conformity assessment procedure has been carried out by the manufacturer;

(b) keep available for inspection by the Secretary of State a copy of the technical documentation, a copy of the declaration of conformity and, if applicable, a copy of the relevant certificate, including any amendments and supplements;

(c) in response to a request from the Secretary of State, provide the Secretary of State with all the information and documentation necessary to demonstrate the conformity of a device;

(d) forward to the manufacturer any request by the Secretary of State for samples, or access to a device and ensure that the Secretary of State receives the samples or has been given access to the device;

(e) cooperate with the Secretary of State on any preventive or corrective action taken to eliminate or, if that is not possible, mitigate the risks posed by devices;

(f) immediately inform the manufacturer about complaints and reports from healthcare professionals, patients and users about suspected incidents related to a device for which they have been designated;

(g) terminate the legal relationship with the manufacturer if the manufacturer acts contrary to its obligations under these Regulations and inform the Secretary of State and, if applicable, the relevant notified body of that termination.

— UK MDR Regulation 77

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ESTABLISH, DOCUMENT, IMPLEMENT AND MAINTAIN, KEEP UP TO DATE AND CONTINUALLY IMPROVE A QUALITY MANAGEMENT SYSTEM

Quality management requirements are better defined in the new Regulations than they were in the MDD and are provided in EU MDR Article 10(9) and UK MDR Regulation 76(13-14):

Manufacturers shall ensure that procedures are in place to keep series production in conformity with the requirements of this Regulation. Changes in device design or characteristics and changes in the harmonised standards or CS by reference to which the conformity of a device is declared shall be adequately taken into account in a timely manner. Manufacturers of devices, other than investigational devices, shall establish, document, implement, maintain, keep up to date and continually improve a quality management system that shall ensure compliance with this Regulation in the most effective manner and in a manner that is proportionate to the risk class and the type of device.

The quality management system shall cover all parts and elements of a manufacturer's organisation dealing with the quality of processes, procedures and devices. It shall govern the structure, responsibilities, procedures, processes and management resources required to implement the principles and actions necessary to achieve compliance with the provisions of this Regulation.

The quality management system shall address at least the following aspects:

(a) a strategy for regulatory compliance, including compliance with conformity assessment procedures and procedures for management of modifications to the devices covered by the system;

(b) identification of applicable general safety and performance requirements and exploration of options to address those requirements;

(c) responsibility of the management;

(d) resource management, including selection and control of suppliers and sub-contractors;

(e) risk management as set out in in Section 3 of Annex I;

(f) clinical evaluation in accordance with Article 61 and Annex XIV, including PMCF;

(g) product realisation, including planning, design, development, production and service provision;

(h) verification of the UDI assignments made in accordance with Article 27(3) to all relevant devices and ensuring consistency and validity of information provided in accordance with Article 29;

(i) setting-up, implementation and maintenance of a post-market surveillance system, in accordance with Article 83;

(j) handling communication with competent authorities, notified bodies, other economic operators, customers and/or other stakeholders;

(k) processes for reporting of serious incidents and field safety corrective actions in the context of vigilance;

(l) management of corrective and preventive actions and verification of their effectiveness;

(m) processes for monitoring and measurement of output, data analysis and product improvement.

— EU MDR Article 10(9)

(13) Manufacturers must ensure that procedures are in place to keep series production in conformity with the requirements of this Part including—

(a) ensuring that changes in device design or characteristics and changes in the designated standards or CS by reference to which the conformity of the device is declared are adequately, and in a timely manner, taken into account;

(b) ensuring that for devices (other than investigational devices) a quality management system, which is proportionate to the risk class and type of device is established, documented, implemented, maintained, kept up to date and continually improved.

(14) The quality management system required by paragraph (13) must—

(a) cover all parts and elements of the manufacturer's organisation dealing with the quality of processes, procedures and devices;

(b) govern the structure, responsibilities, procedures, processes and management resources required to implement the principles and actions necessary to achieve compliance with the provisions of this Part;

(c) provide details of at least the following—

(i) a strategy for regulatory compliance, including compliance with conformity assessment procedures and procedures for management of modifications to the devices covered by the system;

(ii) the identification of applicable general safety and performance requirements and exploration of options to address those requirements;

(iii) the responsibility of the management;

(iv) resource management, including selection and control of suppliers and subcontractors;

(v) risk management as set out in paragraph 3 of Schedule 3;

(vi) clinical evaluation in accordance with regulation 102 and Schedule 14, including PMCF;

(vii) product realisation, including planning, design, development, production and service provision;

(viii) verification of the UDI assignments made in accordance with regulation 91 to all relevant devices and ensuring consistency and validity of information provided in accordance with regulation 93;

(ix) setting-up, implementation and maintenance of a post-market surveillance system, in accordance with regulation 121;

(x) processes for handling communication with the Secretary of State (and authorities in other relevant states), notified bodies, other economic operators, customers and any other stakeholders;

(xi) processes for reporting of serious incidents and field safety corrective actions in the context of vigilance;

(xii) management of corrective and preventive actions and verification of their effectiveness;

(xiii) processes for monitoring and measurement of output, data analysis and product improvement.

— UK MDR Regulation 76(13-14)

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COMPLY WITH THE ANNEX I / SCHEDULE 3 REQUIREMENTS THAT APPLY TO CUSTOM-MADE DEVICES

Under the MDD, manufacturers of custom-made devices are required to follow the relevant Essential Requirements given in Annex I:

> The devices must meet the essential requirements set out in Annex I which apply to them, taking account of the intended purpose of the devices concerned.

— MDD Article 3

These are broadly the same as the General Safety and Performance Requirements (GSPR) set out in EU MDR Annex I and UK MDR Schedule 3.

> A device shall meet the general safety and performance requirements set out in Annex I which apply to it, taking into account its intended purpose.

— EU MDR Article 5(2)

> A device to which this Part applies must meet the general safety and performance requirements set out in Schedule 3 which apply to it, taking into account its intended purpose.

— UK MDR Regulation 5(2)

The obligations have been expanded and include the requirement to establish, implement, document and maintain a risk management system:

> Manufacturers shall establish, document, implement and maintain a system for risk management as described in Section 3 of Annex I.

— EU MDR Article 5(2)

> Manufacturers must establish, document, implement and maintain a system for risk management as described in paragraph 3 of Schedule 3.

— UK MDR Regulation 76(2)

The Annex I / Schedule 3 requirements pertinent to custom-made devices in a dental setting are as follows:

> I. GENERAL REQUIREMENTS
>
> 1. The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their intended use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.
>
> This shall include:
>
> — reducing, as far as possible, the risk of use error due to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and

— consideration of the technical knowledge, experience, education and training and where applicable the medical and physical conditions of intended users (design for lay, professional, disabled or other users).

2. The solutions adopted by the manufacturer for the design and construction of the devices must conform to safety principles, taking account of the generally acknowledged state of the art.
In selecting the most appropriate solutions, the manufacturer must apply the following principles in the following order:

— eliminate or reduce risks as far as possible (inherently safe design and construction),

— where appropriate take adequate protection measures including alarms if necessary, in relation to risks that cannot be eliminated,

— inform users of the residual risks due to any shortcomings of the protection measures adopted.

3. The devices must achieve the performances intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions referred to in Article 1 (2) (a), as specified by the manufacturer.

4. The characteristics and performances referred to in Sections 1, 2 and 3 must not be adversely affected to such a degree that the clinical conditions and safety of the patients and, where applicable, of other persons are compromised during the lifetime of the device as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use.

5. The devices must be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected during transport and storage taking account of the instructions and information provided by the manufacturer.

6. Any undesirable side-effect must constitute an acceptable risk when weighed against the performances intended.

6a. Demonstration of conformity with the essential requirements must include a clinical evaluation in accordance with Annex X.

II. REQUIREMENTS REGARDING DESIGN AND CONSTRUCTION

7. Chemical, physical and biological properties

7.1. The devices must be designed and manufactured in such a way as to guarantee the characteristics and performances referred to in Section I on the 'General requirements'. Particular attention must be paid to:

— the choice of materials used, particularly as regards toxicity and, where appropriate, flammability,

— the compatibility between the materials used and biological tissues, cells and body fluids, taking account of the intended purpose of the device,

— where appropriate, the results of biophysical or modelling research whose validity has been demonstrated beforehand.

7.2. The devices must be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to the patients, taking account of the intended purpose of the product. Particular attention must be paid to the tissues exposed and to the duration and frequency of exposure.

7.3. The devices must be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products they must be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use.

7.6. Devices must be designed and manufactured in such a way as to reduce, as much as possible, risks posed by the unintentional ingress of substances into the device taking into account the device and the nature of the environment in which it is intended to be used.

8. Infection and microbial contamination

8.1. The devices and manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the patient, user and third parties. The design must allow easy handling and, where necessary, minimize contamination of the device by the patient or vice versa during use.

8.6. Packaging systems for non-sterile devices must keep the product without deterioration at the level of cleanliness stipulated and, if the devices are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system must be suitable taking account of the method of sterilization indicated by the manufacturer.

9. Construction and environmental properties

9.1. If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system must be safe and must not impair the specified performances of the devices. Any restrictions on use must be indicated on the label or in the instructions for use.

9.2. Devices must be designed and manufactured in such a way as to remove or minimize as far as is possible:

— the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features,

— risks connected with reasonably foreseeable environmental conditions, such as magnetic fields, external electrical influences, electrostatic discharge, pressure, temperature or variations in pressure and acceleration,

— the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given,

— risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.

13. Information supplied by the manufacturer

13.1. Each device must be accompanied by the information needed to use it safely and properly, taking account of the training and knowledge of the potential users, and to identify the manufacturer.

This information comprises the details on the label and the data in the instructions for use.

As far as practicable and appropriate, the information needed to use the device safely must be set out on the device itself and/or on the packaging for each unit or, where appropriate, on the sales
packaging. If individual packaging of each unit is not practicable, the information must be set out in the leaflet supplied with one or more devices.

Instructions for use must be included in the packaging for every device. By way of exception, no such instructions for use are needed for devices in Class I or IIa if they can be used safely without any such instructions.

13.3. The label must bear the following particulars:

(a) the name or trade name and address of the manufacturer. For devices imported into the Community, in view of their distribution in the Community, the label, or the outer packaging, or
instructions for use, shall contain in addition the name and address of the authorised representative where the manufacturer does not have a registered place of business in the Community;

(b) the details strictly necessary to identify the device and the contents of the packaging especially for the users;

(e) where appropriate, an indication of the date by which the device should be used, in safety, expressed as the year and month;

(g) if the device is costum-made [sic], the words 'custom-made device';

(h) if the device is intended for clinical investigations, the words
'exclusively for clinical investigations';

(i) any special storage and/or handling conditions;

(k) any warnings and/or precautions to take;

(l) year of manufacture for active devices other than those covered by (e). This indication may be included in the batch or serial number;

13.4. If the intended purpose of the device is not obvious to the user, the manufacturer must clearly state it on the label and in the instructions for use.

— *MDD Annex I*

CHAPTER I

GENERAL REQUIREMENTS

1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.

2. The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.

3. Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall:

(a) establish and document a risk management plan for each device;

(b) identify and analyse the known and foreseeable hazards associated with each device;

(c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse;

(d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4;

(e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; and

(f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4. 4. Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, Manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority: (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c) provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users. Manufacturers shall inform users of any residual risks.

5. In eliminating or reducing risks related to use error, the manufacturer shall: (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).

6. The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.

7. Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.

8. All known and foreseeable risks, and any undesirable side-effects, shall be minimised and be acceptable when weighed against the evaluated benefits to the patient and/or user arising from the achieved performance of the device during normal conditions of use.

CHAPTER II

REQUIREMENTS REGARDING DESIGN AND MANUFACTURE

10. Chemical, physical and biological properties

10.1. Devices shall be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Chapter I are fulfilled. Particular attention shall be paid to:

(a) the choice of materials and substances used, particularly as regards toxicity and, where relevant, flammability;

(b) the compatibility between the materials and substances used and biological tissues, cells and body fluids, taking account of the intended purpose of the device and, where relevant, absorption, distribution, metabolism and excretion;

(c) the compatibility between the different parts of a device which consists of more than one implantable part;

(d) the impact of processes on material properties;

(e) where appropriate, the results of biophysical or modelling research the validity of which has been demonstrated beforehand;

(f) the mechanical properties of the materials used, reflecting, where appropriate, matters such as strength, ductility, fracture resistance, wear resistance and fatigue resistance; (g) surface properties; and (h) the confirmation that the device meets any defined chemical and/or physical specifications.

10.2. Devices shall be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to patients, taking account of the intended purpose of the device, and to the persons involved in the transport, storage and use of the devices. Particular attention shall be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.

10.3. Devices shall be designed and manufactured in such a way that they can be used safely with the materials and substances, including gases, with which they enter into contact during their intended use; if the devices are intended to administer medicinal products they shall be designed and manufactured in such a way as to be compatible with the medicinal products concerned in accordance with the provisions and restrictions governing those medicinal products and that the performance of both the medicinal products and of the devices is maintained in accordance with their respective indications and intended use.

10.5. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by the unintentional ingress of substances into the device taking into account the device and the nature of the environment in which it is intended to be used.

10.6. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, unless they come into contact with intact skin only. Special attention shall be given to nanomaterials.

11. Infection and microbial contamination

11.1. Devices and their manufacturing processes shall be designed in such a way as to eliminate or to reduce as far as possible the risk of infection to patients, users and, where applicable, other persons. The design shall:

(a) reduce as far as possible and appropriate the risks from unintended cuts and pricks, such as needle stick injuries,
(b) allow easy and safe handling,
(c) reduce as far as possible any microbial leakage from the device and/or microbial exposure during use, and
(d) prevent microbial contamination of the device or its content such as specimens or fluids.

11.2. Where necessary devices shall be designed to facilitate their safe cleaning, disinfection, and/or re-sterilisation.

11.7. Packaging systems for non-sterile devices shall maintain the integrity and cleanliness of the product and, where the devices are to be sterilised prior to use, minimise the risk of microbial contamination; the packaging system shall be suitable taking account of the method of sterilisation indicated by the manufacturer.

14. Construction of devices and interaction with their environment

14.1. If the device is intended for use in combination with other devices or equipment the whole combination, including the connection system shall be safe and shall not impair the specified performance of the devices. Any restrictions on use applying to such combinations shall be indicated on the label and/or in the instructions for use. Connections which the user has to handle, such as fluid, gas transfer, electrical or mechanical coupling, shall be designed and constructed in such a way as to minimise all possible risks, such as misconnection.

14.2. Devices shall be designed and manufactured in such a way as to remove or reduce as far as possible:

(a) the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features;

CHAPTER III

REQUIREMENTS REGARDING THE INFORMATION SUPPLIED WITH THE DEVICE

23. Label and instructions for use

23.1. General requirements regarding the information supplied by the manufacturer Each device shall be accompanied by the information needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user, or any other person, as appropriate. Such information may appear on the device itself, on the packaging or in the instructions for use, and shall, if the manufacturer has a website, be made available and kept up to date on the website, taking into account the following:

(a) The medium, format, content, legibility, and location of the label and instructions for use shall be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use shall be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams.

(b) The information required on the label shall be provided on the device itself. If this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit, and/or on the packaging of multiple devices.

(c) Labels shall be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification ('RFID') or bar codes.

(g) Residual risks which are required to be communicated to the user and/or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer.

23.2. Information on the label

The label shall bear all of the following particulars:

(a) the name or trade name of the device;

(b) the details strictly necessary for a user to identify the device, the contents of the packaging and, where it is not obvious for the user, the intended purpose of the device;

(c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business;

(d)if the manufacturer has its registered place of business outside the Union, the name of the authorised representative and address of the registered place of business of the authorised representative;

(j) where there is no indication of the date until when it may be used safely, the date of manufacture. This date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable;

(k) an indication of any special storage and/or handling condition that applies;

(m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device, and to any other person. This information may be kept to a minimum in which case more detailed information shall appear in the instructions for use, taking into account the intended users;

(p) if the device is custom-made, the words 'custom-made device';

(q) an indication that the device is a medical device. If the device is intended for clinical investigation only, the words 'exclusively for clinical investigation';

— EU MDR Annex I

PART 1

General requirements

1. Devices must—

(a) achieve the performance intended by their manufacturer;

(b) be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose;

(c) be safe and effective and not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.

2. The requirement in this Schedule to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.

3.—(1) Manufacturers must establish, implement, document and maintain a risk management system.

(2) Risk management is to be understood as a continuous iterative process throughout the entire lifecycle of a device, which requires regular systematic updating and, in carrying out risk management, manufacturers must—

(a) establish and document a risk management plan for each device;

(b) identify and analyse the known and foreseeable hazards associated with each device;

(c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse;

(d) eliminate or control the risks referred to in sub-paragraph (c) in accordance with the requirements of paragraph 4;

(e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability;

(f) based on the evaluation of the impact of the information referred to in paragraph (e), if necessary amend control measures in line with the requirements of paragraph 4.

4.—(1) Risk control measures adopted by manufacturers for the design and manufacture of the devices must conform to safety principles, taking account of the generally acknowledged state of the art.

(2) To reduce risks, manufacturers must manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable.

(3) In selecting the most appropriate solutions, manufacturers must, in the following order of priority—

(a) eliminate or reduce risks as far as possible through safe design and manufacture;

(b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and

(c) provide information for safety (warnings, precautions, contra-indications) and, where appropriate, training to users;

(d) inform users of any residual risks.

5. In eliminating or reducing risks related to use error, the manufacturer must—

(a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety);

(b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).

6. The characteristics and performance of a device must not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.

7. Devices must be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.

8. All known and foreseeable risks, and any undesirable side-effects, must be minimised and be acceptable when weighed against the evaluated benefits to the patient or user arising from the achieved performance of the device during normal conditions of use.

PART 2

Requirements regarding design and manufacture

Chemical, physical and biological properties

10.—(1) Devices must be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in paragraphs 1 to 9 are fulfilled.

(2) Particular attention must be paid to—

(a) the choice of materials and substances used, particularly as regards toxicity and, where relevant, flammability;

(b) the compatibility between the materials and substances used and biological tissues, cells and body fluids, taking account of the intended purpose of the device and, where relevant, absorption, distribution, metabolism and excretion;

(c) the compatibility between the different parts of a device which consists of more than one implantable part;

(d) the impact of processes on material properties;

(e) where appropriate, the results of biophysical or modelling research the validity of which has been demonstrated beforehand;

(f) the mechanical properties of the materials used, reflecting, where appropriate, matters such as strength, ductility, fracture resistance, wear resistance and fatigue resistance;

(g) surface properties;

(h) the confirmation that the device meets any defined chemical or physical specifications.

(3) Devices must be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to—

(a) patients, taking account of the intended purpose of the device;

(b) persons involved in the transport, storage and use of the device, and particular attention must be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.

(4) Devices must be designed and manufactured in such a way that they can be used safely with the materials and substances, including gases, with which they enter into contact during their intended use.

(5) If the devices are intended to administer medicinal products they must—

(a) be designed and manufactured in such a way as to be compatible with the medicinal products concerned in accordance with the provisions and restrictions governing those medicinal products;

(b) ensure that the performance of both the medicinal products and of the devices is maintained in accordance with their respective indications and intended use.

(11) Devices must be designed and manufactured in such a way as to reduce, as far as possible, the risks posed by the unintentional ingress of substances into the device, taking into account the device and the nature of the environment in which it is intended to be used.

(12) Unless they come into contact with intact skin only, devices must be designed and manufactured in such a way as to reduce, as far as possible, the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, and special attention must be given to nanomaterials.

Infection and microbial contamination

11.—(1) Devices and their manufacturing processes must be designed in such a way as to eliminate or to reduce as far as possible the risk of infection to patients, users and, where applicable, other persons and the design must—

(a) reduce as far as possible and appropriate the risks from unintended cuts and pricks, such as needle stick injuries;

(b) allow easy and safe handling;

(c) reduce as far as possible any microbial leakage from the device or microbial exposure during use;

(d) prevent microbial contamination of the device or its content such as specimens or fluids.

(2) Where necessary devices must be designed to facilitate their safe cleaning, disinfection or re-sterilisation.

(7) Packaging systems for non-sterile devices must—

(a) maintain the integrity and cleanliness of the product;

(b) where the devices are to be sterilised prior to use, minimise the risk of microbial contamination;

(c) be suitable taking account of the method of sterilisation indicated by the manufacturer.

Construction of devices and interaction with the environment

14.—(1) If the device is intended for use in combination with other devices or equipment—

(a) the whole combination, including the connection system must be safe and must not impair the specified performance of the devices;

(b) any restrictions on use applying to such combinations must be indicated on the label or in the instructions for use;

(c) connections which the user has to handle, such as fluid, gas transfer, electrical or mechanical coupling, must be designed and constructed in such a way as to minimise all possible risks, such as misconnection.

(2) Devices must be designed and manufactured in such a way as to remove or reduce as far as possible—

(a) the risk of injury, in connection with their physical features, including the volume or pressure ratio, dimensional and where appropriate ergonomic features;

PART 3

Requirements regarding instructions for use

Label and instructions for use

23.—(1) Each device must be accompanied by the information (which may appear on the device itself, on the packaging or in the instructions for use) needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user, or any other person, as appropriate.

(2) The information in paragraph (1) must, if the manufacturer has a website, be made available and kept up to date on the website.

(3) The label and instructions for use must take into account the following—

(a) that the medium, format, content, legibility, and location of the label and instructions for use must be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended users and, in particular, instructions for use must be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams;

(b) the information required on the label must be provided on the device itself or, if this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit, or on the packaging of multiple devices;

(c) labels must be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification ('RFID') or bar codes;

(g) residual risks which are required to be communicated to the user or other person must be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer;

Information on the label

(4) The label must bear the following particulars—

(a) the name or trade name of the device;

(b) the details strictly necessary for a user to identify the device, the contents of the packaging and, where it is not obvious for the user, the intended purpose of the device;

(c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business;

(d) if the manufacturer has its registered place of business outside the United Kingdom, the name and address of the person placing the device on the market;

(j) where there is no indication of the date until when it may be used safely, the date of manufacture and this date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable;

(k) an indication of any special storage or handling condition that applies;

(m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device, and to any other person (this information may be kept to a minimum in which case, more detailed information must appear in the instructions for use, taking into account the intended users);

(p) if the device is custom-made, the words 'custom-made device';

(q) an indication that the device is a medical device and, if the device is intended for clinical investigation only, the words 'exclusively for clinical investigation';

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PREPARE DOCUMENTATION

Under the MDD, manufacturers of custom-made devices are required to prepare documentation regarding the design, manufacture and performance of the devices they produce, which must be kept available for the MHRA:

> For custom-made devices, documentation, indicating manufacturing site(s) and allowing an understanding of the design, manufacture and performances of the product, including the expected performances, so as to allow assessment of conformity with the requirements of this Directive.
>
> The manufacturer must take all the measures necessary to ensure that the manufacturing process produces products which are manufactured in accordance with the documentation mentioned in the first paragraph;

— MDD Annex VIII (3.1)

This requirement remains the same under the EU MDR and the UK MDR:

> 2. The manufacturer shall undertake to keep available for the competent national authorities documentation that indicates its manufacturing site or sites and allows an understanding to be formed of the design, manufacture and performance of the device, including the expected performance, so as to allow assessment of conformity with the requirements of this Regulation.
>
> 3. The manufacturer shall take all the measures necessary to ensure that the manufacturing process produces devices which are manufactured in accordance with the documentation referred to in Section 2.

— EU MDR Annex XIII (2-3)

2. The manufacturer must undertake to keep available for the Secretary of State documentation that indicates its manufacturing site or sites and allows an understanding to be formed of the design, manufacture and performance of the device, including the expected performance, so as to allow assessment of conformity with the requirements of Part VIII.

3. The manufacturer shall take all the measures necessary to ensure that the manufacturing process produces devices which are manufactured in accordance with the documentation referred to in paragraph 2.

— UK MDR Schedule 13 (2-3)

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PREPARE STATEMENT

The MDD introduced the concept of the statement:

> Custom-made devices being placed on the market and put into service if they meet the conditions laid down in Article 11 in combination with Annex VIII; Class IIa, IIb and III devices shall be accompanied by the statement referred to in Annex VIII, which shall be available to the particular patient identified by name, an acronym or a numerical code.

— MDD Article 4(2)

> The statement must contain the following information:
>
> for custom-made devices:
>
> — the name and address of the manufacturer,
>
> — data allowing identification of the device in question,
>
> — a statement that the device is intended for exclusive use by a particular patient, together with the name of the patient,
>
> — the name of the medical practitioner or other authorized person who made out the prescription and, where applicable, the name of the clinic concerned,
>
> — the specific characteristics of the product as indicated by the prescription,

— a statement that the device in question conforms to the essential requirements set out in Annex I and, where applicable, indicating which essential requirements have not been fully met, together with the grounds;

— MDD Annex VIII (2-2.1)

This requirement remains the same – custom-made devices must be accompanied by the statement referred to in the MDD Annex VIII counterparts, EU MDR Annex XIII and UK MDR Schedule 13:

Custom-made devices shall be accompanied by the statement referred to in Section 1 of Annex XIII, which shall be made available to the particular patient or user identified by name, an acronym or a numerical code.

— EU MDR Article 21(2)

Custom-made devices must be accompanied by the statement referred to in paragraph 1 of Schedule 13 which must be identified by name, an acronym or a numerical code.

— UK MDR Regulation 86(3)

Under the EU MDR and the UK MDR, the information that has to be included in the statement is largely the same, but there are some additional requirements, which are highlighted below:

For custom-made devices, the manufacturer or its authorised representative shall draw up a statement containing all of the following information:

— the name and address of the manufacturer, and of all manufacturing sites,

— if applicable, the name and address of the authorised representative,

— data allowing identification of the device in question,

— a statement that the device is intended for exclusive use by a particular patient or user, identified by name, an acronym or a numerical code,

— the name of the person who made out the prescription and who is authorised by national law by virtue of their professional qualifications to do so, and, where applicable, the name of the health institution concerned,

— the specific characteristics of the product as indicated by the prescription,

— a statement that the device in question conforms to the general safety and performance requirements set out in Annex I and, where applicable, indicating which general safety and performance requirements have not been fully met, together with the grounds,

— where applicable, an indication that the device contains or incorporates a medicinal substance, including a human blood or plasma derivative, or tissues or cells of human origin, or of animal origin as referred to in Regulation (EU) No 722/2012.

— EU MDR Annex XIII (1)

For custom-made devices the manufacturer or its authorised representative must draw up a statement containing all of the following information—

(a) the name and address of the manufacturer, and of all manufacturing sites;

(b) if applicable, the name and address of the person placing the product on the market;

(c) data allowing identification of the device in question;

(d) a statement that the device is intended for exclusive use by a particular patient or user, identified by name, an acronym or a numerical code;

(e) the name of the person who made out the prescription and, where applicable, the name of the health institution concerned;

(f) the specific characteristics of the product as indicated by the prescription;

(g) a statement that the device in question conforms to the general safety and performance requirements set out in Schedule 3 and, where applicable, indicating which general safety and performance requirements have not been fully met, together with the grounds;

(h) where applicable, an indication that the device contains or incorporates a medicinal substance, including a human blood or plasma derivative, or tissues or cells of human origin, or of animal origin as referred to in Regulation (EU) No 722/2012.

— UK MDR Schedule 13(1)

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RETAIN A COPY OF THE STATEMENT

Under the MDD manufacturers were required to retain a copy of the statement for at least five years:

> The information contained in the declarations concerned by this Annex shall be kept for a period of time of at least five years. In the case of implantable devices the period shall be at least 15 years.

— MDD Annex VIII (4)

Under the EU MDR and UK MDR this has changed to at least ten years:

> The statement referred to in the introductory part of Section 1 shall be kept for a period of at least 10 years after the device has been placed on the market. In the case of implantable devices, the period shall be at least 15 years. Section 8 of Annex IX shall apply.

— EU MDR Annex XIII (4)

> The statement referred to in paragraph 1(g) must be kept for a period of at least 10 years after the device has been placed on the market and, in the case of implantable devices, the period must be at least 15 years.

— UK MDR Schedule 13(4)

The UK MDR adds an additional paragraph concerning the trading status of the manufacturer during the retention period:

> The statement referred to in paragraph 4 must be kept so that it is available to the Secretary of State throughout the relevant period specified in paragraph 4 irrespective of the continued status (and whether the person continues trading or not) of the manufacturer or person placing the product on the market.

— UK MDR Schedule 13(5)

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REVIEW AND DOCUMENT EXPERIENCE GAINED IN THE POST-PRODUCTION PHASE

Post-market surveillance is a requirement under the MDD:

> The clinical evaluation and its documentation must be actively updated with data obtained from the post-market surveillance. Where post-market clinical follow-up as part of the post-market surveillance plan for the device is not deemed necessary, this must be duly justified and documented.

— MDD Annex X (1.1c)

The post-production requirements were provided in MDD Annex VIII(5):

> For custom-made devices, the manufacturer must undertake to review and document experience gained in the post-production phase, including the provisions referred to in Annex X, and to implement appropriate means to apply any necessary corrective action. This undertaking must include an obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them and the relevant corrective actions:
>
> (i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;

(ii) any technical or medical reason connected with the characteristics or performance of a device for the reasons referred to in subparagraph (i) leading to systematic recall of devices of the same type by the manufacturer.

— MDD Annex VIII (5)

These are comparable with EU MDR Annex XIII(5) and UK MDR Schedule 13(6):

The manufacturer shall review and document experience gained in the post-production phase, including from PMCF as referred to in Part B of Annex XIV, and implement appropriate means to apply any necessary corrective action, In that context, it shall report in accordance with Article 87(1) to the competent authorities any serious incidents or field safety corrective actions or both as soon as it learns of them.

— EU MDR Annex XIII(5)

The manufacturer must—

(a) review and document experience gained in the post-production phase, including from PMCF as referred to in Part B of Schedule 14;

(b) implement appropriate means to apply any necessary corrective action;

(c) report in accordance with regulation 125 to the Secretary of State any serious incidents or field safety corrective actions or both as soon as it learns of them.

—UK MDR Schedule 13(6)

The post-market clinical follow-up requirements are expanded and provided in EU MDR Annex XIV Part B and UK MDR Schedule 14 Part B:

5. PMCF shall be understood to be a continuous process that updates the clinical evaluation referred to in Article 61 and Part A of this Annex and shall be addressed in the manufacturer's post-market surveillance plan. When conducting PMCF, the manufacturer shall proactively collect and evaluate clinical data from the use in or on humans of a device which bears the CE marking and is placed on the market or put into service within its intended purpose as referred to in the relevant conformity assessment procedure, with the aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks on the basis of factual evidence.

6. PMCF shall be performed pursuant to a documented method laid down in a PMCF plan.

6.1. The PMCF plan shall specify the methods and procedures for proactively collecting and evaluating clinical data with the aim of:

(a) confirming the safety and performance of the device throughout its expected lifetime,

(b) identifying previously unknown side-effects and monitoring the identified side-effects and contraindications,

(c) identifying and analysing emergent risks on the basis of factual evidence,

(d) ensuring the continued acceptability of the benefit-risk ratio referred to in Sections 1 and 9 of Annex I, and

(e) identifying possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.

6.2. The PMCF plan shall include at least:

(a) the general methods and procedures of the PMCF to be applied, such as gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of clinical data;

(b) the specific methods and procedures of PMCF to be applied, such as evaluation of suitable registers or PMCF studies;

(c) a rationale for the appropriateness of the methods and procedures referred to in points (a) and (b);

(d) a reference to the relevant parts of the clinical evaluation report referred to in Section 4 and to the risk management referred to in Section 3 of Annex I;

(e) the specific objectives to be addressed by the PMCF;

(f) an evaluation of the clinical data relating to equivalent or similar devices;

(g) reference to any relevant CS, harmonised standards when used by the manufacturer, and relevant guidance on PMCF; and

(h) a detailed and adequately justified time schedule for PMCF activities (e.g. analysis of PMCF data and reporting) to be undertaken by the manufacturer.

7. The manufacturer shall analyse the findings of the PMCF and document the results in a PMCF evaluation report that shall be part of the clinical evaluation report and the technical documentation.

8. The conclusions of the PMCF evaluation report shall be taken into account for the clinical evaluation referred to in Article 61 and Part A of this Annex and in the risk management referred to in Section 3 of Annex I. If, through the PMCF, the need for preventive and/or corrective measures has been identified, the manufacturer shall implement them.

— EU MDR Annex XIV (5-8) (Part B)

4.—(1) PMCF must be addressed in the manufacturer's post-market surveillance plan.

(2) When conducting PMCF, the manufacturer must proactively collect and evaluate clinical data from the use in or on humans of a device which bears the CE marking and is placed on the market or put into service within its intended purpose as referred to in the relevant conformity assessment procedure, with the aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks on the basis of factual evidence.

5.—(1) PMCF must be performed pursuant to a documented method laid down in a PMCF plan.

(2) The PMCF plan must specify the methods and procedures for proactively collecting and evaluating clinical data with the aim of—

(a) confirming the safety and performance of the device throughout its expected lifetime;

(b) identifying previously unknown side-effects and monitoring the identified side effects and contraindications;

(c) identifying and analysing emergent risks on the basis of factual evidence;

(d) ensuring the continued acceptability of the benefit-risk ratio referred to in paragraph 1 and 9 of Schedule 3;

(e) identifying possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.

(3) The PMCF plan must include at least—

(a) the general methods and procedures of the PMCF to be applied, such as gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of clinical data;

(b) the specific methods and procedures of PMCF to be applied, such as evaluation of suitable registers or PMCF studies;

(c) a rationale for the appropriateness of the methods and procedures referred to in paragraphs (3)(a) and (b);

(d) a reference to the relevant parts of the clinical evaluation report referred to in paragraph 3(4) and to the risk management referred to in paragraph 3 of Schedule 3;

(e) the specific objectives to be addressed by the PMCF;

(f) an evaluation of the clinical data relating to equivalent or similar devices;

(g) reference to any relevant standards when used by the manufacturer, and relevant guidance on PMCF;

(h) a detailed and adequately justified time schedule for PMCF activities (e.g. analysis of PMCF data and reporting) to be undertaken by the manufacturer.

6. The manufacturer must analyse the findings of the PMCF and document the results in a PMCF evaluation report that must be part of the clinical evaluation report and the technical documentation.

7.—(1) The conclusions of the PMCF evaluation report must be taken into account —

(i) for the clinical evaluation referred to in regulation 102 and Part A of this Schedule;

(ii) in the risk management referred to in paragraph 3 of Schedule 3;

(2) If, through the PMCF, the need for preventive or corrective measures has been identified, the manufacturer must implement them.

— UK MDR Schedule 14 (4-7) (Part B)

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REPORT SERIOUS INCIDENTS AND FIELD SAFETY CORRECTIVE ACTIONS

Any serious incidents and field safety corrective actions must be reported to the MHRA as described in EU MDR Article 87(1) and UK MDR Regulation 125(1).

1. Manufacturers of devices made available on the Union market, other than investigational devices, shall report, to the relevant competent authorities, in accordance with Articles 92(5) and (7), the following:

(a) any serious incident involving devices made available on the Union market, except expected side-effects which are clearly documented in the product information and quantified in the technical documentation and are subject to trend reporting pursuant to Article 88;

(b) any field safety corrective action in respect of devices made available on the Union market, including any field safety corrective action undertaken in a third country in relation to a device which is also legally made available on the Union market, if the reason for the field safety corrective action is not limited to the device made available in the third country. The reports referred to in the first subparagraph shall be submitted through the electronic system referred to in Article 92.

— EU MDR Article 87(1)

Manufacturers of devices made available on the market, other than investigational devices, must report, to the Secretary of State the following—

(a) any serious incident involving devices made available on the market, except expected side-effects which are clearly documented in the product information and quantified in the technical documentation and are subject to trend reporting pursuant to regulation 126;

(b) any field safety corrective action in respect of devices made available on the market, including any field safety corrective action undertaken in a third country in relation to a device which is also legally made available on the market, if the reason for the field safety corrective action is not limited to the device made available in the third country.

— UK MDR Regulation 125(1)

Reports and responses to MHRA incident investigations must be submitted to the regulator's Manufacturer's On-line Reporting Environment via this website: https://aic.mhra.gov.uk/

SUMMARY

This table outlines the requirements for dental professionals who prescribe, manufacture and / or fit medical devices under the MDD, the EU MDR and the UK MDR:

Requirement	MDD		EU MDR		UK MDR 2019	
	Article/ Annex	Paragraph/ Section	Article/ Annex	Paragraph/ Section	Regulation/ Schedule	Paragraph
1. Register with the Medicines and Healthcare products Regulatory Agency	11	6	21	2	86	4
2. Appoint a person responsible for regulatory compliance	–		15		80	
3. Appoint an authorised representative in the EU or NI(for manufacturers outside the EU or NI placing devices on the EU or NI market) or a UK responsible person (for manufacturers outside GB placing devices on the GB market)	14	2	11		77	

Requirement	MDD		EU MDR		UK MDR 2019	
	Article/ Annex	Paragraph/ Section	Article/ Annex	Paragraph/ Section	Regulation/ Schedule	Paragraph
4. Establish, document, implement and maintain, keep up to date and continually improve a quality management system	–		10	9	76	13-14
5. Follow Annex I / Schedule 3 requirements applicable to custom-made devices (includes: establish, implement, document and maintain a risk management system)	3		5	2	71	2
	–		10	2	76	2
	I		I		3	
6. Prepare documentation	VIII	3-3.1	XIII	2-3	13	2-3
7. Prepare statement	4	2	21	2	86	3
	VIII	2-2.1	XIII	1	13	1
8. Retain copy of the statement	VIII	4	XIII	4	13	4
9. Review and document experience gained in the post-production phase	X	1.1c	XIV	5-8 (Part B)	14	4-7 (Part B)
10. Report serious incidents and field safety corrective actions	VIII	5	XIII	5	13	6

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