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European Medicines Agency

Provisional mandate, objectives and rules of procedure for the Nitrosamines Safety Operational Experts Group (NS OEG)

These mandate, objectives and rules of procedures will be incorporated in and adapted as required to the general rules of procedures governing all Working Parties, Operational Expert Groups and Drafting Groups.

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1. General considerations

The Nitrosamines Safety Operational Experts Group (NS OEG) is replacing the former NS SWP expert group which had been established by the European Medicines Agency (EMA) in order to support the operational work of the Safety Working Party (SWP) related to the risk assessment of nitrosamines. Due to the continuous and numerous requests to the Non-clinical working party (NcWP) on nitrosamines issues related to impurities and the lack of a sufficient number of experts in this field within the same group, a dedicated operational expert group (NS OEG) composed of experts from the network and the NcWP has been created. This NS OEG will include experts with specific expertise in the field of risk assessment of mutagenic impurities and QSAR predictive toxicology.

The NS OEG will also contribute to a harmonised EU approach for assessment of the nitrosamines acceptable intakes (AI) and will interact with international regulators to seek international harmonisation and facilitate regulatory convergence.

2. Mandate and objectives

Mandate

The NS OEG is mandated by EMA and its scientific committees to determine acceptable intake (AI) of nitrosamine impurities newly detected in pharmaceutical products for human use.

The NS OEG will communicate the EU position at international fora e.g., NITWG, and facilitate cross regional convergence in close collaboration with international partners.

The NS OEG will report to the Non-clinical Domain Governance and inform the EMA committees and working parties as needed.

For the performance of its duties, the NS OEG will liaise with the NcWP.

The NS OEG will be dismantled when requests on new nitrosamines cease and work on the ICH M7 (guideline to calculation of compound-specific acceptable intakes) addendum is completed.

Objectives

The main tasks of the NS OEG comprise:

1. Perform the risk assessment of new nitrosamines and define an AI when requested by Committees (e.g., CMDh or CHMP).
2. Give input on AI assessed by international regulators, e.g., FDA, Health Canada and Swiss Medic.
3. Upon request by the Non-clinical Domain Governance, provide recommendations on matters relating directly or indirectly to the safety of nitrosamine-containing medicinal products.
4. Engage with relevant groups, including EMA offices and the Nitrosamines Quality OEG (NQ OEG) to ensure harmonisation across the EU and to optimise resources.
5. Set up communication platforms with Industry and hold Industry interested parties' meetings once or twice a year, as relevant.
6. Contribute to the development of approaches and guidelines for the risk assessment of nitrosamines in partnership with international regulators.
7. Develop training for the risk assessment of nitrosamines as part of the NTC non-clinical curriculum.

3. Composition and rules of participation

Core membership:

The NS OEG is composed of experts selected from the European experts' database according to their specific expertise, most of them belonging to the former SWP nitrosamines Expert group. A lead is nominated by the Non-clinical Working Party (NcWP) to manage the work of the group.

The group may be enlarged or reduced at a later stage if required, depending on workload considerations. A review of the composition will take place after the first year of operation. Membership will be reviewed on a regular basis, based on activity level and evolving needs.

Members are expected to support the activities which are described in the non-clinical domain work plan in relation to the safety assessment of nitrosamines.

Membership implies a commitment to participate actively in the work of the group, regularly attend the entire meetings of the OEG and take part in correspondence between meetings.

NS OEG members are expected to provide scientific leadership across the EU Network on relevant topics including training.

Criteria to be considered for OEG Core membership:

- Background/knowledge/training in toxicology, metabolism or chemistry
- Proven experience of performing the risk assessment of impurities in medicinal products
- Solution-oriented and self-motivated

4. Meeting frequency

Virtual plenary meetings

- Virtual meetings will be organised on a monthly basis. Ad hoc meetings can be organised if required.
- Meeting duration will be determined based on the topics in the agenda.
- One face-to-face meeting per year is foreseen.

Meetings with international regulators

- Where appropriate, it is aimed to have meetings with key regulators from other regions to try to achieve cross-regional convergence. For this aim selected experts of the OEG could take part in the meetings representing the expert view of the OEG.

Reimbursement:

- NS OEG members will be reimbursed in accordance with EMA reimbursement rules.

5. Rules of procedure

5.1. Responsibilities of the Lead

The NS OEG lead is responsible for the efficient conduct of the business of the OEG and shall in particular:

- Plan the work of the OEG together with the EMA Secretariat and the NcWP lead.
- Monitor, together with the EMA Secretariat, that the rules of procedure are respected.

- Ensure that, at the beginning of each meeting, any potential conflict of interest is declared regarding any item to be discussed by the OEG.
- Aim to achieve consensus on issues discussed by the OEG.
- Ensure, together with the OEG, the EMA Secretariat and the NcWP lead, regulatory and scientific consistency of the OEG's recommendations.
- Co-ordinate, together with the EMA Secretariat, the work of the OEG that is relevant to other working parties (i.e., QWP) of the Agency.
- Report on the activities of the OEG to the CHMP, CMDh or other working parties as appropriate.

5.2. Organisation of meetings and reporting arrangements

- The members of the NS OEG agree on the dates of the regular meetings on an annual basis. Some ad-hoc meetings may be organised if required.
- The draft agenda for every meeting shall be circulated, together with the related documents, by the EMA Secretariat, in consultation with the Lead.
- When a member of the OEG is unable to participate in a meeting, part of a meeting, or discussion topic due to a conflict of interest, he/she must inform the Secretariat in advance in writing.
- A position from the NS OEG shall be transmitted to the NcWP for endorsement which can also be done in a written procedure. After NcWP endorsement the position will be forwarded to CHMP for adoption.
- Discussion at the NcWP may happen if there is a critical issue that needs to be addressed by the whole working party.
- Agendas and minutes of the meetings of the NS OEG shall be circulated to the NcWP for written information and an update may be provided at their plenaries.
- A report shall be prepared on an annual basis summarising the work of the NS OEG in the context of the 3-year non-clinical domain work plan.

5.3. Guarantees of independence

The specific provisions for handling Declarations of Interests and confidentiality undertakings as defined in the European Medicines Agency policy on the handling of competing interests of scientific committees' members and experts (EMA/MB/89351/2020) are applicable to members of the NS OEG and ad-hoc experts participating in NS OEG activities.

The members of the NS OEG and ad-hoc experts shall not have any direct interests in the pharmaceutical industry that could affect their impartiality. They shall undertake to act in the public interest and in an independent manner and shall make an annual declaration of interests. The Declarations of Interests of the NS OEG members shall be made available to the public through the Agency's website.

Members of the NS OEG shall declare at the beginning of each meeting any specific interests that could be considered prejudicial to their independence with respect to the points of the agenda.

5.4. Code of conduct

Members of the NS OEG and experts participating in the EMA's activities shall abide by the principles set out in the European Medicines Agency Code of Conduct (EMA/385894/2012).

6. Agency secretariat

Under the authority of the Executive Director, the EMA Secretariat shall provide technical, scientific and administrative support to the NS OEG. This includes the following:

- Provide technical and scientific support to rapporteurs and other members of the NS OEG;
- Provide legal, regulatory and scientific support to the NS OEG;
- Prepare and co-ordinate the work of the NS OEG in consultation with the Lead;
- Ensure, if appropriate, that the timelines laid down by EU legislation for the adoption of the opinions are complied with;
- Organise meetings of the NS OEG ensuring, together with the respective rapporteurs, the timely availability of meeting documents;
- Facilitate the necessary contacts between the NS OEG, relevant working parties, committees and other EU and non-EU groups;
- Ensure adequate co-ordination of the work carried out within the NS OEG, the EMA scientific committees and other concerned working parties and/or groups;
- Contribute to the overall quality assurance and assurance of scientific and regulatory consistency of the documents/recommendations of the NS OEG in cooperation with the Lead, as appropriate;
- Support the preparation of relevant meeting records where needed (e.g. agendas, minutes);
- Contribute to the identification of experts.

7. Coordination group and consistency group

Not applicable.

8. Relationship with other WPs, committees and groups

As indicated above, in order to ensure harmonisation across EU and to optimise resources, the NS OEG will develop formal links to relevant scientific committees, working parties and expert groups.

In addition, it is foreseen that the NS OEG develops and implements an agile and proactive communication pathway between industry and regulators, establishing formal links with:

- International regulators active in this area (e.g., FDA, Health Canada and Swiss Medic) with regular meetings and exchange of information;
- Industry interested parties, as identified by the NS OEG.

9. General provisions

The members of the NS OEG shall be bound, even after the cessation of their duties, not to disclose any information, which, by its nature, must be covered by individual professional secrecy. When

participating in international or other fora on behalf of the EMA/CHMP, members shall ensure that the views expressed are those of the EMA/CHMP.

When participating in international or other fora not specifically on behalf of the EMA/CHMP, members shall make clear that the views expressed are their own views and not those of the EMA/CHMP.