Inspection Division
Survey market inspection Unit

Inspection campaign summary report

TOPIC: Implantable defibrillation leads

Abstract: An inspection campaign was conducted between November 2013 and June 2014, among defibrillation lead manufacturers by the Inspection Direction of ANSM. Six inspections were performed in three manufacturers' and one distributor's site.

The objective of this campaign was to ensure that the manufacturers take into account the regulatory requirements for CE marking in terms of manufacture and control, performances and safety demonstration of the defibrillation leads put on the French market.

Inspected operators generally follow the process of putting on the market of these leads.

However for one of the manufacturers, a high number of deviations was noted during the inspections of two of its sites. ANSM therefore enjoined the manufacturer to comply.

Moreover, it should be noted the absence in this campaign of a major European manufacturer, because the Competent Authority of the country concerned declined the ANSM request for inspection of this manufacturer.

Keywords: Inspection, medical device (MD), defibrillation lead (DL), EC marking, ethylene oxide sterilization.

I. HEALTH STAKES

ANSM exercises a special surveillance on medical devices at risk. It is in this context that fits the inspection campaign on the defibrillation leads (DL) as an implantable medical device (IMD). The objectives of these inspections are to verify the manufacturer's compliance to the applicable regulatory requirements for demonstrating the safety and performances of these devices and to ensure, if necessary, the implementation of the necessary corrective actions.

The heart rhythm disorders are the causes of approximately 40,000 deaths per year in France, as sudden death for adult people resulting of an uncontrolled runaway of cardiac contractions.

The defibrillation leads are connected to a pulse generator housing which is placed under the skin. The leads consist of sheathed electrical conductors and electrodes, they are introduced, intravenously, in the heart.
Some recent models of defibrillators offer for leads subcutaneous implantation (such as housing) instead of cardiac implantation, they were not included in this campaign.

II. REGULATORY REFERENCES

The aim of these inspections was to assess the compliance with the provisions of the Directive 90/385/EEC of the European Parliament amended by the Directive 2007/47/EC and with the French Public Health Code and its implementing regulations concerning active implantable medical devices, particularly defibrillation leads put on the French market.

III. CONDUCT OF THE CAMPAIGN OF INSPECTIONS

1. Objectives

The inspection campaign on defibrillation leads was intended to check out the following points:

- manufacturing conditions considering the regulatory requirements;
- compliance and comprehensiveness of the EC mark regulatory file;
- regulatory obligations taken into account by the operators as responsible of the marketing including the management of claims and vigilance reports on medical devices.

2. Inspected operators

The Inspection Division led the campaign between 2013 and early 2014. The inspected operators are or belong to large groups that have subsidiaries in several countries. Three foreign manufacturers (USA) and a French distributor were inspected. For North American manufacturers, inspections have taken place in two of the three North American headquarters and their three production sites in Puerto Rico. A total of six sites has been inspected during the campaign. The staff of the inspected sites is between 500 and 4300 employees.

It should be noted in this summary, the absence of a major European group: BIOTRONIK, for which the German competent authority, responsible for the implementation of the regulatory requirements applicable to medical devices in its territory, has not responded favorably to the ANSM request to carry out an inspection in Germany for this campaign on the defibrillation leads.

It was not identified marketing in France of other leads that those being the subject of this campaign.

The list of operators inspected is in Appendix 1

3. Terms of the campaign

The inspections were carried out by five inspectors and have been the subject of preliminary information to the operators.

The inspections were lead according to a consistent and predefined methodology which includes the verification of the following items**:**

- the staff management conditions dedicated to the main activities with responsibility (organizational charts, functions' forms, empowerment, delegation, training);
- the quality management system (documentation system, internal/external audits);
- the EC certificates for implantable medical devices placed on the market;
- the comprehensiveness of technical files, in particular on the preclinical and clinical studies, compliance with essential requirements, risks management, labeling and instructions for use of the devices;
- the conditions of manufacturing, control and batch release of products;
- the qualification of the special processes as the validation of sterilization with ethylene oxide;
- the production (hygiene, facilities, maintenance, storage, manufacturing, inspection, packaging;
- the management of non-conformities, claims, medical device vigilance as well as the process provided in case of product recalls.

IV RESULTS – FINDINGS

This campaign has shown that the inspected manufacturers of defibrillation leads generally meet the requirements imposed by the EC marking, except one which brings almost 50% of the deviations on the overall campaign.

Most operators have:

- made mandatory declarations and communications to ANSM, for the placing on the French market of their leads;
- a system of quality management sufficiently documented ;
- conditions of production and traceability satisfactory;
- management of non-conformities / claims and vigilance well suited.

However, areas for improvement were identified during this campaign on:

- The formalization of qualification and validation processes for obtaining and maintaining sterility in particular on the following issues:

    - implementation of procedures in particular on validation frequencies of sterilization with ethylene oxide ;
    - existence of qualification plans for each site and for each EtO sterilization chamber ;
    - validation of EtO re-sterilization on the MD performance and the packaging strength ;
    - controlled atmosphere areas qualification with adequate particulate controls in terms of frequency and particle sizes.

- In terms of risk analysis, major deviations were on:
  - lack of comprehensive risk analysis plan including risk reduction measures;
  - acceptance of risks' level too high and/or an unsatisfactory approach for the calculation of the residual risk;
- Batch release management by the production unit. It was noted in particular the lack of independence between the production activities and batch release where the intervention of an independent qualified person is expected;

- Management of staff dedicated to the main activities of responsibility (organizational charts, functions' forms, empowerment and delegation) must allow accurate description of the functions of a responsible person.

The deviation distribution is presented in Appendix 2.

An injunction was addressed to one operator following inspections of its two sites in May and June 2014 (Minnesota and Puerto Rico) involved in the production of defibrillation leads. The failures that led to this injunction are related to incomplete demonstration of products biocompatibility, to important gaps on validation processes of sterilization and desorption of ethylene oxide residues and parametric release methodology used by the company after sterilization.
This injunction was published on the ANSM website.

IV. CONCLUSION

Defibrillation leads placed on the French market, with the exception of those covered by the injunction above-mentioned are:

• globally in line with the regulation and with the essential requirements applicable to them;
• manufactured, packaged, sterilized, labeled and controlled in satisfactory conditions.

Regarding the leads covered by the injunction, ANSM enjoined the manufacturer to carry out corrective actions, to comply with the regulation.

Appendix 1

List of the inspected operators

St JUDE MEDICAL
MEDTRONIC (2 sites)
BOSTON SCIENTIFIC (2 sites)
SORIN CRM

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Appendix 2