
Annet Visscher | NVFG 18-APR-2023
AE REPORTING UNDER THE MDR
18 april 2023
ACS NVFG MD middag
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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
Safety reporting to Authorities clear for Pre-market Investigations
Grey areas for PMCF Investigations and the EC
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Medical Devices: a diverse sector

Over 500.000 products (10.000 generic groups) + IVDs !

Clinical trials with medical devices D. Bouchez

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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

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MDR – Clinical study safety reporting

- Articles 62 – 82
  - ***Art 80 – AE recording and reporting***
  - ***Art 87 – Incident reporting***
  - ***Art 86 - PSUR***
- 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

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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***.

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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

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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;

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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

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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;

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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***;

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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;

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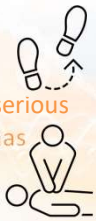
MDR – Clinical trial types & reporting reqs

- Art 62/ 74.2 (Conformity studies with device or application without CE mark)
  - Art 80; MDCG 2020-10
- Art 74.1 (PMCF Interventional studies conform IFU)
  - In principle, Articles 87 to 90 (vigilance), ***but***
  - Art 80 shall apply "where a causal relationship between the serious adverse event and the preceding ***investigational procedure*** has been established"
- Art 82 (other studies)
  - Clinical investigations, not performed pursuant to any of the purposes listed in Article 62(1)
  - Articles 87 to 90 (vigilance)
  - Local requirements



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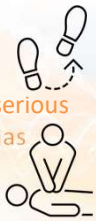
MDCG 2020-10: other post-market clinical investigations may be subject to safety reporting requirements in line with this guidance due to national requirements following MDR Article 82, but there is no such general requirement.



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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).

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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.

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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 -> report to EC all SAE's and DD's that could have led to a SADE, **if required.**

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MDR EUDAMED

- Art 73

  The Commission sha[illegible]ration with the Member States, set up, man[illegible]ain ***an electronic system***: … (e) for reporting [illegible]erse events and device deficiencies and relat[illegible]s 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.

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Netherlands & Belgium

useful links

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

https://www.famhp.be/sites/default/files/Guideline%20Submission%20of%20Clinical%20Investigation%20according%20to%20MDR_version%201.0_4.pdf

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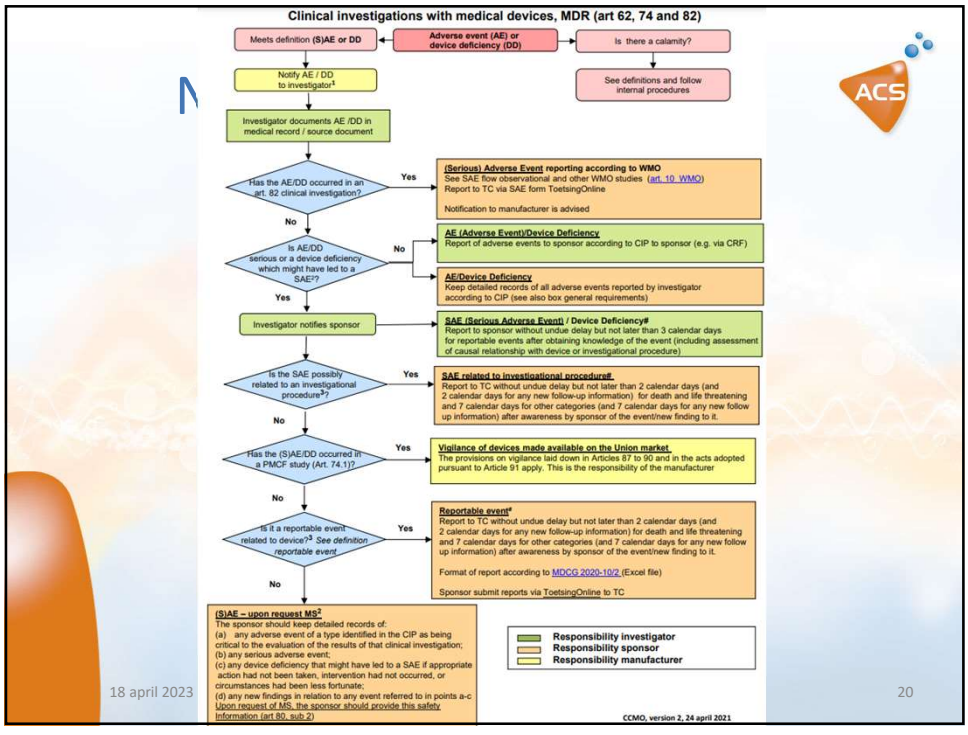

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Netherlands – AE reporting

- 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 (SAE's except those exempt per ***CIP***)
- Non-WMO/ safety reports -> 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!

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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

ISO 14155: 2020 may be of help.

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Questions?

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