Annet Visscher | NVFG 18-APR-2023

AE REPORTING UNDER THE MDR

Topics

- MDR background
  - Adverse Event reporting clinical studies essential part
- Clinical study regulatory bodies
  - Competent Authorities & Ethics Committee
- Guidance documents
  - MDCG 2020-10, ISO 14155
- Different study types
  - Art's 62, 74.2, 74.1, 82
- Conclusion

Medical Devices: a diverse sector

Over 500.000 products (10.000 generic groups) + IVDs !

Clinical trials with medical devices D. Bouchez

MDR – Enhance safety

- MDR:
  - ensure the quality and safety of medical devices on the European market throughout their entire life cycle
  - simplify/ unify safety reporting
  - not a clinical trial regulation

MDR – Clinical study safety reporting

- Articles 62 – 82
  - ***Art 80 – AE recording and reporting***
  - ***Art 87 – Incident reporting***
- ANNEX XV - Clinical Investigations – methodology & documentatie
  - 3.1.4 Plans for safety reporting
- Local law/ Int'l guidance/ ISO 14155
  - Section 7.4.2 (AE's), 7.4.3 (DD's), etc

MDR – AE reporting applicability

- Art 120 – transition period

  Clinical investigations which have started to be conducted in accordance with Article 10 of Directive 90/385/EEC or Article 15 of Directive 93/42/EEC prior to 26 May 2020 may continue to be conducted. As of 26 May 2020, however, the ***reporting of serious adverse events and device deficiencies shall be carried out in accordance with this Regulation***.

Definitions - Clinical Studies

- Clinical Investigation (MDR)
  - Any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device
- Post-market Clinical Follow-Up (PMCF) Investigation (MDR)
  - Clinical investigation to further assess, within the scope of its intended purpose, a device which already bears the CE marking
- Pre-market clinical investigation (MDCG 2020-10)
  - Clinical investigation with non-CE marked devices, or with CE-marked devices used outside the intended use(s) covered by the CE-marking

Definitions - SAE

‘serious adverse event’ (SAE) means ***any adverse event*** that led to

a) death,

b) serious deterioration in the health of the subject, that resulted in any of the following (i) life-threatening illness or injury, (ii) permanent impairment of a body structure or a body function, (iii) hospitalisation or prolongation of patient hospitalisation, (iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, (v) chronic disease,

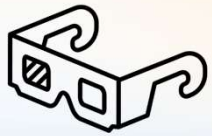
c) foetal distress, foetal death or a congenital physical or mental impairment or birth defect;

Definitions - AE

‘adverse event’ means any untoward medical occurrence, unintended disease or injury or any untoward clinical signs, including an ***abnormal laboratory finding***, in subjects, ***users or other persons***, in the context of a clinical investigation, whether or not related to the investigational device

Definitions - DD

‘device deficiency’ (DD) means any inadequacy in the identity, quality, durability, reliability, safety or performance of an ***investigational device***, including malfunction, ***use errors*** or ***inadequacy in information supplied*** by the manufacturer;



Definitions - Incident

‘incident’ means any malfunction or deterioration in the characteristics or performance of a ***device made available on the market***, including ***use-error*** due to ergonomic features, as well as any ***inadequacy in the information*** supplied by the manufacturer and any undesirable ***side-effect***;

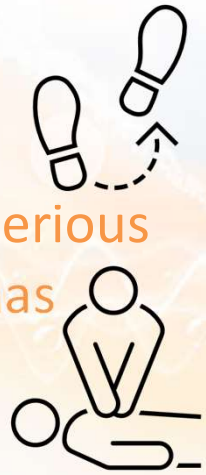
Definitions – Serious Incident

‘serious incident’ means any incident that directly or indirectly ***led, might have led or might lead*** to any of the following: (a) the death of a patient, user or other person, (b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health, (c) a serious public health threat;

MDR – Clinical trial types & reporting reqs

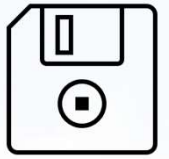
- Art 62/ 74.2 (Conformity studies with device or application without CE mark)
  - Art 80; MDCG 2020-10
- Art 74.1 (PMCF Inte
  - In principle, Artic
  - Art 80 shall appl
    adverse event a
    been established
- Art 82 (other studie
  - Clinical investigations, no
    purposes listed in Article 62
  - Articles 87 to 90 (vigilance)
  - Local requirements

MDCG 2020-10: other post-market clinical investigations may be subject to safety reporting requirements in line with this guidance due to national requirements following MDR Article 82, but there is no such general requirement.



MDR – AE recording/ reporting

- The ***sponsor*** shall ***record***
  - any AE identified in the ***CIP*** as being critical
  - any SAE, and
  - any DD that might have led to a SAE



- The sponsor shall ***report***, without delay to all Member States in which the clinical investigation is being conducted
  - (a) any serious adverse event that has a causal relationship with the investigational device, the comparator or the investigation procedure
  - (b) any DD that might have led to a serious adverse event;
  - (c) any new findings in relation to any event referred to in (a) and (b).

MDR – vigilance reporting

- Manufacturers shall
  - establish a post-market surveillance system to actively and systematically gathering, ***recording*** and analysing data on the quality, performance and safety of ***a device*** throughout its entire lifetime
  - ***report*** 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.

MDR – AE reporting CA/ EC

- The sponsor shall report, without delay to all ***Member States***…

- Reporting to the ***Ethics Committee*** referenced in guidance docs though
  - MDCG 2020-10 –> Member States may also require separate reporting to the Ethics Committee(s)
  - ISO 14155 -> The sponsor … shall … c) report or ensure the reporting, to the EC by the PI (s), of all SAE's and device deficiencies that could have led to a serious adverse device effect, if required by the ***CIP*** or by the EC

MDR EUDAMED

- Art 73

  The Commission shall, in collaboration with the Member States, set up, manage and maintain ***an electronic system***: … (e) for reporting on serious adverse events and device deficiencies and related updates referred to in ***Article 80***.

- MDCG 2021-1

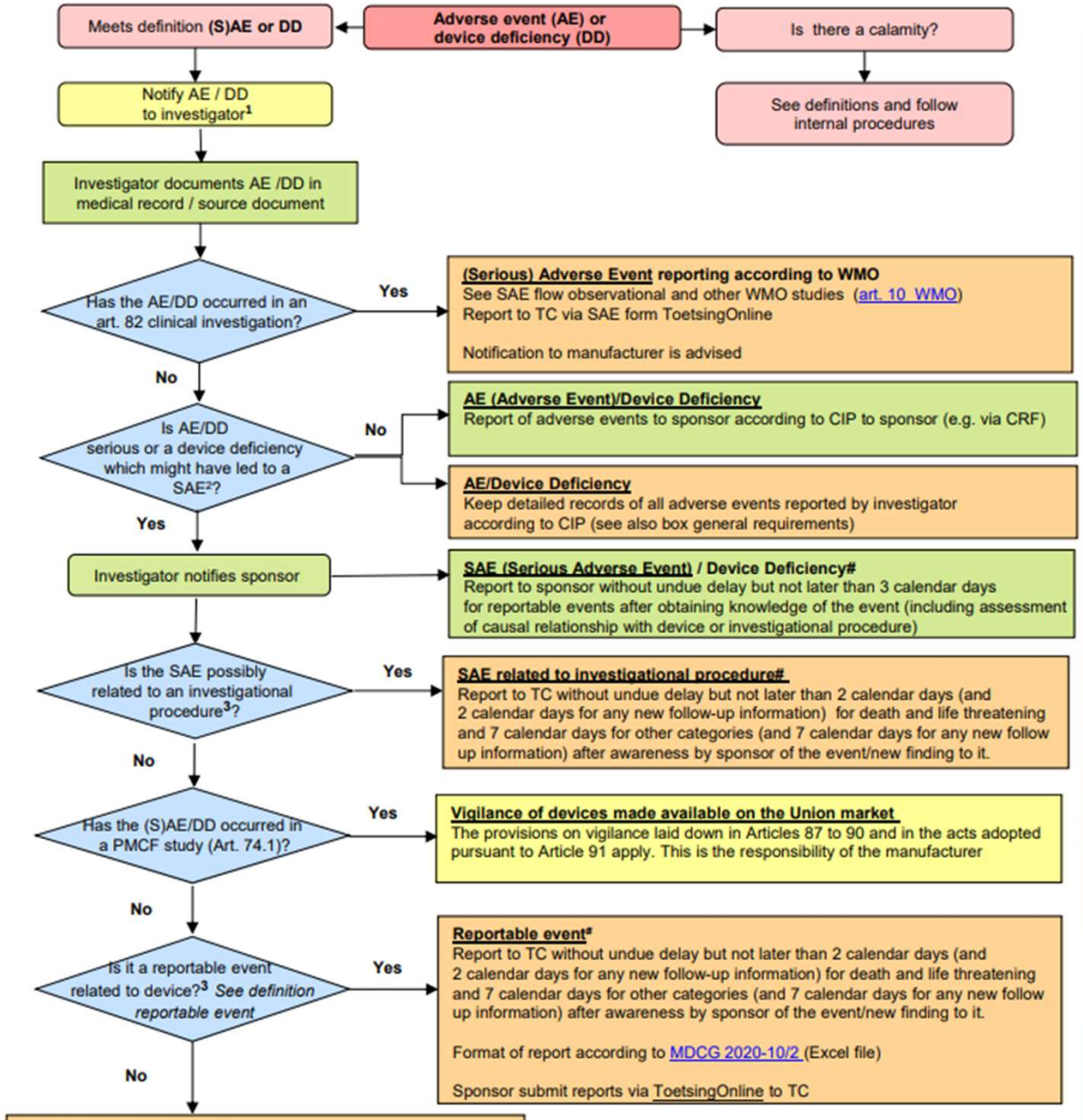
  SAE and DD reporting should take place via the respective ***national procedures*** applicable to clinical investigations and as described in the MDCG Guidance on safety reporting in clinical investigations.

Netherlands – AE Flowchart

https://www.ccmo.nl/onderzoekers/klinisch-onderzoek-naar-medische-hulpmiddelen/tijdens-en-na-onderzoek-naar-medische-hulpmiddelen/veiligheidsrapportage

https://www.ccmo.nl/onderzoekers/publicaties/publicaties/2021/05/08/flowchart-ongewenste-voorvallen-onderzoek-met-medische-hulpmiddelen

Clinical investigations with medical devices, MDR (art 62, 74 and 82)



Netherlands – AE reporting

- Upload in ToetsingOnline until Eudamed is available
  - Clinical investigations art's 62 and 74 (WMO): MDCG 2020-10/2 table (all reportable events)
    - 62 & 74.2 - SADE's and DD's that might have led to a SAE, and
    - 74.1 - SAE related to investigational procedure
  - Other clinical investigations art 82 (WMO): SAE form ToetsingOnline (SAE's except those exempt per ***CIP***)
- Non-WMO -> devices@ccmo.nl and EC
- Int'l studies
  - Include reportable AE's from 3rd country
  - Inform all other CA's involved at the same time!

In conclusion

- Straight forward MDR to CA
  - Art's 62 & 74.2 -> reportable events;
  - Other studies -> serious incidents except documented (known) side-effects.
- Unclarities/ grey area's
  - EC requirements may create (local) nuances;
  - PMCF studies;
  - EUDAMED – local regs

Questions?

info@appliedclinicalservices.com

+31 6 5330 2680

https://appliedclinicalservices.com/
https://medicaldevicesclinical.wordpress.com/

Applied Clinical Services BV | EU Medical Device Clinical Research Consulting

Clinical Evidence Strategies | Clinical Project Managment | Monitoring | Clinical Audits