MENTOR

Mentor Medical Systems B.V.

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Agence Nationale de Sécurité du Médicament et des Produits de Santé
Direction de l'Inspection
Pôle inspection des essais et des vigilances
A l'attention de
143/147 boulevard Anatole France
93285 SAINT-DENIS
France

Ref: MV-Mentor–20102015-LC1-15IPV019
Code : di_ins001_,01_LT05_v03

Registered letter with recorded delivery

Leiden, The Netherlands, 21 December 2015

Dear ,

In response to your letter dated 24th of November 2015, received at Mentor Medical Systems BV on 02nd of December 2015, regarding the inspection performed on 20 - 22 October 2015, enclosed please find our response to the preliminary inspection report. The action plans to correct the audit non-compliances are included. The action plan contains references to the audit non-compliances, non-compliance description, proposed actions, and completion dates as required. Based on this action plan, we hereby assure you that we are committed to addressing the non-compliances in a timely manner.

Please contact me if you need additional information or clarification on the proposed corrective actions.

Sincerely yours,

Management Representative, Plant Quality Manager
Mentor Leiden

Copy.

, ANSM
, Worldwide Director of Quality and Regulatory Compliance, Mentor
, Sr. Director Quality Operations, Mentor
, EMEA QA/RA Manager, Mentor
Plant Manager Mentor Leiden

Finding Identification #: D1

FINDING DESCRIPTION:

The processing of the MV cases, as described in the corresponding procedure used by MENTOR MEDICAL SYSTEMS B.V, is not completely compliant with the European legislation in force (MDD Annex II point 3.1) considering the findings detailed in Annex 2 to this Inspection report, which implies to update this procedure so that :

1. Any serious incident or risk of serious incident, whether expected/foreseeable or not, shall be reported to the concerned competent authority ;
2. Any serious incident or risk of serious incident, regardless of its likelihood of occurrence, shall be reported to the concerned competent authority (as an example, this shall apply to ALCL cases) ;
3. In case of doubt on the causality of the medical devices and thus on the reportability of an event, there should be a pre-disposition to report

INVESTIGATION

Mentor internal observation OBS-014664 was originated on 3rd December, 2015 to investigate and address the nonconformance D1 observed during 2015 ANSM Inspection.

Mentor acknowledges the importance of ensuring a robust Medical Device Vigilance (MDV) process to ensure the protection of health and safety of patients, users and others by reducing the likelihood of reoccurrence of incidents elsewhere.

SOP-TX-113, Regulatory Agency Reporting, Rev. 30, is the current procedure that defines Mentor requirements for Health Authority reporting, including requirements for submission of MDV reports to ANSM. The current procedure documents Mentor policy related to US Medical Device Reporting (MDR) decision making, but does not clearly define Mentor's MDV reporting policy or the process for MDV reporting of serious incidents. In addition, the procedure does not include a process for determining MDV reportability of incidents where the causality is unknown.

DOP-QA-4002, Processing of a Complaint File and Investigation Guidelines, Rev. 26 includes specific guidance on the information to be collected from complainants related to these cases. For ALCL cases, the following information is to be collected as available beyond standard requirements:

- Summary of symptoms, confirmed diagnosis, date of diagnosis, pathology/test findings, complete breast implant history, relevant medical history (i.e. environmental exposure, cancer, allergies), any recent medications/ preparations used and treatment outcome;
- Complete breast implant history as available, including prior surgeries with non-Mentor breast implants, the dates of implantation, brands and types of implants (saline or silicone), and types of implant surface (textured or smooth); and
- Anatomic site of ALCL including side, whether the ALCL was primarily in this site and pathologically confirmed, date of pathology confirmation and report findings, whether a fibrous capsule is involved, whether patient has persistent and/or late onset seroma, identification of any masses near the breast implant, and identification of capsular contracture with Baker Grade.

It was observed that current procedures do not indicate that ALCL cases be subject to MDV reporting. In practice it was confirmed that all cases are reported to the relevant Health Authorities. Procedures will be updated to document this practice as described above.

Root Causes: Method

The root cause of this issue is that the procedure is unclear and lacking the details required per MEDDEV 2.12-1 Rev. 8. In addition, the Medical Device Vigilance policy applied by Mentor is not adequately documented.

ACTION PLAN

#	Description	Planned Completion Date
2	SOP-TX-113, Regulatory Agency Reporting procedure and related procedures will be revised to: • Document Mentor process related to MDV reporting, including treatment of ALCL cases; and • Clarify the process for determining MDV reportability of incidents where the causality is unknown.	March 30, 2016
3	Training will be provided to employees involved in MDV reporting, based on the procedural and policy revisions implemented to SOP-TX-113 Regulatory Agency Reporting and related procedures.	April 30, 2016

***Finding Identification #:* D2**

FINDING DESCRIPTION:

The description of the MV cases processing, in MENTOR MEDICAL SYSTEMS B.V and/or MENTOR French affiliate documentation system, is not complete (MDD Annex II point 3.2, claimed ISO 13485 standard points 4.2.1 d et 4.2.2 b) insofar the documentation system :

1. Does not mention the reporting process agreed between MENTOR and ANSM regarding the BIs related incidents occurred in France, which concerns :
    - The individual cases prone to Immediate notification ;
    - The clustered cases prone to periodic (yearly) notification :
        i. via the Periodic summary reports (PSRs) ;
        ii. via the Trend reports in case of detection of drift, simultaneously to the aforesaid PSRs.
2. Does not include any procedure of preparation and submission of the PSRs to ANSM.

INVESTIGATION

Mentor internal observation OBS-014665 was originated on 3rd December, 2015 to investigate and address the nonconformance D2 observed during 2015 ANSM Inspection.

Vigilance procedures in France are not enough detailed on what needs to be reported.
They do not refer to the ANSM table "Critères de déclaration des incidents PMI par les fabricants" neither to the PSRs. In addition, there is no work instruction describing how to prepare and submit a PSR to the ANSM.

Root Causes: Method

1) The vigilance reporting criteria defined by the ANSM in its document called "Critères de déclaration des incidents PMI par les fabricants" did not change actual practices of reporting by Mentor France from previously known criteria. As a result, it can be stated that the procedure FR-PR-

3-0002 Vigilance and Field Action did not specifically state the requirements as stated in "Critères de déclaration des incidents PMI par les fabricants".

2) As per the ANSM requirements, PSRs were submitted to the ANSM (cf the last e-mail sent to the ANSM with PSRs for 2014 in attachments), however, no procedure was updated on the process doing so. As a result, it can be stated that the procedure is lacking this instruction.

ACTION PLAN

#	Description	Planned Completion Date
1	Update the French local procedure PR-FR-3-0002 "Vigilance and Field Actions" to include details on the reporting process for incidents related to BIs, occurring in France. The table "Critères de déclaration des incidents PMI par les fabricants" will be included into this SOP	January 31, 2016
2	Create a Work Instruction to explain the process to prepare and submit PSRs to the ANSM (work instruction # 100386533)	January 31, 2016
3	Train people involved in this process on new revision of SOP PR-FR-3-0002 and WI # 100386533	February 18, 2016

Finding Identification #: D3

FINDING DESCRIPTION:

Regarding the continuity of the MV activity, a record of presence of the Head of the Product Evaluation Department, since the beginning of the year 2015, was presented during the inspection and is referenced 13 in this Inspection report. Nevertheless, the records certifying the presence of the Product Evaluation Department Head's delegates within the same period are not implemented, which does not allow to document the continuity of the MV activity.

The continuity of the MV activity within MENTOR organization is not enough documented, which induces a risk that MV cases may not all be processed and reported with the required due diligence (MDD Annex II items 3.1 and 3.2 b), in the absence of records demonstrating the continuous presence of the Product Evaluation Department Head's or of his delegates.

INVESTIGATION

Mentor internal observation OBS-014661 was originated on 3rd December, 2015 to investigate and address the nonconformance D3 observed during 2015 ANSM Inspection.

PR-0000626 Good Documentation Practices Procedure Rev: 7 was reviewed. The procedure provides detailed instructions on delegation requirements at Mentor, and requires use of 100205740 Franchise Form for Delegation to document approval of delegates. It was confirmed that the Head of the Product Evaluation Department has approved forms in place to delegate authority to other qualified team members in the event of her absence.

In addition, Mentor practice is to regularly review critical processing timelines related to medical device vigilance in order to ensure integrity and continuity of the process. Examples of metrics under regular monitoring include the percentage of cases resolved within 60 days and the percentage of open cases aged greater than 90 days. The Mentor medical device vigilance system relies on a team of trained and qualified individuals working to approved procedures, and the absence of a single individual (including the Head of the Product Evaluation Department) would not impact the integrity of this system.

Discussions with Quality Leadership on this issue determined that the monthly metrics being distributed and the quarterly Management Review being conducted could be fortified to ensure additional control. Current procedures only require presentation of critical processing parameters during quarterly management review. Additional oversight by the Mentor Management Representative is required. A procedure will be implemented to ensure critical process parameters related to medical device complaint handling and vigilance reporting are reviewed and discussed each month at a meeting attended by leadership. Examples of metrics that may be reviewed include timeliness of complaint entry, timeliness of MDV submission, and timeliness of complaint resolution. The Mentor Management Representative will participate in the monthly meeting. Updates to the Management Review process are addressed in the response to ANSM remark R9. These improvements will further ensure that all complaints are processed and reported with the required due diligence.

Root Causes: Method

The root cause of this issue is lack of visibility of critical processing parameters related to complaints to the Mentor Management Representative. Current procedures do not require periodic review of the complaint process and reportability status.

ACTION PLAN

#	Description	Planned Completion Date
1	Implement a procedure to ensure critical process parameters related to medical device complaint handling and vigilance reporting are reviewed and discussed in a periodic basis at a meeting attended by leadership. The Mentor Management Representative will participate in the monthly meeting. The procedure will include clear process to ensure continuity of the MV process and documented provisions for authority delegation.	March 30, 2016
2	Training will be provided to employees involved in MDV reporting, based on the procedural revisions implemented.	April 15, 2016

Finding Identification #: D4 Major

FINDING DESCRIPTION:

The management of the individual complaints and MV cases by MENTOR is not satisfactory, which compromises the proper processing and notification of the serious incidents occurred in France to ANSM, (MDD Annex II Item 3.1, claimed ISO 13485 standard items 7.2.3, 8.4 and 8.5, Meddev 2.12/1 points 5.1 .7 and 5.3), insofar :

1. MENTOR reported an MV case of silicone granuloma to ANSM more than 8 months after its reception by the French affiliate, whereas silicone granulomas correspond to serious incidents prone to immediate notification (point 2) ;
2. The evaluation of the ALCL cases is limited to the analysis of the medical and scientific literature which states that risks of ALCLs on patients bearing BIs are not to be excluded, without further investigations (point 1) ;
3. The production batch records (DHR) are not systematically reviewed and challenged In the processing of the complaints and MV cases, particularly when these cases refer to known and anticipated incidents, which excludes any assessment of the production impacts (points 1, 4, 6) ;
4. TRACKWISE™ database does not provide the traceability of:
    a. the source documents attesting the actual dates of receipts of the complaints and MV cases communicated to MENTOR staff, with the notifiers details ;
    b. the documents attesting the reporting of the serious incidents to the concerned competent authorities ;
    c. requests and/or reminders which should be addressed to the notifiers in order to collect information on the complaints and MV cases, which may jeopardize the proper evaluation of the incidents gravity and of the causality of the BIs involved (point 3).
5. TRACKWISE™ database decision tree may be empty of any Information (point 9) or may refer to decisions which are not consistent with the European legislation and guidelines in force regarding the gravity and the reportability of some MV cases, insofar silicone granulomas and surgical interventions related to explantations, which are serious incidents prone to immediate notification, are not ranked as such in this database, which may jeopardize the reporting of the serious incidents with the required due diligence to the concerned European competent authorities (point 5, 7).

INVESTIGATION

Mentor Internal CAPA CAPA-005472 was originated on 7th December, 2015 to investigate and address the nonconformance D4 observed during 2015 ANSM Inspection.

Complaint reference was received by the Mentor French affiliate on February 13, 2013. The case involved an incident of silicone granuloma. Upon receipt of the complaint, the French affiliate recognized that no product brand or model was provided. Given the uncertainty of whether a Mentor product was involved, the affiliate chose to not report the incident to ANSM. Mentor acknowledges that this was a mistake, and that Mentor should have a predisposition to report in cases where information is unclear or absent. Mentor agrees with ANSM that all cases of silicone granuloma are subject to MDV reporting.

SOP-TX-113, Regulatory Agency Reporting, Rev. 30, is the current procedure that defines Mentor requirements for Health Authority reporting, including requirements for submission of Medical Device Vigilance (MDV) reports to ANSM. The current procedure documents Mentor policy related to US Medical Device Reporting (MDR) decision making, but does not clearly define Mentor's MDV reporting policy or the process for MDV reporting of serious incidents. In addition, the procedure does not include a process for determining MDV reportability in cases where information is unclear or absent. Mentor will update procedures to clarify this process, and include provisions for documenting consultation with a qualified clinician in cases where information is unclear or absent. Additional process updates are described in the response to nonconformance D1 observed during 2015 ANSM Inspection, which also relates to MDV processing.

DOP-QA-4002, Processing of a Complaint File and Investigation Guidelines, Rev. 26, describes the procedure for processing and investigating product complaints. As described in the response to nonconformance D1 observed during 2015 ANSM Inspection, the procedure includes specific guidance on the information to be collected from complainants related to complex medical cases, including cases of ALCL. In addition, the procedure documents a policy on when to conduct DHR review. The procedure does not require a DHR review in all MDV cases. Mentor agrees that all investigations related to MDV cases should include a DHR review. Mentor will update procedures to clarify this process.

At this time, the TRACKWISE database is currently used by Mentor Customer Quality associates and not used by the regional affiliates including the French affiliate. Incident reports submitted by the local affiliates to their applicable competent authority are not always provided to Mentor and, therefore, the data is not always available in TRACKWISE. Details of these complaints, including the actual date of receipt, documents attesting the reporting of the serious incidents to the concerned competent authorities, and requests addressed to the notifiers are documented in affiliate databases. Mentor has recognized that this state is not ideal, and has committed significant investment to the implementation of a new global complaint database to replace TRACKWISE. This system will be utilized by Mentor as well as all regional affiliates to document complaints, complaint investigations, and any MDV reports submitted to competent authorities. Mentor is in the late stages of this project implementation, with "go-live" scheduled for May 2016. Complete implementation of the system is expected by July 31, 2016.

The policy and procedures related to MDV reporting will be updated to align with ANSM expectations as described in the response to nonconformance D1 observed during 2015 ANSM Inspection.

Root Causes: Method

The root cause of this issue is that the procedure is unclear and lacking the details required per MEDDEV 2.12-1 Rev. 8. In addition, the Medical Device Vigilance policy applied by Mentor is not adequately documented.

In addition, business systems such as TRACKWISE being used to document complaint investigation and not integrated with systems used to document MDV decisions by local affiliates.

ACTION PLAN

#	Description	Planned Completion Date
1	Update SOP-TX-113, Regulatory Agency Reporting, and related procedures to predispose Mentor to report in cases where information is unclear or absent. The procedure will be updated to include provisions for documenting consultation with a qualified clinician in cases where information is unclear or absent. The local French procedure PR-FR-3-0002 "Vigilance and Field Actions" will be updated, these changes will be implemented accordingly.	March 30, 2016
2	Train the employees involved in this process revision, including local affiliates as required.	April 30, 2016
3	Perform an evaluation on form 100220996 Registre des Réclamations, from 2010 to 2015, to verify if there are other cases which have not been reported because of lack of information. Report these cases to the ANSM if applicable.	January 29, 2016
4	Update DOP-QA-4002, Processing of a Complaint File and Investigation Guidelines, to require DHR review in all MDV cases.	February 29, 2016
5	Train the employees involved in the DOP-QA-4002 process revision.	March 15, 2016
6	Implement a new global complaint database to replace TRACKWISE in the US and France.	July 31, 2016

Finding Identification #: R1

FINDING DESCRIPTION:

MENTOR shall update and complete its procedures regarding the management of its documentary system (procedures, records and archiving), so that they clearly mention:

1. The management of the training of all the addressees concerned by the new documents and updates of the existing documents ;
2. A period of archiving at least equivalent to that laid down by the European legislation in force (MDD Annex II point 6.1), regarding the EC Declarations of conformity, EC Certificates of the medical devices, decisions and reports from the notified body, which shall be at least:
    a. 15 years after the last product has been manufactured, in the case of implantable devices;
    b. 5 years after the last product has been manufactured, for the other devices.
    c. The restrictions of access to the complaints and MV documents in paper, to the only authorized staff.

INVESTIGATION

Mentor internal observation OBS-014672 was originated on 3rd December, 2015 to investigate and address the recommendation R1 observed during 2015 ANSM Inspection.

Mentor Leiden has a procedure, SOP-1007 Training rev 34, which specifies the training management process specifically to the Mentor Leiden site. The procedure described the interrelation with the documentary system (Adaptiv) and the training management system (ComplianceWire). However, it is acknowledged that improvements can be made to procedure SOP-1007 to further clarify interrelation between systems used.

Procedure 100095458, Franchise Record Retention Schedule rev 11 was reviewed as part of this observation. The incorrect retention period (Act+10) was included for 'site registrations', which is the terminology used to describe QS Certificates, EC certificates and Declaration of Conformity.

Mentor Leiden follows PR553-005, Franchise Policy for Records Management Compliance (currently in revision 14) where it is stated in that *"Records and information shall be protected, and access to them controlled according to their value"*. As this is a high level franchise document, it does not state the specific requirements to restrict access to paper complaint and MV documents. Because the paper documents reside in the Irving site, the Irving records retention policy (SOP-TX-151 rev 9) was reviewed and it was identified that the procedure misses the specific restriction to paper complaints and MV records.

Root Causes: Method

For all the three specific descriptions, it was recognized that the procedure is not clear and concise and does not specify the items as mentioned by the ANSM.

ACTION PLAN

#	Description	Planned Completion Date
1	Update Procedure SOP-1007 to better specify the interrelation between the different automated systems that are used as part of the training process.	March 31, 2016

#	Description	Planned Completion Date
2	Update Procedure 100095458 to change the retention period for 'site registrations' to 15 years after the last product has been manufactured. Additionally, update the record description to clearly describe that 'site registrations' include the QS Certificates, EC certificates and Declaration of Conformity.	March 31, 2016
3	Update Mentor Texas procedures (SOP-TX-151) to specifically include restriction of access for paper to authorized staff only	March 31, 2016
4	Training people who are involved on the revised/ updated procedures as stated in action 1-3 of this recommendation.	April 15, 2016

***Finding Identification #:* R2**

FINDING DESCRIPTION:

MENTOR MEDICAL SYSTEMS B.V shall update and complete its procedures regarding the management of the skills and habilitations of its staff, insofar the documentation system does not mention the modalities of initial and periodic trainings to the risks associated to the BIs, intended to the staff involved or likely to be involved in the communications of complaints and MV cases (staff in charge of the management of complaints and MV, any other staff that may direct such communications to the staff in charge of the management of complaints and MV ...).

Such modalities shall include:

- periodic and nominative training plans of the staff ;
- nominative records attesting the trainings followed by the staff and the assessment of the effectiveness of such trainings.

INVESTIGATION

Mentor internal observation OBS-014673 was originated on 3rd December, 2015 to investigate and address the recommendation R2 observed during 2015 ANSM Inspection.

Mentor has implemented broad training related to complaint reporting. Mentor employees are trained to report all potential complaints to the Complaint Handling Department. In addition, Mentor has documented PL-0000087 Franchise Policy on Complaint Handling, Rev. 3, which outlines basic requirements related to complaint handling. Industry best practices dictate that non-specialized employees should not attempt to evaluate the risks associated with complaints, to avoid any impediment to reporting. Further investigation revealed that the training presentation requires update and that annual reoccurrence training should be assigned to all employees. Training material will be developed to define requirements for all employees, affiliates, contractors, and manufacturing partners with regards to complaint identification, timely reporting and support of complaint investigations. The training will be deployed to all Mentor employees, affiliates, and contractors. Annual recertification will be required.

Root Causes: Method

The root cause of this observation is that the training curriculum for Mentor associates is lacking periodic training on handling of potential product complaints.

ACTION PLAN

#	Description	Planned Completion Date
1	Training material will be developed to define requirements for all employees, French affiliates, contractors, and manufacturing partners with regards to complaint identification, timely reporting and support of complaint investigations.	March 30, 2016
2	The training will be deployed to Mentor employees and contractors that are involved on complaint identification, timely reporting and support of complaint investigations. Annual retraining will be required.	April 30, 2016

Finding Identification #: ***R3***

FINDING DESCRIPTION:

The Work Instruction DOP-QA-4002 mentions which data are needed for the assessment of the causality of the medical devices involved in the reported incidents, but does not precise the methodology with which the final decision of causality is made and supported.

The procedures and/or work instructions used by MENTOR MEDICAL SYSTEMS B.V in the processing of the complaints and MV cases should be completed so that they precise clearly the methodology with which the final decision of causality of the medical devices involved in the reported incidents is made and supported.

INVESTIGATION

Mentor internal observation OBS-014674 was originated on 3rd December, 2015 to investigate and address the recommendation R3 observed during 2015 ANSM Inspection.

DOP-QA-4002, Processing of a Complaint File and Investigation Guidelines, Rev. 26, describes the procedure for processing and investigating product complaints. In DOP-QA-4002, Processing a Complaint File and Investigation Guidelines, root cause determination is a required process within the investigation. In cases where the determination cannot be made, the procedure requires an explanation. However, a detailed methodology for root cause determination is not clearly defined.

Discussions with Quality Leadership on this issue determined that not all complaint investigations support a root cause analysis. Complaint investigation and testing supports determination of an assignable cause (the cause of the nonconformity) and confirmation of the complaint. Frequent or severe complaints are escalated to the "CAPA" process for further investigation, root cause determination, and corrective action. If any customer complaint is not followed by corrective action, the reason is documented and approved.

As described in the response to nonconformance D1 observed during 2015 ANSM Inspection, SOP-TX-113, Regulatory Agency Reporting procedure and related procedures will be revised to clarify the process for determining MDV reportability of incidents where the causality is unknown. As described in the response to nonconformance D4 observed during 2015 ANSM Inspection, SOP-TX-113, Regulatory Agency Reporting, and related procedures will be updated to predispose Mentor to report in cases where information is unclear or absent. The procedure will be updated to include provisions for documenting consultation with a qualified clinician in cases where information is unclear or absent.

Complaint investigation procedures will be clarified to ensure documentation of Mentor's policy related to root cause investigation of reported complaints.

Root Causes: Method

The root cause of this observation is that Mentor procedures do not clearly define the root cause determination methodology used in the complaint handling process.

ACTION PLAN

#	Description	Planned Completion Date
1	DOP-QA-4002, Processing a Complaint File and Investigation Guidelines, will be revised to document a clearly defined root cause determination methodology.	February 16, 2016
2	Employees involved in the new revision of DOP-QA-4002 Processing a Complaint File and Investigation Guidelines will be trained.	February 28, 2016

Finding Identification #: R4

FINDING DESCRIPTION:

The description of the corrective and preventive actions (CAPAs/FSCAs) management, in MENTOR MEDICAL SYSTEMS B.V documentation system, should be completed so that it mentions provisions regarding the communications to the notified body of the CAPAs/FSCAs :

1. Implemented on medical devices design and/or manufacturing processes and/or labelling, further to each serious incident (to prevent its recurrence) (Meddev 2.12/1 point 5.4.4) ;
2. likely to induce substantial changes to all the medical devices concerned, not only on class III medical devices (MDD Annex II point 3.4).

INVESTIGATION

Mentor internal observation OBS-014667 was originated on 3rd December, 2015 to investigate and address the recommendation R4 observed during 2015 ANSM Inspection.

PR-0000109 rev 9, Franchise Procedure for Field Action, states that the authorized representative should "communicate with European, Competent Authority, notified body and other health authorities as needed".

Specifically for the communication of the activities (to prevent reoccurrence) that resulted from product risk escalations, PR551-002, Franchise Procedure for Handling Product Risk Escalation and Quality Review Board rev 34 and PR575-001 Franchise Procedure for Corrective And Preventive Action (CAPA) rev 48, were reviewed. These procedures do not specifically mention provisions regarding communications to the notified body in relation to the preventive actions instituted.

Root Causes: Method

Method, the procedures do not specify provisions regarding communications the notified body on implementations resulting from escalations. Mentor will implement/update the procedures to include provisions to communicate activities following from product risk escalations to the notified body. As this procedure is applicable to all medical devices, this will concern all medical device classes.

ACTION PLAN

#	Description	Planned Completion Date
1	Review current procedure on the requirements to inform TUV on ANSM recommendation to have provisions included regarding the communications to the notified body on actions to prevent reoccurrence.	March 31, 2016
2	Implement/update the procedures to include provisions to communicate activities following from product risk escalations to the notified body if deemed necessary.	April 30, 2016
3	Training people who are involved on the revised/ updated procedures that state the provisions to communicate activities following from product risk escalations to the notified body.	May 15, 2016

Finding Identification #: R5

FINDING DESCRIPTION:

In the QMS (documentation System)

The product recall process description, In MENTOR MEDICAL SYSTEMS B.V documentation system, should be clarified and completed, at least regarding the medical devices marketed In France, so that it :

1. Mentions that any medical device recall motivated by a technical or medical reason related to a serious incident shall be reported immediately to the European competent authorities on the territory of which the recall is to be conducted (MDD Annex II item 3.1) or that any message intended to the concerned competent authorities and to the patients and/or users, within the framework of such a situation, should be communicated in advance (48 h for example) to the concerned competent authorities ;
2. Precises the reconciliation intended to document the efficency of the recall, with a systematic recall full balance sheet recapitulating the quantities of product units :
    a. produced and/or in production ;
    b. present in stocks ;
    c. likely to be outside stocks (samples sent for analysis, samples given to the staff for demonstration ... for examples) ;
    d. marketed and recallable (unused) ;
    e. marketed and not recallable (used).
3. Plans the evaluation of the efficiency of the recall process by simulations of recall involving the distribution stakeholders until the final clients.

INVESTIGATION

Mentor internal observation OBS-014668 was originated on 3rd December, 2015 to investigate and address the recommendation R5 observed during 2015 ANSM Inspection.

PR-0000109 rev 9, Franchise Procedure for Field Action, states that the authorized representative should "communicate with European, Competent Authority, notified body and other health authorities as needed". The procedure does not define a time requirement for notification to Competent or Notified bodies. Further, the procedure does not provide for definition of effectiveness criteria for the successful closure of field actions.

During creation of the procedure, there were no requirements in standards for conducting of simulated field actions. It is recognized that when an extended period of time has elapsed since conducting a field action, it is good practice to conduct a simulated action to ensure proper execution of actions.

Root Causes: Method

PR-0000109 rev 9, Franchise Procedure for Field Action, does not adequately define the timing for reporting of actions, the criteria for effectiveness checks and did not include a best practice of conducting simulated field actions.

ACTION PLAN

#	Description	Planned Completion Date
1	Update PR-0000109 to include time requirements for reporting, effectiveness check criteria, and to include simulations when there has been a significant elapsed time in conducting a field action.	April 30, 2016
2	Training people who are involved on the new revision of PR-00000109	May 15, 2016

Finding Identification #: R6

FINDING DESCRIPTION:

The Post Market Surveillance (PMS) process described in MENTOR documentation system and related to experience gained from devices in the post-production phase should be completed, so that It lays down provisions related to the construction and update of a consolidated survey report for each category of BIs since their first marketing, with a presentation of :

1. The incidents outcomes broken down by :
    a. Typologies of incidents ;
    b. Regions of occurrence of the incidents (Worldwide I Europe /local countries) ;
    c. Years of occurrence ;
    d. Years of sales and/or implantation;
    e. Sales volumes or numbers of BIs implanted per year (in order to assess the significance of the reported cases) ;
    f. Surface (smooth or textured) of the BIs (In order to allow the inter-comparison of the Benefit/Risk ratio of the textured BIs versus smooth BIs) ;
2. An exhaustive list of the typologies of reported incidents, from the most frequent to the rarest ones ;
3. A methodology of identification of the key points, issues and stakes stemming from these data.

INVESTIGATION

Mentor internal observation OBS-014670 was originated on 3rd December, 2015 to investigate and address the recommendation R6 observed during 2015 ANSM Inspection.

As part of the investigation, SOP-CO-046 Post Market Surveillance (PMS) Rev 6 and related template FORM-CO-057 were reviewed. In addition, a review of existing PMS output was performed.

The existing procedure requires that PMS plans incorporate the monitoring of many specific data sources, including product quality complaints and adverse events. The existing system requires the PMS report include a general summary of product performance for the relevant time period, and overall data trending for key PMS sources identified in the PMS Plan. The plans span the relevant time period, not a period starting with first marketing of the product. In addition, detail related to regions of occurrence of the incidents, years of occurrence, and years of sales and/or implantation may be omitted. Each of the requested breakdowns was reviewed and an assessment was made to determine whether they will be included in the PMS program.

Analysis Request	**Response**
1. The incidents outcomes broken down by: a. Typologies of incidents ;	Current reports include tables describing the typologies of complaints, but explanation of the typologies is missing. In future reports, additional detail describing the harms identified (typologies) will be included.
b. Regions of occurrence of the incidents (Worldwide I Europe /local countries);	Regional analysis is not currently included in reports. In future reports, additional detail regarding regional analysis will be included. For example: analysis will be performed to determine whether certain regions report disproportionately high rates of certain cases.
c. Years of occurrence ;	In future reports, additional detail will be included if certain complaint typologies are new or increasing. Existing reports already identify trends in recent typologies.
d. Years of sales and/or implantation;	The existing method of normalizing complaint rates uses manufacturing volume, not sales or

e. Sales volumes or numbers of BIs implanted per year (in order to assess the significance of the reported cases) ;	implantation volume. Analysis will be performed to determine whether sales volume, implantation volume, or another factor is a more appropriate factor to use in normalization of complaint rates. The normalization calculation, relevant factors, and a justification will be included in future PMS reports.
f. Surface (smooth or textured) of the BIs (In order to allow the inter-comparison of the Benefit/Risk ratio of the textured BIs versus smooth BIs);	Analysis by surface type is not currently included in reports. In future reports, additional analysis will be included to provide detail on surface type (smooth or textured) as it relates to complaint rates. Comments regarding the acceptability of smooth versus textured surface will be documented, and an independent benefit/risk assessment will be performed if required.
2. An exhaustive list of the typologies of reported incidents, from the most frequent to the rarest ones ;	Existing reports include overall complaint rates. In future reports, additional analysis will be performed and documented regarding each of the complaint typologies, including the most frequent to the rarest ones.
3. A methodology of identification of the key points, issues and stakes stemming from these data.	Existing reports document key points, issues, and conclusions regarding the performance, safety and efficacy of the product. In addition, adequacy of the clinical evaluation, including a review of literature, is documented. Existing reports identify any required changes to the PMS plan, if necessary. No changes are proposed.

In conclusion, opportunities to improve the existing method of document post-market surveillance were identified. Existing procedures do not adequately capture requirements deemed necessary by the Regulator. Several changes are proposed to be implemented.

Root Causes: Method

The root cause of this issue is that existing procedures do not adequately capture requirements deemed necessary by the Regulator.

ACTION PLAN

#	Description	Planned Completion Date
1	SOP-CO-046 Post Market Surveillance (PMS) and related templates will be updated based on the comprehensive review of Regulator feedback. See the investigation for a complete list of identified changes.	March 31, 2016
2	Train employees to newly implemented PMS requirements.	April 18, 2016
3	Revise post-market surveillance reports based on newly implemented requirements. Mentor PMS Report for Gel Breast Implants and Mentor PMS Report for Saline Breast Implants will be properly updated . This accelerated revision recognizes the importance of revising the PMS reports for long-term implantable products. PMS Reports for other products will be revised during their standard revision cycle.	July 29, 2016 revision date for Gel Breast Implants and Saline Breast Implants; other PMS reports will be revised during their standard cycle

Finding Identification #: ***R7***

FINDING DESCRIPTION:

MENTOR LLC and MENTOR MEDICAL SYSTEMS B.V should complete the job descriptions and the documentation related to the delegations of its staff, insofar :

1. The delegation form related to activities under the responsibility of the Head of the Product Evaluation Department is not signed by the delegates themselves, which does not certify that they know and accept these delegations ;
2. The job description of MENTOR MEDICAL SYSTEMS B.V Plant Quality Assurance Manager does not mention his activities related to complaints and MV.

INVESTIGATION

Mentor internal observation OBS-014675 was originated on 3rd December, 2015 to investigate and address the recommendation R7 observed during 2015 ANSM Inspection.

1. Although a process for handling delegation records is in place (PR-0000626, rev 7), the process doesn't require delegates to acknowledge and accept task/activities delegates to them.
2. According to PR-0000372 (rev 11) every employee need to have an accurate job description describing all responsibilities for a job function.

Root Causes:

1. Method – The current delegation process doesn't require delegates to acknowledge and accept task/activities delegates to them.
2. Man – It was missed to add the responsibilities/activities of the Plant Quality Assurance Manager regarding the complaints-process and MV in the job description (PD-0108, rev 5).

ACTION PLAN

#	Description for part 1	Planned Completion Date
1	Evaluate whether process for acknowledgement/acceptance of delegates for task/activities delegated to them needs to be defined in local Mentor Irving procedure or in Franchise Procedure	February 28, 2016
2	Update procedure to include acknowledgement/acceptance of delegates	April 15, 2016
3	Make assessment for all Mentor Irving delegation memos, and update memos following the new requirements.	April 15, 2016
4	Update PD-0108 to add responsibilities of Plan QA regarding complaint process	January 31, 2016
5	Training Plant QA Manager and delegates on the new revision of PD-0108	February 15, 2016
6	Create quiz and test whether applicable associates understand their responsibilities regarding up to date job descriptions.	March 15, 2016

Finding Identification #: R8

FINDING DESCRIPTION:

MENTOR should complete the audits covering its complaints and MV management, so that their scope cover the assessment of the quality and timeliness of:

- The MV serious incidents communications to the concerned European competent authorities mentioned in this inspection report;
- The responses to the requests of the competent authorities.

INVESTIGATION

Mentor internal observation OBS-014662 was originated on 3rd December, 2015 to investigate and address the recommendation R8 observed during 2015 ANSM Inspection.

The Internal Audit Report related to Complaint Process IA-002636 was reviewed as part of this investigation and noticed that several complaints files were assessed and the applicable procedures were reviewed. The auditor was a qualified lead auditor with several years of experience within the medical device industry.

A review on procedure 100369706 Work Instruction for the Internal Audit Process – Mentor Leiden Only rev. 1 was also performed. In relation to this recommendation, it was acknowledged that that there is a lack of guidance specific to the materiovigilance requirements per MDD, ISO13485 and MEDDEV 2.12/1, Therefore, procedure not adequately defined is considered the root cause for this observation.

Root Causes: Method

Procedure 100369706 Work Instruction for the Internal Audit Process – Mentor Leiden Only, was not adequately defined. The procedure did not detail guidance specific to materiovigilance requirements.

ACTION PLAN

#	Description	Planned Completion Date
1	Update procedure 100369706 Work Instruction for the Internal Audit Process – Mentor Leiden Only to include guidance on how to conduct an internal audit on Materiovigilance Process	February 15, 2016
2	Training the internal auditors on the new revision of Procedure 100369706	February 28, 2016

Finding Identification #: R9

FINDING DESCRIPTION:

MENTOR MEDICAL SYSTEMS B. V's management reviews should be completed in order to:

1. Cover the assessment of the quality and timeliness of :
    a. the MV serious Incidents communications to the concerned European competent authorities;
    b. the responses to the requests of the competent authorities.

2. Develop the key points, issues and stakes stemming from the PMS data regarding the question of ALCLs related to BIs.

INVESTIGATION

Mentor internal observation OBS-014663 was originated on 3rd December, 2015 to investigate and address the recommendation R9 observed during 2015 ANSM Inspection.

Previous management reviews have been checked to verify if Health Authority reporting timeliness and PMS data have been presented (meeting 29Jul15, 22Jan15, 15Jul14). All management reviews have included the health authority reporting timeliness and PMS data.

The procedure PR550-006 rev 36, Franchise procedure for the Management Review of the Quality System, was reviewed as part of this investigation. The procedure states that both Health Authority reporting timeliness as well as PMS data, needs to be presented during the Management Review.

The template used to perform the Management Review Process is generic in nature, which defines the minimum requirements that each site needs to cover during Management Review Process. Mentor Leiden acknowledges that the Management Review Procedure PR550-006 establish that each site can add more information on this template in order to adjust site needs.

Root Causes: Man

Man, omission error. By means of this recommendation, Mentor will include more "in-depth" analysis of the PMS and incident reporting in the future management reviews to include:

a) The MV serious Incidents communications to the concerned European competent authorities;
b) The responses to the requests of the competent authorities.
c) Key points, issues and stakes stemming from the PMS data regarding the question of ALCLs related to BIs.

ACTION PLAN

#	Description	Planned Completion Date
1	Perform more "in-depth" analysis of the PMS and incident reporting in the future management reviews to include: a) The MV serious Incidents communications to the concerned European competent authorities; b) The responses to the requests of the competent authorities. c) Key points, issues and stakes stemming from the PMS data regarding the question of ALCLs related to BIs.	March 31, 2016
2	Perform a refresh training to Leadership Team on requirements of PR550-006 current revision.	January 15, 2016

Finding Identification #: R10

FINDING DESCRIPTION:

1. Appropriate actions so that its complaints and MV management database includes fields that shall summarize the information and the evaluations made with regards to each key point of the processing of each case, with the attached supporting documents or references, concerning :
    - The date and mode of reception of the source document related to the case notification to MENTOR (letter, fax, e-mail, report of phone call ...), with the identification of the notifier and MENTOR staff addressee;
    - The gravity of the case (serious I non serious);
    - The causality of the medical device(s) involved (established, possible, excluded or unknown)
    - The risk(s) related to the patient;
    - Potentialities of use error;
    - Potentialities of misuse;
    - The reportability of the incident to the concerned competent authorities;
    - The reference of the notification of the incident (Is serious) to the concerned competent authorities;
    - The final evaluation, conclusion and decision related to the case;
    - The criteria triggering the closure of the case.

2. A quality control of the data entered in this database.

INVESTIGATION

Mentor internal observation OBS-014676 was originated on 3rd December, 2015 to investigate and address the recommendation R10 observed during 2015 ANSM Inspection.

DOP-QA-4002, Processing of a Complaint File and Investigation Guidelines, Rev. 26, describes the procedure for processing and investigating product complaints. In the procedure, Attachment 1 "Failure Investigation Guidelines" provides the critical components of each investigation, including:

- Documentation of sufficient attempts for missing/incomplete information and device return;
- A description of the problem, issue or discrepancy;
- Results of Product Evaluation laboratory examination and testing of devices;
- Summarization of complaint trends for the identified failure;
- Summarization of other similar complaints for the lot number(s) provided;
- Determination of root cause or an explanation of why the root cause could not be determined;
- Corrective action(s) taken or rationale why no action will be taken;
- A conclusion statement; and
- Aging, observation and failure coding.

This procedure and other complaint handling procedures do not require documentation of the date, identification of the notifier, whether the complaint represents an MDV reportable case, or the causality of the medical device involved. In practice all of these parameters are captured in the TRACKWISE database. Mentor procedures require revision to clarify that these parameters will be documented in each complaint file.

DOP-QA-4004 Product Evaluation Coding System, Rev 23 provides failure codes that are assigned to each complaint file. These codes enable robust trend analysis, and capture the gravity of the case (serious versus non-serious). In addition, select codes identify complaints with potential of use error or potential of misuse.

A risk analysis is not performed as part of each complaint. Current procedures require periodic risk assessment per a defined schedule. Mentor procedures require revision to ensure each complaint includes a thorough risk assessment.

As described in the response to nonconformance D4 observed during 2015 ANSM Inspection, Mentor will be implementing a new global complaint database to replace TRACKWISE. Although TRACKWISE is a validated system and is compliant with the regulations, some fields are missing that would improve the processing of complaints.

- The source of the complaint is not documented (i.e., phone, mail, e-mail, etc.).
- There is a field in TrackWise to document whether the event was reported to the competent authorities, but it does not reference which competent authority or the date the report was submitted. The TRACKWISE database is not used by the regional affiliates including the French affiliate. Details of these complaints, including the actual date of receipt, documents attesting the reporting of the serious incidents to the concerned competent authorities, and requests addressed to the notifiers are documented in affiliate databases.

As previously described, Mentor has recognized that this state is not ideal, and has committed significant investment to the implementation of a new global complaint database to replace TRACKWISE. This system will be utilized by Mentor as well as all regional affiliates, and complete implementation of the system is expected by July 31, 2016.

Root Causes: Method

The root cause of this issue is that Mentor procedures are unclear and lacking required details.

In addition, business systems such as TRACKWISE being used to document complaint investigation and not integrated with systems used to document MDV decisions by local affiliates.

ACTION PLAN

#	Description	Planned Completion Date
1	Update complaint handling procedures to clarify information required to be documented in all complaint files. In addition, the updated procedures will ensure that each complaint includes a thorough risk assessment.	February 26, 2016
2	Train the employees to the procedural revision.	March 11, 2016
3	Implement a new global complaint database to replace TRACKWISE in the US and France.	July 31, 2016

Finding Identification #: R11

FINDING DESCRIPTION:

MENTOR MEDICAL SYSTEMS B.V should assess the efficiency of its recall process and the proactivity of its partners (customers and distributors) in this matter by conducting periodic recall simulations, documented with:

1. Reconciliations that shall summarize the quantities of product units :
    a. produced and/or In production ;
    b. present in stocks;
    c. likely to be outside stocks (samples sent for analysis, samples given to the staff for demonstration ... for examples) ;
        i. marketed and recallable (unused) ;
        ii. marketed and not recallable (used).
2. Conclusions and potential areas of improvements that may be deemed necessary, following such simulations.

INVESTIGATION

Mentor internal observation OBS-014669 was originated on 3rd December, 2015 to investigate and address the recommendation R11 observed during 2015 ANSM Inspection.

During creation of the procedure, there were no requirements in standards for conducting of simulated field actions. It is recognized that when an extended period of time has elapsed since conducting a field action, it is good practice to conduct a simulated action to ensure proper execution of actions.

Root Causes: Method

PR-0000109 rev 9, Franchise Procedure for Field Action, does not adequately define a time period to conducting simulate field actions to assess the efficiency of the recall process.

ACTION PLAN

#	Description	Planned Completion Date
1	Update PR-0000109 to include time requirements for reporting, effectiveness check criteria, and to include simulations when there has been a significant elapsed time in conducting a field action.	April 30, 2016
2	Training people who are involved on the new revision of PR-00000109	May 15, 2016

***Finding Identification #:* R12**

FINDING DESCRIPTION:

Mentor should complete its BIs post-market survey reports, so that the PMS reports present:

- The analysis of the incidents outcomes broken down by BI surfaces (smooth and textured), In order to allow the inter-comparison of the Benefit/Risk ratio of the textured BIs versus smooth BIs ;
- The exhaustive list of the typologies of reported Incidents, from the most frequent to the rarest ones ;
- The in depth analysis of the key points, issues and stakes stemming from the data related to ALCL cases, including the demonstration of the preservation of the BIs' Benefit/Risk ratio.

INVESTIGATION

Mentor internal observation OBS-014671 was originated on 3rd December, 2015 to investigate and address the recommendation R12 observed during 2015 ANSM Inspection.

A complete investigation into post-market survey report feedback is provided in the response to nonconformance R6 observed during 2015 ANSM Inspection.

Root Causes: Method

Refer to the investigation into post-market survey report feedback provided in the response to nonconformance R6 observed during 2015 ANSM Inspection.

ACTION PLAN

#	Description	Planned Completion Date
N/A	Refer to the action plan listed on remark R6	Refer to action plan listed on R6

ATTACHEMENT I

Evidence of last PSRs submitted to the ANSM (June 1st of 2015) according to investigation performed on observation D2.

Rapports périodiques
de sécurité - Implants

Document End

[BuSFR]

De: je ,
Envoyé: lundi 1 juin 2015 13 15
À: li L
Objet: Rapports périodiques de sécurité - Implants mammaires Mentor - Perthese

Importance: Haute

Bonjour ,

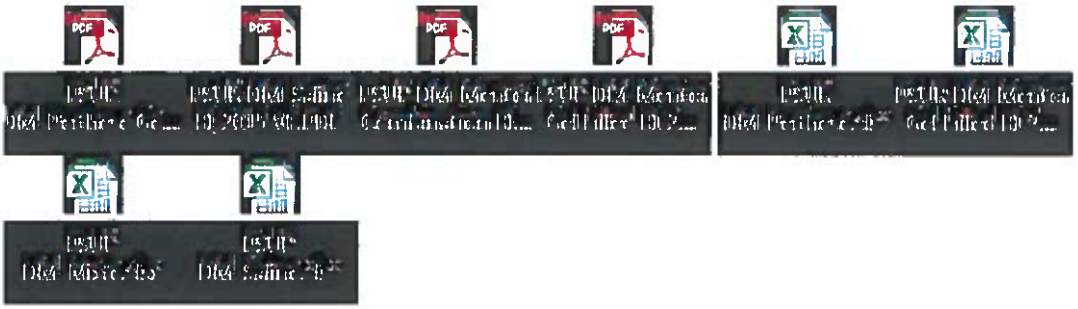
Je vous prie de trouver ci joint les rapports de sécurité suivants :

- Implants mammaires gel Perthese
- Implants mammaires gel Mentor
- Implants salins Mentor
- Implants mixtes gel/solution saline Mentor

Je reste à votre disposition pour toute information complémentaire,

Bien cordialement,

EMEA Quality & Regulatory Affairs Manager
PEROUSE PLASTIE/MENTOR
PSUR DM_Saline



De :
Envoyé : jeudi 26 février 2015 18:29
À :

Objet : Rapports périodiques de sécurité - Implants mammaires.

Madame, Monsieur,

Veuillez trouver ci-joint les versions finales anglaise et française du rapport périodique de sécurité, sans la mention "projet".

Vous en souhaitant bonne reception,

Cordialement

Coordination des vigilances

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Confidentialité

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