NEWSLETTER JUNE 2019

Finalization of the Guidance on Characterization of Ultrahigh Molecular Weight Polyethylene (UHMWPE) Used in Orthopedic Devices

https://www.fda.gov/media/95791/download

Characterization of Ultrahigh Molecular Weight Polyethylene (UHMWPE) Used in Orthopedic Devices

Guidance for Industry and Food and Drug Administration Staff

Document issued on April 26, 2019.

The draft of this document was issued on February 12, 2016.

FDA has developed this guidance document for members of industry who submit and FDA staff who review testing of orthopedic devices using ultrahigh molecular weight polyethylene (UHMWPE) material. This guidance is intended to assist you in determining the appropriate information and testing to submit in Premarket Notifications (510(k)s), De Novo requests, Premarket Approval (PMA) applications, Humanitarian Device Exemptions (HDEs), and Investigational Device Exemptions (IDEs) for orthopedic devices that contain UHMWPE.

This guidance addresses the characterization and testing of UHMWPE materials used in class II and class III orthopedic devices, including spinal devices. These materials include conventional UHMWPE, highly crosslinked UHMWPE, highly crosslinked UHMWPE containing antioxidants (e.g., α-tocopherol (an isomer of vitamin E)), and non-conventional UHMWPE. This document outlines the information we recommend you include in a submission to FDA to characterize the UHMWPE material (e.g., material description, sterility, biocompatibility, mechanical properties, and chemical properties).

This guidance document does not address nor discuss device-specific functional testing, such as impingement testing, wear testing, or interconnection strength testing.

Second Notified Body for MDR in NANDO database

NANDO database was updated in April 2019 to include the second Notified Body under the European Medical Devices Regulation (EU) 2017/745 (MDR). **TÜV SÜD Product Service GmbH Zertifizierstellen** has in fact successfully completed the Joint Assessment for designation to the MDR.

State-of-play of joint assessments of Notified Bodies in the MDR and IVDR sectors

As of April 23, 2019 the **NB applications** sent to SANTE/F were **38 for MDR** and **9 for IVDR** with an overall scope coverage, namely the entirety of MDR and IVD codes.
The preliminary assessment reports (**PARs**) received by SANTE/F were **27 for MDR** and **6 for IVDR**.
Regarding the post-assessment activities, 11 CAPA (Corrective And Preventive Action) plans were received by SANTE/F and reviewed by JAT (Joint Assessment Team). 3 JAT opinions are under preparation, **7 JAT opinions** have been already issued, and 1 CAPA plan is undergoing official translation.

Manual on borderline and classification in the community regulatory framework for medical devices

https://ec.europa.eu/docsroom/documents/35582

The new version of the Manual on borderline and classification for medical devices, Version 1.22, has been published in May. Three new borderline cases has been added: automated external defibrillator storage units (AEDs), lubricants intended for alleviation of vaginal dryness, and medication decision support software.
AEDs are intended by the manufacturer for use in emergency situations and are usually designed to function as intended within certain environmental conditions e.g. within temperature and humidity ranges that are specified in the instructions for use and on the device labelling.
To ensure AEDs are available for use in an emergency situation, they are often stored in public locations (e.g. shopping centres and public streets). Due to the varying environmental conditions that the AED can be exposed to in these locations, AEDs are stored in storage units which claim to maintain the AEDs within the recommended environmental conditions. An AED is a medical device in accordance with the MDD. The question is whether the AED storage units could be considered as an accessory to the AED.
An AED storage unit is intended to be used with an individual AED to store it in the environmental conditions in which the AED was designed to function. The AED storage unit protects the AED from extreme environmental conditions in the location where it is stored so that the AED performs as intended when needed in an emergency situation.
An AED storage unit that is intended to maintain the specified environmental conditions required for an AED to perform as intended, should be qualified as an accessory to a medical device as per Article 1 (2) b of the MDD. An AED storage unit that uses a power supply to achieve its intended purpose should be classified as class I under Rule 12 of the Annex IX of the MDD. If no power supply is used, the unit should be classified as class I under Rule 1.
On the other hand, an AED storage unit that is not intended to maintain the required environmental conditions for the AED should not be qualified as an accessory to a medical device.
Pill organiser boxes are intended for storing the pills in dedicated compartments for a given period for administration at the right time. There are different kinds of boxes: boxes for one day, boxes for one week, 7-day boxes consisting of seven daily compartments and others. The purpose of these boxes is to facilitate and control medication.
Although taking the correct dose of medication at the right time is an important part of medical treatment, tools facilitating this do not fulfil the definition of a medical device, because they are not intended to diagnose, prevent, monitor, treat or alleviate disease themselves. The box is only a convenient tool to help the patient remember whether or not they have taken their medication. These pill organiser boxes should not be qualified as medical device.
Water- or silicone- based lubricants intended by the manufacturer for the alleviation of vaginal dryness during sexual intercourse should be qualified as medical devices, since they are intended for replacement of a physiological process and thereby comply with the definition of medical device.
After sexual intercourse, it is expected, or at least likely, that part of the lubricant will remain in the body for more than 60 minutes and not more than 30 days. This is an inherent characteristic of the product and is considered part of its intended (normal) use and not as accidental use (as stated in section 3.2 of MEDDEV 2.4/1 rev. 9).
Lubricants intended for the alleviation of vaginal dryness during sexual intercourse are therefore invasive devices intended for short term use (more than 60 minutes and not more than 30 days), unless demonstrated otherwise by the manufacturer. According to Rule 5, these lubricants should be classified in class IIa.
In case the manufacturer can provide sufficient evidence to prove that the lubricant does not remain in the human body beyond 60 minutes after application, the lubricant may be considered to be intended for transient use and should then be classified in class I (Rule 5).

The medication decision support software is intended to be used by healthcare professionals for optimising patient medicinal therapy by identifying possible contraindications, medicinal product interactions and need for dosage adjustments.
The software uses a patient's clinical data and applies a number of rules, of varying complexity, to generate an output. The simplest rules may depend on a single condition being met. These typically use data relating to prescribed medication that is stored in the internal dataset. Other rule-based principles may be more complex and may depend on several conditions being met for a recommendation to be made. Certain rules can have preference for one condition over another.
The output information from the software is used by the healthcare professional to refine and optimise the individual patient's medicinal therapy treatment plan e.g. to give advice to remove a particular medicinal product to avoid possible interactions, to highlight adverse reactions to medicinal products, to provide treatment options for previously untreated conditions etc.
The software is intended to be used for the purpose of prevention, monitoring, treatment or alleviation of a disease and should therefore be qualified as a medical device.

Medical Device Coordination Group clarifies device and UDI registration timelines under MDR and IVDR

On 15 April 2019, the Medical Device Coordination Group (MDCG) released two new documents:

- MDCG 2019-4 Timelines for registration of device data elements in EUDAMED
- MDCG 2019-5 Registration of legacy devices in EUDAMED.

The MDCG 2019-4 document clarifies the inconsistencies of the timelines in the legal text and defines that devices (that are place on the market after Date of Application of the Regulations regardless if covered by Directive or Regulation certificate) should be registered in Eudamed 18 months after the date of application – until 26 November 2021 for MDs and 26 November 2023 for IVDs.
This 18-month registration timeline applies if the new database is fully functional by 25 March 2020. If Eudamed is not fully functional on time, then the registration deadline is 24 months after the date of publication of the OJEU notice about Eudamed functionality.
However, devices might need to be registered sooner (earlier than 18/24 months after Date of Application) i.e. registration is obligatory in case of serious incident and field safety corrective action reporting.

The MDCG 2019-5 document clarifies that devices with valid Directive certificate which will be placed on the market after Date of Application (the so called "legacy devices") are required to be registered in Eudamed (this is applicable to both medical devices after the 26 May 2020 and in vitro diagnostic medical devices after 26 May 2022).
They will need two other unique access keys (IDs) to replace the Basic UDI-DI and UDI-DI for the sake of the workability of Eudamed. For this purpose, a Eudamed DI will be assigned to the device instead of the Basic UDI-DI and a Eudamed ID will be assigned by Eudamed instead of the UDI-DI allowing the system to work and to keep the design of Eudamed as close as possible to the MDR design. These Eudamed DI and Eudamed ID will be unique for a given legacy device.
In case a legacy device has been already registered in Eudamed and that same device becomes at any point in time an MDR compliant device, that MDR device should be considered as a new device requiring a new registration (due to the change in the applicable legislation) with a Basic UDI-DI and UDI-DI in Eudamed.

Consultation on draft guideline on quality requirements for medical devices in combination products

https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-quality-requirements-drug-device-combinations_en.pdf

29 May 2019
EMA/CHMP/QWP/BWP/259165/2019
Committee for Medicinal Products for Human Use (CHMP)

Guideline on the quality requirements for drug-device combinations

Draft

On 3 June 2019 EMA has released a draft guideline on the quality requirements for medical devices in human medicines that include a medical device (known as drug device combinations or DDC) for a 3-month public consultation.
The guideline addresses the new obligations in MDR, in particular the requirements under Article 117. This article foresees that the marketing authorisation application should include a CE certificate or declaration of conformity for the device or, in certain cases, an opinion from a NB on the conformity of the device.
The guideline covers devices that are necessary for the administration, dosing or use of the medicine. They can be integral, co-packaged or referred to in the product information of the medicine but obtained separately. It specifies which information about the device needs to be submitted as part of the initial marketing authorisation application and subsequently during the product lifecycle. It also contains a proposed template for the NB opinion on the conformity of the device to the relevant general safety and performance requirements laid down in MDR.
It is intended that this guideline will increase transparency and consistency of information in regulatory submissions, reducing work for all stakeholders and ultimately improving patient safety.
Stakeholders are invited to send their comments by 31 August 2019 to qwp@ema.europa.eu using the template provided.
EMA will take into account comments received during the consultation, with a view to finalising the guideline before the regulation fully applies on 26 May 2020.

Authorised representative, importer and distributor: a scheme for understanding their obligations

https://www.aboutpharma.com/blog/2019/05/06/mandatario-importatore-e-distributore-uno-schema-per-capirne-gli-obblighi/

An interesting article that reviews the competences of the three economic operators through a summary scheme that better frame their respective duties in the light of MDR.
Authorised representative, importers and distributors acquire a role completely complementary to that of the manufacturer. They are no longer mere subjects in a commercial chain, but they become active players in the safety of the device, throughout its entire life. This profile is clearly explained in the MDR articles that regulate in detail the obligations of each economic operators.
Since many companies have multiple skills, i.e. they are simultaneously manufacturers for some DM and authorized representative, importers and/or distributors for other DM, the scheme proposed in the article can be a useful tool to guide and facilitate within the companies the different requirements and obligations in relation to the different roles they cover.

Use of Symbols to Indicate Compliance with the MDR

https://www.medtecheurope.org/wp-content/uploads/2019/05/190506_MD-labelling_Symbols-guidance.pdf

MedTech Europe
from diagnosis to cure

GUIDANCE

Use of Symbols to Indicate Compliance with the MDR
May 2019

To comply with new MDR requirements in an efficient manner before the relevant international standard is available, MedTech Europe publishes its guidance on graphical symbols to be used on medical devices' labels. The graphical symbols in this guidance have all been validated with users, including patients and healthcare professionals, according to international standards. These symbols have been submitted to ISO and are currently being considered in the revision of ISO 15223-1 Medical Devices - Symbols to be used with medical device labels, labelling and information to be supplied.
The guidance includes symbols for the following information:

1. Medical device
2. Contains human blood or plasma derivatives
3. Contains a medicinal substance
4. Contains hazardous substances
5. Contains biological material of human origin
6. Contains biological material of animal origin
7. Sterilized using vaporized hydrogen peroxide
8. Translation
9. Repackaging
10. Single Patient Multiple use.

Additionally, in Annex 2 of the guidance MedTech Europe recommends symbols to be used with patient implant card.

Alternative methods to animal testing, a working group set up at the Italian Ministry of Health

The Health Minister has signed the establishment of a working group for the promotion of alternative methods to the use of animals in scientific experiments.
"Finally we have equipped ourselves with an instrument of civilization. Monitoring experiments on the use of animals is an ethical but also scientific achievement. We need to balance the interests of research and science with the need to

go beyond traditional methods to reduce to the maximum the number of animals used", said the Health Minister Giulia Grillo.
In addition to institutional representatives, the working group consists of experts on alternative methods in bioethics and animal experimentation.
The body will also make use of the contributions of the stakeholders identified through an expression of interest procedure as per the notice that will be published on the website of the Ministry of Health.
The working group will have to meet monthly and every six months will have to present a report to the minister.

Chemsafe attendance to the AFI Symposium, Rimini, Italy, June 2019

An important attendance of Chemsafe people occurred this year during the 59° Annual AFI Symposium in Rimini, ITALY.
A workshop on June Wednesday 5, morning was organized by Chemsafe. ***"Le nuove frontiere regolatorie dei Dispositivi Medici: come affrontarle in un contesto Europeo ed Internazionale"***. The workshop was aimed to give an overview on EU Regulation on Medical Devices from a scientific/regulatory perspective and having a glance at the USA and Chinese regulation respectively. International guests were hosted by Chemsafe during workshop. Chemsafe people involved were Mr. Paolo Rossi as Chairman, Alessandra Iavello and Tiziana Nardo of Chemsafe Medical Device Business Unit, as speakers. The workshop was attended by around 50 people.

The following day, our Managing Director Antonio Conto, had a speech in the GMP session regarding the quality of API (Active Principle Ingredients) entitled "***Toxicology evaluation in the quality of API***". The session was attended by around 150 persons. Many interesting questions were posed by the audience.

On June 7, the Conference session dedicated to the Medical Devices was chaired by Alessandra Iavello, Head of the Chemsafe Medical Device Business Unit. The session was attended by around 200 persons with interesting round table at the end and many questions regarding the future new Regulation implementation starting from May 26, 2020.

CHEMSAFE attendance 2019

IKN ITALY
YOUR KNOWLEDGE NETWORK

Milan (ITALY) February 26-2
Regulatory Toxicology, IKN workshop
Teachers: Antonio Conto (Chemsafe), Marco Rodda (Chemsafe)

58TH ANNUAL MEETING
& ToxExpo · MARCH 10–14, 2019

Baltimore (USA), March 10-14
USA SOT (Society of Toxicology), Exhibition booth + two poster presentations, 4 people

London (USA), March 20-21
BCPA PESTEX, 1 people attending

Nurnberg (GE), May 21-23
MEDTECHLive, Exhibition booth + 3 people

Basel (CH), May 7-9
VITAFOODS 2019, Exhibition booth + oral presentation, 4 people

Rimini (ITALY) June 5-7
AFI 59° SIMPOSYUM, Exhibition booth + MD workshop organization, 6 people + talk in the Quality of API session

Bruxelles, June 12-13
CHEMICAL WATCH EXPO: GLOBAL CHEMICAL REGULATION, Exhibition booth + oral presentation, 2 people

Helsinki (FI), September 8-11
EUROTOX 2019, Exhibition booth + two poster presentations