EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Nitrosamine Implementation Oversight Group (NIOG)

Workplan and topics for QWP & SWP IP Meetings

NIOG - Industry Associations Meeting

31st March 2021

Workplan

- NIOG will discuss topics **raised by relevant stakeholders** :
  - *Pharmaceutical industry associations*
  - *CMDh, Committees, working parties*
  - *International regulatory partners (via International Groups: Nitrosamine International Strategic Group - NISG, Nitrosamine International Technical Working Group - NITWG)*
- Topics prioritised taking into account, as appropriate, stakeholder feedback
- Includes topics for interaction with industry at working party IP meetings

Quality Topics

Topic	Description	Priority	Party for follow-up
1. New science around nitrosamine formation	***New scientific evidence around nitrosamine formation, risk factors and root causes including risks associated with biologics***	***High***	***QWP for discussion at QWP IP meeting***
2. Investigations and root causes	***New root causes and investigation findings*** • ***Update on Metformin root cause investigations***	***High***	***QWP for discussion at QWP IP meeting***
3. Purge studies and calculations	***The use of tools from ICH M7 to discharge risk, for example, purge studies and calculations***	***High***	***QWP for discussion at QWP IP meeting***
4. Analytical methods	***Technical aspects of analytical methods***	***Medium***	***QWP for discussion at QWP IP meeting***
5. Support for OMCL Market Surveillance	*Scientific input to OMCL market surveillance testing plan for nitrosamines as recommended by LLE*	*Medium*	*NIOG*
6. Risk for medical devices	*Risk factors for medical devices with short term drug contact which are not covered in the Q&A*	*Low*	*QWP*

Multi-disciplinary Topics

Topic	Description	Priority	Party for follow-up
1. ICH M7 revision	***Scope and timing of ICH M7 revision***	***High***	***QWP & SWP for discussion at SWP & QWP IP meetings***
2. Products with multiple nitrosamines	***Management of products with multiple nitrosamines – cumulative control options***	***High***	***QWP & SWP for discussion at QWP IP meetings***
3. Nitrosamines in products used in clinical drug-drug interaction trials	Guidance for use of investigational medicinal products contaminated with nitrosamines in clinical drug-drug interaction trials	High	CHMP
4. Sartans Lessons Learnt Exercise outcome	Monitoring progress on drafting/updating of scientific guidance as recommended by Sartans Lessons Learnt Exercise report	Medium	QWP, SWP, GMDP IWG

QWP IP Preparation – Proposed Timelines

- 9th April: Draft agenda to industry associations
- 23rd April: Industry feedback on draft agenda
- 30th April: final agenda
- 7th May: List of industry topic leads and participants
- 7th May: List of EU network participants
- 10th May: Industry draft presentations due
- 26th May: QWP IP meeting

Safety Topics

Topic	Description	Priority	Party for follow-up
1. Structure-Activity Relationships (SAR)	***Use of Structure-Activity Relationships (SAR) to establish AIs for data-poor nitrosamines, including "complex" nitrosamines - refinement of QSAR tools.***	***High***	***SWP for discussion at SWP IP meeting***
2. In vitro assays	***Use of in vitro assays for confirmation of non-mutagenicity for impurities and mutagenicity testing methodology.***	***High***	***SWP for discussion at SWP IP meeting***
3. Mutagenic / clastogenic APIs	***Policy for control options in mutagenic/clastogenic APIs***	***Medium***	***SWP for discussion at SWP IP meeting***
4. Harmonisation of AI limits	How to deal with potential dis-harmonisation on AI limits for known and newly identified nitrosamines between international regulatory authorities	High	SWP

SWP IP Preparation – Proposed Timelines

- 16th April: Draft agenda to industry associations
- 23rd April: Industry feedback on draft agenda
- 30th April: final agenda
- 7th May: List of industry topic leads and participants
- 7th May: List of EU network participants
- 10th May: Industry draft presentations due
- 25th May: SWP IP meeting

Procedural Topics

Topic	Description	Priority	Party for Follow-up
1. Managing interaction with industry	Interaction between NIOG and Working Parties with industry stakeholders	High	NIOG
2. Risk assessment for line extensions and variations	Harmonisation of EU approach to risk assessments for line extensions and variations	Medium	EMA, CMDh
3. Reporting formats	Facilitate submission of step 1/2/3 responses	Medium	EMA, CMDh

For details on how European authorities will manage the call for review please consult: European Medicines Regulatory Network approach for the implementation of the CHMP Opinion pursuant to Article 5(3) of Regulation (EC) No 726/2004 for nitrosamine impurities in human medicines

Any questions?

Further information

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