RECOMMENDATION 2013/473/EU ON NOTIFIED BODIES AUDITS

Questions and Problems in the Field

RAin Dr. Angela Graf
RECOMMENDATION 2013/473/EU IN NOTIFIED BODY-AUDITS

BAH - Who we are and why do we care about medical devices?

Background and Basics

Questions and Problems in the Field

Conclusion
RECOMMENDATION 2013/473/EU IN NOTIFIED BODY-AUDITS

BAH - Who we are and why do we care about medical devices?

Background and Basics

Questions and Problems in the Field

Conclusion
GERMAN MEDICINES MANUFACTURERS’ ASSOCIATION

- Registered Association („e.V.“), founded 1954 in Cologne
- Offices in Bonn Bad-Godesberg (Main Office) and Berlin
- 40 Employees (therefrom 23 academics: Art Scolars, Biologists, Chemists, Computer Scientist, Economists, Lawyers, Nutritionists, Pharmacists)
- BAH is with more than 460 members the biggest industrial association in the sector of medicines in Germany
- Members are settled in the following business areas:
  - German branche offices of global operating companies
  - Small and medium-sized enterprises (SME)
  - All relevant manufacturers of generic drugs
  - Consulting firms, CROs, Agencies, Publishing Houses etc.
MANUFACTURERS OF SUBSTANCE-BASED AND DENTAL MEDICAL DEVICES ARE BAH MEMBERS

For example
- Nose sprays (seawater-derived)
- Products for the treatment of acute sore throat
- Products for the treatment of gastrointestinal disorders
- Laxatives that absorb water
- Eye drops
- Medicinal clay
- Products for the treatment of infestation with head lice

For example:
- Dental filling material (e.g. composites)
- Dental bondings
- Dental Inlays
- Dental cannulas
- Dental crowns
- Artificial teeths
- Polymerisation activators (light)
## OUR WORLD-WIDE ACTIVITIES

### BAH
- Offices in Bonn and Berlin
- 40 Employees
- Committees (e.g. Medical Devices, Economy, Communication, Phyto-Medicines)
- Bundestag and Bundesrat
- Federal Government
- Higher federal authorities
- Organisations in the context of healthcare
- Associations, Media

### AESGP
- Office in Brusseles
- 6 Employees
- Committees (e.g. Regulatory Affairs, Medical Devices)
- European Commission
- European Parliament
- European Medicines Agency, European Associations, Media

### WSMI
- Office in Ferney-Voltaire (France)
- 5 Employees
- World Health Organisation (WHO)
RECOMMENDATION 2013/473/EU IN NOTIFIED BODY-AUDITS

BAH - Who we are and why do we care about medical devices?

Background and Basics

Questions and Problems in the Field

Conclusion
BACKGROUND

- **2012: Joint Plan for Immediate Action**
  launched by the European Commission’s Directorate-General DG Sanco

- **One of the main objectives:**
  “Ensure that all notified bodies in the context of the conformity assessment make full use of their powers given to them under the current legislation ... including the powers to conduct unannounced inspections.”
  (European Commission Press Release IP/12/119, 9 February 2012)

24 September 2013

- Commission Implementing Regulation (EU) No 920/2013: designation and the supervision of notified bodies
- Commission Recommendation (EU) No 2013/473: audits and assessments performed by notified bodies in the field of medical devices
RECOMMENDATION (EU) NO 2013/473

- Articles
- Annex I – Product Assessment (design & type of examination)
- Annex II – Quality System Assessment
- Annex III – Unannounced Visits

RECOMMENDATION (EU) NO 2013/473

Article 1 Purpose

By providing general guidelines for such assessments and unannounced audits, this Recommendation should facilitate the work of the notified bodies as well as the Member States’ evaluation thereof. This Recommendation does not create any new rights and obligations. The legal requirements applicable to all types of devices and conformity assessments are set out in the Union legislation on medical devices.
2013/473/EU - BINDING RULES?

- Is the “Recommendation 2013/473/EU“ a text without any legally binding obligations but only the interpretation of law in force?*

- Annexes: „Notified Bodies **should** verify / examine / identify / carry out unannounced audits (…)“

„Should“ in the context of legal texts is normally connected with an **elementary rule with exemptions in justified circumstances.**

see also:
2013/473/EU - BINDING RULES?

But:

- Is it legitimate to launch a nonbinding „recommendation“ when there was before already a Commissions Draft for a Medical Device Regulation as a binding rule with the identical aim?

- Some parts of the recommendation do not only interprete the law in force but do establish new rules (e.g. testing of samples, unannounced audits). Does this fit together with the legal character of a „recommendation“?

Is this only a theoretical discussion between lawyers?

→ An inconsistent modus operandi of Notified Bodies within Europe leads to a fragmentation of the legal framework and results in unfair competition.
RECOMMENDATION 2013/473/EU IN NOTIFIED BODY-AUDITS

BAH - Who we are and why do we care about medical devices?

Background and Basics

Questions and Problems in the Field

Conclusion
# Definition of Key Terms

<table>
<thead>
<tr>
<th>Critical Subcontractor</th>
<th>• Subcontractors in charge of processes which are essential for ensuring compliance with legal requirements</th>
</tr>
</thead>
</table>
| Crucial Supplier       | • Supplier of crucial components  
|                         | • Supplier of the entire devices                                                               |

If a process is essential for the compliance or if a component is a crucial component also depend on:
- the complexity of the supplied component (e.g.: some software)
- the complexity of the supplied process (e.g.: sterilization processes)
DEFINITION OF KEY TERMS II

Manufacturer A: Triclosan

- Triclosan is chemically well-defined!
- Triclosan is not a crucial component

Manufacturer B: Dental Medical Device

- Final Inspection Batch Release
- Protective Sealant for Exposed Dentin
  - Mechanical Protection from Abrasion by Sealant
  - Triclosan for Protection from Plaque Formation and Caries Associated Bacteria at the Surface of Sealant

Incoming testing

No Critical subcontractor
No Crucial Supplier
DEFINITION OF KEY TERMS III

- Key terms such as „critical subcontractor“ or „crucial supplier“ should be clarified in order to reach a common understanding among manufacturers and Notified Bodies.

- And…. !!!!!

  Notified bodies may, instead of or in addition to visiting the manufacturer, visit one of the premises of the manufacturer’s critical subcontractors or crucial suppliers if this is likely to ensure more efficient control. (Annex III, Number 2)
DEFINITION OF KEY TERMS IV

- UAAs* should be carried out at suppliers and subcontractors only in justified cases, e.g. insufficient control of the manufacturer or in case of final product suppliers.

- FDA has stopped the auditing of suppliers many years ago. It was taken into account that – for many suppliers – the medical devices industry represents only a small part of the total turnover.

- Auditing just because of formal aspects and not of justified rationale would probably lead to a delivery stop for some medical device companies.

* UAA: Unannounced audit
PRODUCT ASSESSMENT (ANNEX I)

Where the manufacturer has applied for design dossier examination or for a type examination:

- Notified Body should verify
  - if the device is correctly qualified as medical device
  - the classification of the devices and whether the manufacturer has fulfilled the applicable conformity assessment obligations
  - the compliance of the device with the relevant Essential Requirements and with the common technical specifications
  - all documentation related to the device conformity assessment
  - that the clinical data is up to date

- The Notified Body should examine the requirements regarding the design, manufacture and packaging of the device

- The Notified Body should review all relevant preclinical follow-up data, the clinical evaluation and the post-market clinical follow-up.
QUALITY SYSTEM ASSESSMENT (ANNEX II)

Where the manufacturer has applied for an assessment of its quality system:

- The quality system assessment should include audits of the premises of the manufacturer.
- The Notified Body should identify which products the manufacturer identify as covered by the quality system assessment.
- The Notified Body should identify the post-market information available to them or to the manufacturer.
- The Notified Body should review the technical documentation on the basis of the representative sample for class IIa and IIb.
- The Notified Body carry out or ask for relevant tests of the device.
OEM*- PLM**- RELATIONSHIP I

Annex II:

„General advice in case of outsourcing of the production via subcontractors or suppliers”

“Notified bodies should note that manufacturers:

(…)

(b) do not fulfill their obligation to have at their disposal the full technical documentation and/or of a quality system by referring to the technical documentation of a subcontractor or supplier and/or to their quality system;”

* OEM: Original Equipment Manufacturer (i.e. company that „physically“ produces the medical device)

** PLM: Private Label Manufacturer (i.e. company that places the device on the market without producing it itself; manufacturer in the sense of the medical devices law)
OEM-PLM-RELATIONSHIP II

* OEM: Original Equipment Manufacturer (i.e. company that “physically” produces the medical device)
** PLM: Private Label Manufacturer (i.e. company that places the device on the market without producing it itself; manufacturer in the sense of the medical devices law)
OEM-PLM-RELATIONSHIP III

- The reference to the audit report concerning the technical documentation of the OEM’s Notified Body must be possible furthermore together with the stipulation, that the PLM can have full access if necessary.

- An excerpt of the technical documentation is placed at the disposal of the PLM by the OEM, as appropriate.
Annex II, 4:
“For medical devices of Class IIa or IIb, the notified bodies should review the technical documentation on the basis of representative samples (...) Where doubts arise as to the conformity of a device, including its documentation, notified bodies should carry out or ask for relevant tests of the device. (…)”
SAMPLES II

Multi-level Procedure should be best practice:

(1) Testing of samples should be generally performed at the manufacturer's site as an eye witness test.

(2) If the manufacturer is unable to carry out such tests as part of the audit, there should be the possibility to put the samples in quarantine and perform the tests as part of an extended or newly applied audit in the presence of an Notified Body-Auditor.

(3) Only if this is not possible, an external examination of the samples by the Notified Body should be executed; in this case, a cross-check sample remains with the manufacturer.
UNANNOUNCED AUDITS (UAAs)

Article 2c
To verify the day-to-day compliance with legal obligations, notified bodies should, in addition to the initial, surveillance or renewal audits, visit the manufacturer or, if this is likely to ensure more efficient control, one of its subcontractors in charge of processes which are essential for ensuring compliance with legal requirements (‘critical subcontractor’) or a supplier of crucial components or of the entire devices (both: ‘crucial supplier’) without prior notice (‘unannounced audits’) in accordance with Annex III.

Specifications in Annex III
UAAs – ORGANIZATIONAL ASPECTS

- UAAs should not take longer than one day.

- The audit team should consist of 2 persons at the maximum. One of both auditors should be familiar with the audited of the manufacturer and the related manufacturing processes.

- UAAs should take place only once in every 3 years (also for class III medical devices). Exceptions are justified in the suspicion or under vigilance aspects (e.g. increased error rate of a product group).

Aim of UAAs is „to verify the day-to-day compliance with legal obligations“. Purpose in an efficient and practicable control and not to perform a lot of audits with high costs (audit costs of Notified Bodies and subcontractors / suppliers will be passed on the manufacturer).
UAA’S – ORGANIZATIONAL ASPECTS II

- Possibility of a “Matrix-UAA Monitoring“ for manufacturers with a multi-site (e.g. root of number of monitored manufacturer sites).

- It should be legitimate to submit documents that are useful for the clarification of the audit result within a specified time frame after the UAA (e.g. 48 hours).

- The request to inform the NB about processing times should be avoided as it is not practically feasible. Instead, guidelines should be developed how to carry out UAAs if the target product specified in the audit plan is not produced at that time. In this case an adaption of the audit plan to devices currently being manufactured would be quite possible without missing the fundamental objective of the UAA recommendation.
RECOMMENDATION 2013/473/EU IN NOTIFIED BODY-AUDITS

BAH - Who we are and why do we care about medical devices?

Background and Basics

Questions and Problems in the Field

Conclusion
CONCLUSION

- The character of the „recommendation“ is not clear. This will lead to an inconsistent implementation within Europe.
- There are a lot of unsolved questions and problems in the field.
- Manufacturers need legal certainty.
- Dialog between Notified Bodies and Manufacturers is necessary in order to find practical solutions.
RAin Dr. Angela Graf
Bundesverband der Arzneimittel-Hersteller e.V.
Ubierstraße 71-73
53173 Bonn
0228/957 45 – 31
Graf@bah-bonn.de

Thank you for your interest!