FONDAZIONE
PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

Master Biennale di II livello in
Discipline Regolatorie "G. Benzi"

XI FORESIGHT TRAINING COURSE

Changes in Regulatory Sciences in the EU

how to move from a reactive to a multi-stakeholder proactive attitude

25-27 October, 2018

Istituti Clinici Scientifici Maugeri - Via Salvatore Maugeri, 6 - Pavia (Italy)

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The new provisions introduced by Rule 21

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WHERE IT COMES FROM

5.5.2017 EN Official Journal of the European Union L 117/1

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) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 168(4)(c) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee (1),

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure (2),

Whereas:

(1) Council Directive 90/385/EEC (3) and Council Directive 93/42/EEC (4) constitute the Union regulatory framework for medical devices, other than *in vitro* diagnostic medical devices. However, a fundamental revision of those Directives is needed to establish a robust, transparent, predictable and sustainable regulatory framework for medical devices which ensures a high level of safety and health whilst supporting innovation.

(2) This Regulation aims to ensure the smooth functioning of the internal market as regards medical devices, taking as a base a high level of protection of health for patients and users, and taking into account the small- and medium-sized enterprises that are active in this sector. At the same time, this Regulation sets high standards of quality and safety for medical devices in order to meet common safety concerns as regards such products. Both objectives are being pursued simultaneously and are inseparably linked whilst one not being secondary to the other. As regards Article 114 of the Treaty on the Functioning of the European Union (TFEU), this Regulation harmonises the rules for the placing on the market and putting into service of medical devices and their accessories on the Union market thus allowing them to benefit from the principle of free movement of goods.

WHERE IT COMES FROM

Recital 59:

Rules under the old regime applied to invasive devices do not sufficiently take account of the level of invasiveness and potential toxicity of certain devices which are introduced into the human body. In order to obtain a suitable risk-based classification of devices that are composed of substances or of combinations of substances that are absorbed by or locally dispersed in the human body, it is necessary to introduce specific classification rules for such devices. The classification rules should take into account the place where the device performs its action in or on the human body, where it is introduced or applied, and whether a systemic absorption of the substances of which the device is composed, or of the products of metabolism in the human body of those substances occurs.

WHERE IT COMES FROM

Rule 21 has been laid down to give an adequate classification to invasive devices, consisting of substances or associations of substances; it is based on the risk that these substances or their metabolism products are absorbed by the human body, both locally and systemically.

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WHERE IT COMES FROM

MDR 2017/745

AIM:
TO ENSURE A HIGH LEVEL OF SAFETY OF PATIENT

INSTRUMENT:
TO INCREASE THE RISK THRESHOLD OF DM

WHAT DOES IT SAY

Rule 21

Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body

are classified as:

- **class III** if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose;
- **class III** if they achieve their intended purpose in the stomach or lower gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body;
- **class IIa** if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities;
- **class IIb** in all other cases.

WHAT DOES IT SAY

Rule 21

The **medical devices composed of substances** are classified as:

- **class III** if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose;
- **class III** if they achieve their intended purpose in the stomach or lower gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body;
- **class IIa** if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities;
- **class IIb** in all other cases.

WHAT IMPLIES

1st evidence

No substance-based device can be class I anymore

intervention of the ON is always necessary

WHAT IMPLIES

2nd evidence

The medical devices composed of substances, where applicable and in a manner limited to the aspects not covered by this Regulation, **shall comply with** the relevant requirements laid down in Annex I to **Directive 2001/83/EC** for the evaluation of:

- **Absorption, Distribution, Metabolism, Excretion;**
- **local tolerability;**
- **toxicity;**
- **interaction with other devices, medicinal products or other substances**
- **potential for adverse reactions.**

CONSEQUENCES

FOR DESIGN PHASE

Devices shall be designed with a **particular attention** to:

a) the **choice** of materials and **substances** used, particularly as regards **toxicity**;

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.

CONSEQUENCES
FOR TECHNICAL DOCUMENTATION

The documentation shall contain the **results and critical analyses of** all verifications and validation **tests and/or studies** undertaken, including test design, complete test or study protocols, **methods** of data analysis and data summaries and test conclusions, regarding studies in relation to:

- **Absorption, Distribution, Metabolism and E**
- possible **interactions** of th products of metaboli **with other devices, medicinal products** or **stances**, considering the target population, and its associated medical conditions;
- local **tolerability**;
- **toxicity**, including **single-dose** toxicity, **repeat-dose** toxicity, **genotoxicity, carcinogenicity and reproductive and developmental toxicity**, as applicable depending on the level and nature of exposure to the device.

In the absence of such studies, a justification shall be provided

CONSEQUENCES

FOR LABELS

Label and instructions for use shall contain the following:

- the **overall qualitative composition** of the device and **quantitative** information **on the main constituent** or constituents responsible for achieving the principal intended action
- **warnings and precautions**, where appropriate, related to the general profile of **interaction** of the device and its products of metabolism with other devices, medicinal products and other substances
- **contra- indications**
- **undesirable side-effects**
- risks relating to **overdose**

CONCLUSIONS

RULE 21 INDICATES THE WAY

that allows to recognize
the substance-based devices
as medical devices

CONCLUSIONS

RULE 21 INDICATES THE WAY
BUT WE HAVE TO PAY ATTENTION TO:

- Choice of **substances**
- Physical, chemical and microbiological **characterization** of the device, particularly with regard to the **toxicity** of the **substances**
- **Mode of action**, scientifically demonstrated
- **Studies** supporting :
  - the device **classification**
  - the device preclinical and clinical characterization

    studied as for a medicinal product

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Thank you!

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