

**FRENCH NATIONAL AGENCY FOR MEDICINES AND HEALTH PRODUCTS SAFETY  
INSPECTION DIVISION**

Trials and Vigilances Inspection Department

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Réf : MV-Nagor-08122015-C3-15IPV021

**FINAL INSPECTION SUMMARY REPORT**

<b>Company Inspected</b>	<p><b>NAGOR Limited</b> <b>127/129 Deerdykes View</b> <b>Westfield Industrial Estate</b> <b>Cumbernauld, Scotland</b> <b>GLASGOW G68 9HN</b> <b>UNITED KINGDOM</b></p> <p><b>Phone : +(44) 1236 780780</b></p>
<b>Activities</b>	<p><input type="checkbox"/> Non OBL Manufacturer (Responsible for marketing in Europe)</p> <p><input checked="" type="checkbox"/> OBL Manufacturer (Responsible for marketing in Europe)</p> <p><input type="checkbox"/> Medical devices Assembler</p> <p><input type="checkbox"/> European Representative</p> <p><input type="checkbox"/> Importer</p> <p><input checked="" type="checkbox"/> Distributor</p> <p><input type="checkbox"/> Sub-Contractor</p> <p><input type="checkbox"/> Other</p>
<b>Date of inspection</b>	8 <sup>th</sup> to 9 <sup>th</sup> December 2015.
<b>ANSM Inspector</b>	Accompanied by _____, Regulatory Affairs Section Head of the Medicines and Healthcare products Regulatory Agency (MHRA).
<b>Summary of the main stages of the inspection</b>	<p>Reference of the mission : 15IPV021.</p> <p>Mission letter dated 10<sup>th</sup> November 2015.</p> <p>Date of shipment of the preliminary inspection report : 22<sup>nd</sup> January 2016.</p> <p>Dates of receipt of the responses from the Company : 15<sup>th</sup> February 2016.</p>

## **I. ASSESSEMENT OF THE RESPONSES OF THE COMPANY BY THE INSPECTOR**

The findings notified by the inspector in the preliminary inspection report are recalled and summarized in this final report, preceded by a number in 'D' for the deviations and a number in 'R' for the remarks.

The assessment of the responses provided by the company is preceded by the sign « → ».

The term '*satisfactory*' means that the reported response provides evidence of the implementation of appropriate corrective and/or preventive action(s).

The term '*acceptable*' means that the reported response is appropriate in principle, but in the absence of evidence submitted, the implementation of the corrective and/or preventive action(s) could be verified during a next inspection.

The term '*noted*' means that the reported response and corrective and/or preventive action(s) need to be completed or deepened.

The term '*not satisfactory*' means that the response is not adequate to provide a solution to the reported findings.

### **Quality Management System (QMS)**

- R1 NAGOR Ltd should complete its procedure(s) regarding the management of its documentation system, so that they clearly mention 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 medical devices technical documentation, EC declarations of conformity, EC certificates, decisions and reports from the notified body, which shall be at least :
- 15 years after the last product has been manufactured, in the case of implantable devices ;
  - 5 years after the last product has been manufactured, for the other devices.
- **Uncomplete response**, insofar the action plan provided is limited to update the *Archival procedure QP028* by 31<sup>st</sup> March 2016, regarding the archiving of the decisions and reports from the notified bodies for a period of 15 years after the last product was manufactured, without including the medical devices technical documentation and EC declarations of conformity.
- R2 NAGOR Ltd should complete its procedure(s) regarding the management of the skills and habilitations of its staff, so that they mention modalities of initial and periodic trainings intended to the staff involved or likely to be involved in the communications or processing of complaints and MV cases, regarding :
1. The applicable European legal references and guidelines dealing with MV (MDD, MEDDEV 2.7/3, MEDDEV 2.12/1, MEDDEV 2.12/2) ;
  2. The risks associated to the medical devices marketed by NAGOR Ltd ;
  3. The identification of safety and MV cases and their communication to the staff in charge of their processing.
- Response noted, considering the commitments by 29<sup>th</sup> April 2016, to :
- Capture, within the internal training database, the skills and training of the staff involved or likely to be involved in communications or processing of complaints ;
  - Include appropriate training regarding :
    - The applicable European legal references and guidelines dealing with MV (MDD, MEDDEV 2.7/3, MEDDEV 2.12/1, MEDDEV 2.12/2) ;
    - The risks associated to the medical devices marketed by NAGOR Ltd ;
    - The identification of safety and MV cases ;
    - Processing of complaints.
- As mentioned in R2, NAGOR's procedure for staff training shall be updated accordingly.

- D1 The description of the MV management process, in NAGOR Ltd documentation system, is not complete (MDD Annex II point 3.2, claimed ISO 13485 standard points 4.2.1 d, 4.2.1 f) insofar the documentation system :
1. Does not mention the reporting process agreed between ANSM and NAGOR Ltd regarding the incidents related to the BIs marketed in France, in terms of :
    - individual cases prone to immediate notification ;
    - clustered cases prone to periodic (yearly) notification :
      - via the *Periodic summary reports* (PSRs) ;
      - 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.
- ➔ Acceptable response, considering the commitments to update, by 31<sup>st</sup> March 2016, the procedure *QP 025-02* to include :
- an appendix documenting the agreed reporting process between ANSM and NAGOR ;
  - a procedure for preparation and submission of the PSRs to ANM.
- R3 The CAPAs/FSCAs management process described in NAGOR Ltd documentation system should be completed so that it mentions maximum deadlines for closing the CAPAs/FSCAs opened, in order to reduce the risk that some actions might remain unclosed without justification and indefinitely.
- ➔ Acceptable response, considering the commitments to update, by 31<sup>st</sup> March 2016, the CAPA procedure *QP 024* to include a maximum deadline of 18 months for closing the CAPAs.
- R4 The product recall management process described in NAGOR Ltd documentation system should be completed so that it mentions a reconciliation intended to document the efficiency of the recall, with a systematic recall full balance sheet recapitulating the quantities of product units :
- produced and/or in production ;
  - present in stocks or quarantined ;
  - likely to be outside stocks (samples sent for analysis, samples given to the staff for demonstration... for examples) ;
  - marketed and recallable (unused) ;
  - marketed and not recallable (used).
- ➔ Response noted, considering the commitments to generate, by 29<sup>th</sup> April 2016, a work instruction providing a full description of the recall process, actions and the intended objectives required in the event of a product recall. This work instruction shall include all the items mentioned in R4.
- R5 The Post Market Surveillance (PMS) management process described in NAGOR Ltd documentation system should be completed, so that it lays down provisions and metrics related to the construction and update of a consolidated survey report regarding the BIs since their first marketing, with a presentation of :
1. The incidents outcomes broken down by :
    - Typologies of incidents (ruptures, capsular contractures, siliconomas, seromas, breast cancers, ALCL...);
    - Years of occurrence ;
    - Years of sales and/or implantation ;
    - Sales volumes or numbers of BIs implanted, per year (in order to assess the significance of the reported cases) ;
    - 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 the aforementioned data.
- ➔ Response noted, considering the commitments to incorporate, by 30<sup>th</sup> June 2016, the information mentioned in R5 in the next cycle of the management review. NAGOR's *Post Market Surveillance* procedure shall also be updated accordingly.

## **Organization of the staff involved or likely to be involved in MV**

- D2 NAGOR Ltd cannot demonstrate the means implemented in its organization to ensure that each member of its staff that may have knowledge of a case of complaint or MV knows how to communicate the case to the qualified staff in charge of its processing, which might jeopardize the MV treatment and the proper reporting of serious incidents or risks of serious incidents to the concerned competent authorities with the due diligence required (MDD Annex II points 3.1 (7<sup>th</sup> dash) and 3.2 b, claimed ISO 13485 standard point 5.5), insofar :
- NAGOR Ltd organization charts do not mention the name of the qualified staff to whom shall be transmitted any case of complaint or MV ;
  - No track documenting the communication of the e-mail address '*vigilance@nagor.com*', to each member of the company's staff, is available.
- Acceptable response, considering the commitments by 29<sup>th</sup> April 2016 :
- To update the induction process for all staff to include details of the appropriate contacts for the Vigilance Department, with regards to the communication of complaints or MV ;
  - Recirculate the updated induction to all members of NAGOR's staff ;
  - Update the organization charts in order to identify the staff that should be communicated in case of complaint or MV.
- R6 NAGOR Ltd should complete its management of the competences and skills of the staff involved or likely to be involved in the communications of complaints and MV cases (claimed ISO 13485 standard point 5.5.2 c), by keeping records attesting that all this staff is trained or made aware of :
- Its complaints and MV management procedures ;
  - The risks associated to the medical devices marketed by NAGOR Ltd.
- Acceptable response (combined with the response provided to R2), considering the commitments by 29<sup>th</sup> April 2016, to :
- Capture, within the internal training database, the skills and training of the staff involved or likely to be involved in communications or processing of complaints ;
  - Include appropriate training regarding :
    - The applicable European legal references and guidelines dealing with MV (MDD, MEDDEV 2.7/3, MEDDEV 2.12/1, MEDDEV 2.12/2) ;
    - The risks associated to the medical devices marketed by NAGOR Ltd ;
    - The identification of safety and MV cases ;
    - Processing of complaints.
- D3 NAGOR Ltd cannot demonstrate the continuity of its MV activity, which induces a risk that serious incidents or risks of serious incidents might not all be processed and reported with the required due diligence to the concerned competent authorities (MDD Annex II points 3.1 (7<sup>th</sup> dash) and 3.2 b), insofar this company does not keep records demonstrating the continuous presence of at least one member of its qualified staff in charge of reporting those serious incidents or risks of incidents.
- Acceptable response, considering the commitments by 31<sup>st</sup> March 2016, to :
- Generate a record detailing who is responsible for vigilance and who can deputize in the absence of the person responsible ;
  - Manage the continuity of the MV activity via an electronic holiday tracker.

## **Interfaces and Contracts**

- R7 Regarding the interfaces with its distributors, NAGOR Ltd is expected to :
1. Complete its contract template so that it includes provisions in terms of :
    - a) Immediate notification, to the manufacturer, of any complaint and/or MV case related to the concerned medical devices ;
    - b) Identification of the party who is responsible for reporting any serious incident or risk of serious incident to the concerned competent authorities.
  2. Then precise, in response to this inspection report, a short date of implementation of this contract template with all distributors for 2016.

- Response noted, considering the commitments by 30<sup>th</sup> June 2016, to :
  - Roll out the new distribution template agreement and sign up the distributors, or generate and circulate an interim letter to the distributors, to ensure that they are aware of their obligations regarding vigilance activities and to precise who is responsible for reporting any serious incident or risk of serious incident to the competent authority ;
  - Require the distributors to sign and return the aforementioned letter or the new distribution template to NAGOR as evidence of their understanding regarding their obligations.

It is reminded that the new distribution template or letter intended to the distributors shall require immediate notification, to the manufacturer, of any complaint and/or MV case related to the concerned medical devices.

## **Audits**

R8 NAGOR Ltd should improve its audit management by taking the necessary provisions to assure systematically the independence of the auditors regarding the audited activities (claimed ISO 13485 standard point 8.2.2).

- Acceptable response, considering the commitments to verify, by 29<sup>th</sup> April 2016, the internal audit schedule to ensure the independence of the auditors regarding the audited activities.

## **Complaints and materiovigilance (MV) management**

D4 The management of the individual complaints and MV cases by NAGOR Ltd is not completely satisfactory, which compromises the proper processing and notification of the serious incidents or risks of serious incidents to the concerned competent authorities (MDD Annex II item 3.1, claimed ISO 13485 standard items 7.2.3, 8.4 a) and 8.5), insofar :

1. NAGOR Ltd does not have systematically the traceability of the batch records (DHR) reviews and of the results obtained, while processing MV cases (*Annex 2 point 1 of the preliminary inspection report*) ;
2. An incident report communicated to ANSM and related to a case of *BI rupture and capsular contracture* only mentions "*deflation*" and is therefore incomplete (*Annex 2 point 2 of the preliminary inspection report*) ;
3. The date of MV case initial notification, as mentioned in NAGOR registration form, does not systematically correspond to the real date of initial notification attested by the source document (*Annex 2 point 3 of the preliminary inspection report*) ;
4. NAGOR Ltd does not keep under control all its distributors, considering that :
  - One of them had knowledge of an ALCL case but did not communicate it to NAGOR Ltd (*Annex 2 point 4 of the preliminary inspection report*) ;
  - This case was reported late to the concerned competent authority.

- Regarding point 1 : Acceptable response, considering the commitments to document, from 26<sup>th</sup> February 2016, the review of the manufacturing records and their conclusion in the section of the *QR016* related to the complaint history comments.

- Regarding point 2 : The initial incident report communicated to ANSM and checked during this inspection, regarding the case , only stated "*deflation*" and did not mention *rupture and capsular contracture*. The response provided by NAGOR is limited to mention "*Final report communicated to ANSM details capsular contracture and rupture. No actions required*" and is therefore **uncomplete**, considering the absence of commitments to check, from now on, the completeness of each incident report to be communicated to ANSM.

- Regarding point 3 : Acceptable response, considering the commitments to generate, by 31<sup>st</sup> March 2016, a work instruction which will reference that the date of notification is to be from the date that the complaint was received (not from when NAGOR became aware of the complaint).

- Regarding point 4 : Response noted, considering the commitments by 30<sup>th</sup> June 2016, to :
  - Roll out the new distribution template agreement and sign up the distributors, or generate and circulate an interim letter to the distributors, to ensure that they are aware of their obligations regarding vigilance activities and to precise who is responsible for reporting any serious incident or risk of serious incident to the competent authority ;
  - Require the distributors to sign and return the aforementioned letter or the new distribution template to NAGOR as evidence of their understanding regarding their obligations.

It is reminded that the new distribution template or letter intended to the distributors shall require immediate notification, to the manufacturer, of any complaint and/or MV case related to the concerned medical devices.

### **Corrective and preventive actions (CAPAs/FSCAs) management**

D5 The management of the CAPAs/FSCAs by NAGOR Ltd is not completely satisfactory, which compromises the proper processing and notification of the serious incidents or risks of serious incidents to the concerned competent authorities (MDD Annex II item 3.1, claimed ISO 13485 standard items 7.2.3, 8.4 a) and 8.5), insofar NAGOR Ltd does not have the traceability of any confirmation response from a Belgian distributor, to the reminder letter sent by NAGOR Ltd and reminding the distributor duties regarding the communication of MV cases to NAGOR Ltd (*Annex 2 point 5 of the preliminary inspection report*).

→ Satisfactory response, considering the response from the Belgian distributor received by NAGOR on 13<sup>th</sup> December 2015, associated to the distributor's standard operating procedure regarding vigilance.

### **Systematic review of experience gained from devices in the post-production phase (PMS)**

R9 NAGOR Ltd should complete its BIs post-market survey, so that the PMS reports present some written assessments and conclusions comparing the smooth BIs versus the textured BIs, regarding :

1. The incident trends broken down by typologies of incidents, particularly capsular contractures ;
2. The key points, issues and stakes stemming from the data related to ALCL cases ;
3. The global BIs Benefit/Risk ratio including the impact of the surface.

→ Acceptable response, considering the commitments to incorporate, by 30<sup>th</sup> June 2016, the information mentioned in R9 in the next cycle of the management review.

### **Archiving**

R10 NAGOR Ltd should secure the archiving of all the complaints and MV documents in paper format by retaining these documents in premises protected against fire hazards (claimed ISO 13485 standard points 4.2.4, 8.5.1).

→ Acceptable response, considering the commitments to secure, by 29<sup>th</sup> April 2016, the complaints and MV documents against fire risks.

## **FINAL CONCLUSION**

The inspection carried out from 8<sup>th</sup> to 9<sup>th</sup> December 2015 at NAGOR Ltd site located 127/129 Deerdykes View, Westfield Industrial Estate, Cumbernauld, Scotland, allowed to collect the information related to the organization and to the activity of this company regarding materiovigilance.

As a result of this mission, acceptable or noted responses were provided to the findings reported in the preliminary inspection report, except the following points :

- NAGOR Ltd should complete its procedure(s) regarding the management of its documentation system, so that they clearly mention 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 medical devices technical documentation and EC declarations of conformity (R1), which shall be at least :
  - 15 years after the last product has been manufactured, in the case of implantable devices ;
  - 5 years after the last product has been manufactured, for the other devices.
- NAGOR shall check, from now on, the completeness of each incident report to be communicated to ANSM (D4 point 2).

Further corrective and preventive actions should be taken as soon as possible regarding the aforementioned items.

Saint-Denis, 19<sup>th</sup> February 2016.

**ANSM Inspector**

