

Precious Metals and Rhenium Consortium Silver Work Group & Nano Task Force – Joint meeting

Brussels, 4 Sep 2013, 10:30 am-16:30 pm



[1]

Agenda (1)

I. General

1. Welcome and introduction
2. To Do List: Last comments from Ag WG before finalization and use towards Dossier update submission
3. Feed-back from RAS Materials on data-sharing request

II.A Technical items – Effects assessment

Environment

4. Freshwater
5. Marine water
6. Microorganisms
7. Soil
8. Recap of status of PNECs
9. Read-across approach for environmental endpoints

Human Health

10. Mammalian toxicity
11. Read-across approach for human health endpoints

Lunch!

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Agenda (2)

II.B Technical items – Exposure assessment

12. Feed-back from PMC Members on new uses to be registered (if any)
13. Environmental exposure assessment
14. Occupational exposure assessment
15. Waste exposure assessment
16. Prioritisation of technical items according to Dossier update needs and PMC Secretariat resources

III. Administrative items

17. Status of characterization data generation: tour de table
18. Preparation of meeting with RIVM
19. Discussion and agreement on recommended approach towards reviewing the Ag Dossier update
20. PMC response to EU public consultation relating to REACH annexes and nanomaterials: discussion and approval of version for submission by 13 Sep 2013
21. Typical profiles of Ag and Ag compounds: feed-back from Ag WG for inclusion in IUCLID 5 files

[3]

Agenda (3)

IV. General

22. Transport classifications for Ag and Ag compounds in scope
23. AOB, next meetings and closing remarks

[4]

I. General

[5]



1. Welcome and introduction

Caroline Braibant

[6]

Welcome and introduction

- Confidentiality and Competition Law
- Tour de table & Apologies, including presentation of R. Nicolay, new Manager in PMC
- Approval of the agenda
- Status of actions agreed at and approval of minutes of the last conference calls (17 & 18 July 2013)

[7]

Actions 17 July 2013 Ag WG CC

What?	Status
1. Distinguish Agenda items related to the Evaluation preparation from those inherent to the maintenance of the Ag project dossiers	
2. Draft discussion document suggesting outline of testing protocol for 'repeat' oyster test Organise a conference call to discuss and agree on oyster study testing outline	
3. Check whether activated sludge test results will be available before the Ag WG Oct 2013 meeting so it can be reported then	
4. Obtain data from CSIRO as it becomes available, obtain data from NanoFate, and develop a soil SSD for silver	Today
5. Provide list of studies on NM 300 that should be requested for assessment to + questions for RAS Materials (NIA Member)	
6. Develop proposal on additional soil research with CSIRO and circulate to Ag WG for discussion Understand what data is available to CSIRO and under what 'temporary' conditions this data could be shared	
7. Update the marine SSD proposal including all costs (including WCA's time) and tests on ionic Ag to be discussed/pre-approved by the Ag WG Prepare Ag WG recommendation for approval by Mgmt Cttee	
8. Elaborate the BLM proposal including all steps/phases and costs, timeline, etc. to be discussed/pre-approved by the Ag WG Prepare Ag WG recommendation for approval by Mgmt Cttee (using Ag project reserve monies) Identify potential co-sponsors for the (pre-)BLM work	On-going
9. Clarify whether ES with revised SpERCs covers nanoAg and generate updated ENV ES for Ag metal	
10. Review EBRC ES Strategy document and respond to questions outlined in a dedicated e-mail from PMC Secretariat	5/33 responses received
11. Respond to mini-survey from PMC Secretariat	22/33 responses received
12. Prepare proposal for dustiness tests to be discussed/pre-approved by the Ag WG Prepare Ag WG recommendation for approval by Mgmt Cttee	Today
13. Circulate final draft waste ES prepared by ARCHE to Ag WG for comment/review at 4 Sep mtg	
14. Inform PMC Secretariat on any new use of (nano)Ag or Ag compounds that should be assessed and reported to ECHA in a Dossier update	5/33 responses received
15. Assess UBA references and report findings/relevance to Ag WG at 4 Sep meeting	
16. Circulate final invitations and draft agendas for next Ag WG meetings	

[8]

Actions 18 July 2013 Ag WG CC

What?	Status
1. Revert to RIVM requesting specific Agenda items	
2. a) Propose key messages/positions and relevant background documents for circulation to RIVM b) Approve key messages/positions and relevant background documents for circulation to RIVM proposed by PMC representatives participating in 20 Sep meeting with RIVM	Today
3. Update Ag WG on outcome of 20 Sep meeting with RIVM	
4. a) Include clear dossier scope in all PMC dossiers, starting with Ag metal Dossier, based on COM recommendation or one or more of the following approaches: b) Add this task to Ag Substance Evaluation To Do List c) Send extract of Cu Dossiers' CSR illustrating approach to describing the scope of a risk assessment/Dossier	On-going
5. a) Update To Do List integrating all suggestions made and re-circulate to Ag WG for comment b) Provide comments on Updated To Do List to PMC Secretariat c) Prepare final draft To Do List and circulate to Ag WG for approval at 4 Sep 2013 meeting d) Circulate updated versions of the To Do List with description of changes made to Ag WG + upload onto Ag database	Today
6. a) Elaborate a formal proposal for the Ag Dossier review including all options discussed at the 18 Jul cc and circulate to Ag WG b) Discuss and decide on best way forward for review c) Contact recommended reviewers and launch Ag Dossier review logistics d) Report on outcome of Ag Dossier review and agree on final adjustments to the Dossier	Today/On-going
7. a) Add requested items to report before circulation to Silver Institute: b) Confirm agreement to share the WCA report with the Silver Institute c) Circulate updated report to Silver Institute	WCA to make adjustments and send to Silver Institutes
8. a) Generate and include characterisation information in individual Ag metal registration dossiers, and monitor REACH-IT mailbox for ECHA requests for more information on substance identity b) Forward characterisation information to PMC Secretariat c) Aggregate characterisation information and include in joint dossier sections on physico-chemical properties	5/33 responses received On-going
9. Report impure form of AgCl (only used as an intermediate < 10 t/a) in sections 1.2 and 2 of AgCl joint dossier (no need to be included in the AgCl hazard assessment) Look again at the sizes and purities of Ag and Ag compounds that are manufactured and imported and inform PMC Secretariat accordingly so the typical profiles can be included in the relevant dossiers	5/33 responses received On-going
10. a) PMC should support the request for Eurométaux to launch a project on standard phrases for ES of inorganic substances, as part of the review of Chesar (due in ~ 1 year), or as a separate <i>ad hoc</i> project b) Decide on languages in which Ag short ES should be translated at PMC level c) Organise translation of the short ES once these are available, in the number of languages decided by the Ag WG at its next meeting	Today
11. Derive transport classification for all PMC substances and add to PMC inventories	Today
12. Prepare response to public consultation on REACH annexes and circulate to Ag WG for discussion/approval at 4 Sep 2013 Ag WG meeting	Today

[9]



2. To Do List: Last comments from Ag WG before finalization and use towards Dossier update submission

Caroline Braibant

[10]

To Do List

- No comments received on To Do List circulated on 22 July 2013
- Any comment today?
- Next :
 - From now till Dossier update finalisation:
 - Use as progress tracker
 - Before Dossier update submission and after:
 - Use as check-list

[11]



3. Feedback from RAS Materials on data-sharing request

Caroline Braibant

[12]

Status of exchanges with RAS Materials/NIA

Since...

... Reminder sent on 29/08/2013

02/08/2013

- RAS Materials announces not immediately interested in PMC membership + PMC responds data still needed

01/08/2013

- RAS Materials announces possible interest in joining PMC under specific conditions to compensate for data shared + PMC responds

22/07/2013

- List of potentially relevant references sent to RAS Materials + request to agree on data-sharing mechanism

25/04/2013

- List of available studies received from RAS Materials and sent to EBRC and WCA to identify potential useful references

19/04/2013

- Conference call PMC Secretariat-RAS Materials to clarify context/purpose

12/03/2013

- Mail from RAS Materials proposing to share information generated under OECD WPMN

[13]

II.A Technical items – Effects assessment

[14]

Environment

[15]

Regular literature searches

- Reviews of recently published literature conducted every six months (September and March)
 - All dossier information requirements, including PNECs
- List of relevant studies circulated to Ag WG and obtained for reliability assessment
- Reliable studies added to IUCLID dossier and implications for PNEC assessed
- September 2012 review
 - Studies currently being added to IUCLID
- March 2013 review
 - Underway
 - Literature screened for potentially relevant studies
 - Reliability assessment underway – Complete September 2013
- Suggest March review is cut-off for dossier update

[16]



4. Fresh water

[17]

4.1. Status of PNEC_{freshwater}

- Reviews of recently published literature implications for PNEC_{freshwater} assessed
- September 2012 review: No implications for PNEC_{freshwater}
- PNEC_{freshwater} : 40 ng/l (unchanged)

[18]

4.2. Further research on silver speciation and BLM (1)

- Zn, Ni, Mn, Cu (Pb) have developed relationships between water physico-chemistry (e.g pH, DOC, Ca) and chronic ecotoxicity - BLMs
 - Bioavailable EQS for Ni and Pb recently adopted under WFD
 - Zn and Cu relationships used under REACH and ESR
- No comparable relationship currently available for silver
- Proposal to improve the understanding of the speciation behaviour of silver has been further developed since previous working group meeting
 - Precursor to BLM development
 - Would determine how well WHAM software predicts Ag complexation with variable DOM-sulphide and free sulphide concentrations

[19]

4.2. Further research on silver speciation and BLM (2)

- Experimental design would be undertaken by:
 - Scott Smith (Wilfrid Laurier University, Canada)
 - Steve Lofts (Centre for Ecology, UK) – WHAM software developer
 - Adam Peters (wca environment, UK)
- Practical phase would be completed in laboratory of Scott Smith (MSc student) to reduce costs
- Estimated costs over two years are £58k
- Potential to split these costs
 - Unilever (who have worked with wca environment on silver recently and have similar research needs)
 - Matched grant funding (1:1 in kind) from the Government of Canada (proposal under development)
- Exact scope of potential collaboration under discussion

[20]



5. Marine water

[21]

5.1. Oyster Embryo testing

- Proposed to confirm/refute the findings of Ringwood et al. 2010
 - Study reported very sensitive NOEC for nanosilver – K3
- Ag WG Expert conference call 21 Aug 2013 to refine scope of testing
 - Two forms of nanosilver (NM300K and citrate coated)
 - 25 g/L salinity
 - Silica particle control
 - 25 g/L salinity
 - AgNO₃ tests
 - 25 and 35 g/L salinity
 - Single exposure regime (settled) to mimic Ringwood *et al.* 2010
- Clarification of required GLP status of testing received from ECHA
 - GLP not required for supplementary testing
- Revised proposals requested from BEL and Nautilus
 - BEL: £50,000.00
 - Nautilus/Nanocomposix: £20,364.00
- References from Nautilus/Nanocomposix obtained
- No comments received following circulation of minutes of 21 Aug cc
 - greenlight to proceed assumed

[22]

5.2. PNEC_{marine}: RIVM ERL position paper

- In 2012 RIVM published ERL (Environmental risk limits) for silver for use under the WFD
 - Both limits are significantly more sensitive than PNECs in REACH dossier
 - Feedback to RIVM on the derivation of their ERL for silver in freshwater from PMRC dismissed
- Potential that PNEC_{marine} could be challenged during evaluation

Salinity	RIVM ERL (ng/L)	PMRC PNEC (ng/L)
0	10	40
<15	10	860
20	12.7	
25	28.5	
30	53.9	
34	80.6	
35	90.9	

- Review completed; summary note in preparation
 - Will be circulated for discussion/approval at next Ag WG meeting (Oct 2013)

[23]

5.3. Marine SSD

- Existing PNEC_{marine} is based on a deterministic approach
 - Based on most sensitive reliable data
 - Require relatively large Assessment Factors (AF)
 - Vulnerable to new data – PNEC can only go down
- SSD based PNEC attract lower AF (1-5) and are less vulnerable to new data as whole dataset is used during derivation
- Costs and scope finalised
 - **€57,200 + VAT** (€46,410 for BEL and €10,790 for Smithers Viscient).
 - **£4,400 + VAT** for study monitoring
- Circulated to Ag WG by mail, no comments received, tacit consent assumed
- Next: forward to Mgmt Cttee in Sep for approval prior to Assembly meeting in Dec

[24]



6. Microorganisms

[25]

6.1. Status of PNEC_{microorganisms}

- PNEC_{microorganisms} is intended to protect the degradation functions and process performance and efficiency of domestic and industrial sewage treatment plants (STP)
- Nitrifying bacteria are considered to be the most sensitive component of the microbial fauna found in STP
- AF of 1 is applied to NOECs from these types of tests
 - AF for other microbial tests range from 10 – 100
- Two studies report effects on nitrification by ionic silver Resulting in NOECs of 0.025 and 0.05 mg l⁻¹, respectively
- **PNEC_{microorganisms} = 0.025 mg l⁻¹/ AF (1) = 0.025 mg l⁻¹ dissolved silver**
- Available data on the relative toxicity of nanosilver and ionic silver to STP is equivocal
- Confirmatory GLP testing commissioned at Laus (OECD 209)

[26]

6.2 Activated sludge testing: status of testing

- Range-finding testing completed
 - Silver Nitrate
 - 100 mg/L, 100% Inhibition
 - 10 mg/L, 97 % Inhibition
 - 1 mg/L, 0 % Inhibition
 - 0.1 mg/L, 0% Inhibition
 - Nano Silver NM-300K
 - 1000 mg/L, 100% Inhibition
 - 500 mg/L, 100% Inhibition
 - 100 mg/L, <100 % Inhibition (statistically significant)
 - 10 mg/L, 0 % Inhibition
 - 1 mg/L, 0 % Inhibition
 - 0.1 mg/L, 0% Inhibition
- Nanosilver not completely aggregated or absorbed on bacteria
- Protocol for definitive testing (with characterisation) received from Laus for approval (26th August 2013)
- Results of definitive testing anticipated by next Ag WG

[27]



7. Soil

[28]

Status of ECHA's decision on PMC's Soil Testing Proposal



- Soil Testing Proposal officially approved by ECHA (30 July 2013)
- Unanimous decision by MSC
- Proposed scope fully accepted (no changes)
- Deadline: 30 April 2014

[29]

7.1. Soil testing at CSIRO (Testing Proposal): status of testing

- Status
 - Programme proceeding as planned
 - Interim report May 2013 (circulated 27 May 2013)
 - Most toxicity tests and leaching work completed
 - Ageing work ongoing
- Next steps
 - Final report Nov. 2013 (timing re-confirmed in June)
 - Will include results for IUCLID/PNEC_{soil} revision as soon as available (Mid September)
- CSIRO not GLP accredited, but not considered that this will affect the acceptance of the data by ECHA

[30]

7.2. Status of PNEC_{soil}

- In the absence of data current PNEC_{soil} is based on equilibrium partitioning
- **PNEC_{soil_eqp} = 0.794 mg silver kg⁻¹ wet weight**
- The derivation of a definitive PNEC_{soil} is pending the results of CSIRO study and additional ecotoxicity data from EU nanofate project

[31]

7.3. SSD proposal from WCA

- Suggest to use SSD approach
 - Identical rationale to marine SSD discussed previously
 - CSIRO data
 - Nanofate data received for springtails & woodlice (reported in sufficient detail for a K1/K2 quality assessment)
 - EC/LC50 data for additional earthworm species received. Raw data requested
- Bioavailability correction is proposed to be based on soil conditions used in EU RAR for other metals
- Estimated timing for revised PNEC_{soil}: End of September 2013

[32]

7.4. Data-sharing and further research with CSIRO

- CSIRO have agreed to share their proprietary (nano)Ag fate and behaviour data at no cost, assuming that PMC will continue working with CSIRO to tackle knowledge gaps on fate and behaviour of (nano)Ag in due course
- Proposal for additional research received on 21 Aug 2013
- Will be circulated in time for discussion at next Ag WG meeting (Oct)

[33]



8. Recap of Ag PNECs

[34]

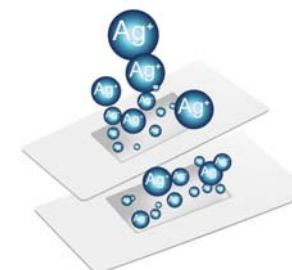
Silver PNECs

Environmental Compartment	Target Organism	PNEC	Value	Basis
Freshwater	Aquatic organisms	$PNEC_{\text{freshwater}}$	$0.040 \mu\text{g l}^{-1}$ dissolved silver	SSD with an AF of 3
Saltwater	Aquatic organisms	$PNEC_{\text{saltwater}}$	$0.86 \mu\text{g l}^{-1}$ dissolved silver	Most sensitive NOEC with an AF of 10
Sediment ¹	Benthic organisms	$PNEC_{\text{sed}}$	1.2 mg kg^{-1} (dry weight)	Most sensitive NOEC with an AF of 10
Sediment ¹	Benthic organisms	$PNEC_{\text{marine sediment}}$	1.2 mg kg^{-1} (dry weight)	Most sensitive NOEC with an AF of 10
Agricultural Soil	Terrestrial organisms	$PNEC_{\text{soil}}$	0.794 mg kg^{-1} (wet weight)	Equilibrium partitioning approach using $PNEC_{\text{freshwater}}$
Sewage Treatment Plant	Microorganisms	$PNEC_{\text{microorganisms}}$	0.025 mg l^{-1} dissolved silver	Most sensitive NOEC with an AF of 1

[35]

1: For the purposes of Tier 3 assessment under REACH both the $PNEC_{\text{sed}}$ and the $PNEC_{\text{marine sediment}}$ are normalised to the EUSES default sediment organic carbon content of 5%. $PNEC_{\text{sed, OC5\%}} = 438.13 \text{ mg kg}^{-1}$ (dry weight)
AF: Assessment Factor

9. Read-across approach for environmental endpoints



[36]

9.1. Status of documentation according to ECHA's latest Guidance

- Environmental read-across approach assumes toxicity is driven solely by Ag ion, with little to no influence of size, surface area, coating, etc.
- Latest ECHA guidance will be reviewed to ensure that read-across strategy adopted is documented sufficiently and according to ECHA's recommended format in Ag Dossier
 - WCA and EBRC liaising on best approach to report read-across in various sections of dossier + in dedicated document

[37]

9.2. Status of presentation to ECHA's NMWG

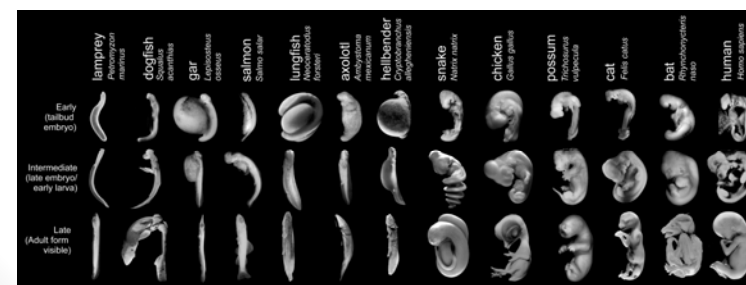
- ECHA NanoMaterials Working Group's mandate is to discuss scientific and technical questions relevant to REACH and CLP processes dealing with nanomaterials and provide recommendations on strategic issues
- Three sub-groups have been formed, in order to address the following topics in more detail:
 - Characterisation
 - Read-across
 - Organic nanomaterials
- Zn association active in NMWG and Read-across subgroup on behalf of NFM sector
- Zn has presented read-across approach from Zn ion to ZnO and others and has been requested to collect other metal case-studies where read-across from metallic ion applies
- PMC has opportunity to present Ag read across approach at 1-2 Oct 2013 NMWG meeting
 - EBRC and WCA are preparing slides on the topic
 - Slides will be circulated to Ag WG, Zn, EM and ECHA NMWG Subgroup on Read-across by 20 Sep 2013

[38]

Human health

[39]

10. Mammalian toxicity



[40]

Overview of *previous* HH database and assessment in REACH silver dossiers (for background information)

- substance specific data/read-across for acute toxicity endpoints, irritation/corrosivity and phys-chem. hazards
- generic “grouping” assessment based on Ag (ion) for sensitisation and genetic toxicity (both endpoints “negative”) – two read-across categories formed (i) soluble and (ii) poorly soluble
- very limited data was available for repeated dose, repro/developmental toxicity and carcinogenicity
 - in 2010, only a dev-tox study by NTP with silver acetate was available
 - there were formal data-gaps for repeated dose toxicity, fertility and carcinogenicity
 - initially, in 2010, a testing proposal for a 90-day oral study was submitted
 - later withdrawn following discussion with ECHA and awareness of on-going NTP study (dossier update 2012)
 - also, 90-day oral studies with nanoAg became available (published)

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Current DNELs - inhalation

- Workers, inhalation
- (i) poorly soluble Ag substances
 - metallic silver: 0.1 mg/m³
 - basis: SCOEL OEL, 1993, based on argyria (limited epidemiological data)
 - re-calculated to other poorly soluble Ag compounds (Ag₂O, Ag halides)
- (ii) Soluble Ag substances
 - DNEL for sol. Ag substances only applied to AgNO₃: 0.01 mg Ag/m³
 - basis: EU indicative OEL, 2006
- General population, inhalation
 - metallic and poorly soluble compounds: 0.04 mg Ag/m³
 - basis: same starting point as used by SCOEL, higher assessment factor
 - soluble Ag compounds: 0.004 mg Ag/m³
(same factor 10 between soluble and insoluble as for workers)

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Current DNELs - oral

- General population, oral
 - metallic and poorly soluble compounds: 1.2 mg Ag/kg/day
 - basis: published 90-day oral study on nanoAg (NOAEL = 30 mg/kg/day)
 - soluble Ag compounds: 0.02 mg Ag/kg/day
 - basis: Tamimi et al. (1998) study with Ag containing mouth wash applied in the oral cavity (in lack of any better data!)
 - clear data gap recognised in 2010 registrations, anticipated to be closed by NTP data (conduct of “own” RDT studies legally excluded...)

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Update literature search – new data

- update literature search conducted in early August 2013 (previous one was performed in August 2012)
- ca. 50 potentially relevant new publications on human health identified and obtained as full texts
- Almost all sources refer to nanoAg, and can be broken down as follows:
 - in-vivo RDT studies
 - in-vitro cytotoxicity, genotoxicity and bioaccessibility testing
 - toxicokinetic and mechanistic studies
 - several reviews (screened for relevant primary data not identified already)

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Key new data to be included + discussed in dossier updates: ORAL

- nanoAg data on acute tox, sensitisation and gentox: most endpoint records are already added to IUCLID template
- repeated dose oral (+repro):
 - NanoAg:
 - Kim et al. (2008/2010): 28/90-day (already in IUCLID, but may require review of discussion)
 - Hadrup et al. (2012): 28-day study (separate publication on neurotoxicity)
 - NTP 90-day study (not fully reported)
 - Hong et al. (2013) OECD 422 combined RDT + repro/dev tox screening ("no evidence of toxicity")
 - Ag acetate
 - Hadrup et al. (2012): 28-day study
 - NTP 90-day study (not fully reported)

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Kim et al. (2008...): 28/90 day oral study with NanoAg

- Material: silver nano particles (52.7 - 70.9 nm; average 60 nm), purchased from NAMATECH Co., Ltd. (Korea)
- Method: 28-day (2008) and 90-day (2010) oral toxicity study (OECD 407/408)
- 28-day:
 - Doses: 30, 300 and 1000 mg/kg/day
 - Key findings: Increased incidences of bile duct hyperplasia around the central vein were observed in livers at all doses in a dose-dependent way, but authors did not conclude on a NOAEL or LOAEL, because of uncertainties on the findings.
- 90-day:
 - Doses: 30, 125 and 500 mg/kg/day
 - NOAEL: 30 mg/kg/day
 - LOAEL: 125 mg/kg/day based on incidence of liver damage by increased levels of alkaline phosphatase and cholesterol

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Hong et al. (2013): OECD 422 combined RDT + repro/dev tox screening

- Material: citrate-capped silver nanoparticles (7.9 ± 0.95 nm) from ABC Nanotech (Daejeon, Korea)
- Method: combined repeated-dose toxicity study with reproduction/developmental toxicity (OECD 422; GLP)
- Doses: 62.5, 125 and 250 mg/kg/day
- Results:
 - no deaths
 - in a few rats non dose-dependent symptoms of alopecia, salivation and yellow discolouration of the lung were seen
 - no statistically significant effects for haematology, biochemistry and histopathology
 - toxicity endpoints of reproduction/developmental screening test showed no evidence of toxicity
 - tentative NOAEL = 250 mg/kg/bw

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Hadrup et al. (2012): 28-day study with nanoAg + Ag acetate

- Material:
 - "14 nm nanoparticulate silver (Ag-NP) stabilised with polyvinylpyrrolidone"
 - Ag acetate solution (with PVP added)
 - Method: conduct similar to OECD 407
 - Doses:
 - nanoAg: 2.25, 4 and 9 mg/kg/day
 - Ag acetate: 14 mg/kg/day
 - Results:
 - nanoAg: NOAEL: 9 mg/kg/day (highest dose)
 - Ac acetate: caused *reduced bw gain, increased ALP, decrease in plasma urea and lower absolute and relative thymus weights, indicating toxicity of Ag-acetate.*
- Hadrup et al. (2012):
- *another publication investigating effects on neurotransmitter levels; interpreted by authors as signs of neurotoxicity(!)*

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NTP 90-day study oral with NanoAg + Ac acetate

- Study conducted at US FDA National Center for Toxicological Research, together with NTP
- Materials/doses:
 - nanoAg (10, 75 and 110 nm) at 9, 18, 36 mg/kg/day
 - Ag acetate: 100, 200 and 400 mg/kg/day
- Preliminary toxicological results (Slides BfR Conference, Feb 2012):
 - The oral administration of AgOAc at doses of 200 mg/kg bw and higher induced significant decreases in body weight and increased morbidity in rats. Severe gastroenteritis listed as cause of death.
 - No overt dose response pathologies were observed for AgNPs. Renal disease listed as cause of death for 2 rats exposed to AgNP 110 nm and 1 rat exposed to AgNP 10 nm.

Further relevant studies

- repeated dose inhalation:
 - NanoAg:
 - 28-day + 90-day studies by Korean group (Song, Sung, Ji ...) (several publication since 2007 on various aspects of these studies: standard parameters for these study types, but also on lung function, recovery...)
- repeated dose, supportive data on other routes
 - de Jong (RIVM (!), 2013): 28-day intravenous study with nanoAg; not of relevance for RC, but perhaps for mechanistic aspects
- human data, not considered useful for DNEL derivation, e.g.
 - 2013 human time-exposure study of orally dosed nanoAg (Munger et al.)
 - 2012 argyria case report (Stafeeva et al.)
 - 2013 study on argyria (no argyria despite release of Ag from implants)
 - 2011 health surveillance study on nanoAg workers (Lee et al.)

Sung et al. (2008/2009): 90 day inhalation studies with nanoAg

- Material: silver nanoparticle (particles < 55 nm; diameters log normally distributed between 6 and 55 nm; count median particle diameter 18 nm (GSD: 1.5))
- Method: Repeated dose inhalation toxicity (OECD 413; GLP)
- Doses: 49, 133 and 515 $\mu\text{g}/\text{m}^3$ (analytical concentration)
- Results:
 - NOAEC: 133 $\mu\text{g}/\text{m}^3$ based on minimal bile-duct hyperplasia in males and females, chronic alveolar inflammation and macrophage accumulation in the lungs of males and females, and erythrocyte aggregation in females.
 - Lung function: "the decreases in the tidal volume and minute volume and other inflammatory responses after prolonged exposure to silver nanoparticles would seem to indicate that nanosized particle inhalation exposure can induce lung function changes, along with inflammation, at much lower mass dose concentrations when compared to submicrometer particles."

Song et al. (2013): Recovery from AgNPs induced lung effects (exposure 12 weeks)

- Material: Silver nanoparticle (14 – 15 nm diameter)
- Method: guideline compliance not explicitly stated
- Doses: 49, 117 and 381 $\mu\text{g}/\text{m}^3$
- Results:
 - „The present results suggest a potential persistence of lung function changes and inflammation induced by silver nanoparticle exposure above the no observed adverse effect level“.

de Jong (2013): 28-day intravenous study with nanoAg

- Material: BioPure silver nanoparticles (21.0 ± 2.6 nm diameter and 107 ± 7.6 nm diameter), purchased from NanoComposix, San Diego, CA, USA
- Method: repeated dose oral toxicity study (OECD 407) with adjustments
- Doses (intravenously; once daily):
 - 20 nm nanosilver: 0.0082, 0.025, 0.074, 0.22, 0.67, 2 and 6 mg/kg bw/day
 - 100 nm nanosilver: 6 mg/kg bw/day
- Results:
 - Findings: growth retardation; increase in spleen weight and size; increase in absolute T and B cell populations, AgNPs accumulation in spleen, liver and lymph nodes, clinical chemistry showed liver damage; decrease in several red blood cell parameters; immune parameters were effected

Gromadzka-Ostrowska et al. (2012): AgNPs effects on epididymal sperm in rats

- Material: spherical silver nanoparticles (nominal diameter: 20 ± 5 nm and 200 ± 50 nm), purchased from PlasmaChem (Berlin, Germany)
- Method: guideline compliance not explicitly stated
- Doses (intravenously; single dose):
 - Group 1 (20 nm AgNPs): 5 mg/kg
 - Group 2 (20 nm AgNPs): 10 mg/kg
 - Group 3 (200 nm AgNPs): 5 mg/kg
- Results:
 - „a size-dependent (20 nm and 200 nm), dose-dependent (5 and 10 mg/kg bw) and time-dependent (24 h, 7 and 28 days) decrease in the epididymal sperm count“
 - DNA damage in germ cells increased
 - 200 nm AgNPs: testes seminiferous tubule morphometry showed changes
 - „no change of body weight, adipose tissue distribution and the frequency of abnormal spermatozoa was observed“.
 - 200 nm AgNPs seemed to be less toxic than 20 nm AgNPs

Key new data to be included
+ discussed in dossier updates

- preparation of endpoint study records in IUCLID for these key new data is in progress
- further, several new publication were found relating to
 - nanoAg dissolution / bioaccessibility
 - in-vivo and in-vitro toxicokinetics (PS and coating influential ?)
 - discussions on nanoAg particle effect vs. effects of ionic Ag
- Key mechanistic question:
Ag-NP (oral/inh) to blood stream directly vs. gastric dissolution, with secondary tissue precipitation as Ag/S/Se particulates
- other “marginally” relevant articles to be included as “short entries” in IUCLID dossier and used in discussions

Discussion thought starters

- acute toxicity and data on irritation/corrosivity to be kept separate in each substance dossier
- for RDT and CMR, reconsider read-across/grouping/category/template approach:
- currently, only two categories considered:
 - Ag metal (powder and massive , together with “poorly soluble” substance: Ag_2O , AgCl , AgBr , AgI , Ag_2SO_4 , Ag_2CO_3 (the latter two do not require a CSA/CSR due to <10 tpa)
 - soluble substance: so far, only AgNO_3 of relevance
- separate category for nanoAg required?

Discussion thought starters

- evaluation of literature on nanoAg indicates that:
 - any toxicity whatsoever is due to ionic silver rather than a NP effect
 - in other words: there is no clear indication that NP-Ag has any enhanced toxicity; however, no comparison with sol or insol Ag possible (yet)
- currently available data do not allow a quantitatively clearly defined “cut-off” point between soluble and insoluble compounds
- silver ion release and systemic bioavailability depends on particle size, exposure route, coatings (for nanoAg) etc...
- conservative, worst case consideration of nanoAg as soluble Ag difficult to avoid (lack of data on “metallic” silver)
- inhalation DNELs so far based on SCOEL (insoluble) and EU IOEL (soluble)
- currently, no information that would necessitate revision of these DNELs
- oral DNELs to be reviewed based on NTP study (still not available in full)

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Next steps and timing

- by end October
 - EBRC to complete IUCLID dataset (human health section), including endpoint study records, endpoint summaries/discussions
 - EBRC revise DNEL report
 - EBRC to generate new CSR chapters on human health
- by mid November
 - PMRC members and secretariat to review and comment on human health sections IUCLID and CSR
 - EBRC to amend phys-chem section in Ag metal dossier with nanoAg data
- by end November
 - EBRC to address consortium comments on IUCLID and CSR and finalise
- early December
 - editorial merging of CSRs and Exposure scenarios with environmental sections

58

11. Read-across approach for human health endpoints

[59]

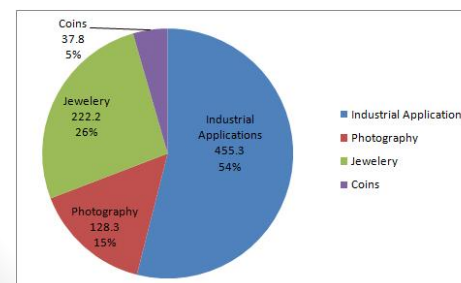
- Cf. item 9 above

[60]

II.B Technical items – Exposure assessment

[61]

12. Feed-back from PMC Members on new uses to be registered (if any)



[62]

Ag & Ag compounds: only one new use for AgNO₃

- Minutes and annexes of 17 & 18 July Ag WG conference calls were circulated on 22 Jul with a list of questions
- One question (question b)) invited PMC Members to report on any (new) use of Ag and/or Ag compounds
- 5/33 responses received
- None of the respondents had any new use to report
- EBRC and WCA will proceed with CSR + ES on the assumption that only one new use (reported previously) needs addition

[63]

13. Environmental exposure assessment



[64]

Revised spERCs and nanoAg



- SpERCs used for Exposure Assessment in 2010 dossier have been refined (v2.1)
 - Release factors to air have changed, but insignificantly
 - no or little difference to the PECs and RCRs
 - Release factors for water have decreased significantly (5-10x) as silver has a high partition co-efficient ($K_d = 190,546$)
 - Aquatic PECs and RCRs will improve significantly
 - Release factors to soil removed (previous SpERCs estimated direct releases to soils, which would be illegal)
 - Soil assessment should now be based on deposition from air and sewage application only
- Dependence on higher tier modelling likely to be reduced
- Also, assumed only six ES are relevant for nanoAg (9.1-9.5 + 9.8)

[65]

Draft updated ENV ES: timing

- ES will be revised based on v2.1 SpERCs
- Work on-going, will be completed by mid-Oct 2013 (in time for next Ag WG meeting)

[66]

14. Occupational exposure assessment



[67]

Feed-back on PMC mini-survey on nanoAg in Ag ES

- Mini-survey sent on to 33 PMC Members involved in Ag and/or Ag compounds
- By 30 Aug, 24 responses had been received
- From 24 responses, 5 indicated involvement in nanoAg (6 originally anticipated, 1 missing one may be among pending respondents)
 - 4 current, 1 future involvement
 - 2 EU importers, 2 EU manufacturers
 - Volumes are between < 100 up to = or > than 500 kg, with maximum of 750 kg projected by 2018
 - Total of 8 manufacturing/using sites reported (accumulative number, actual sites unknown, may be less than 8)
- As regards questions on EBRC's report:
 - All uses of nanoAg are covered
 - Only 'consumer' product in which nanoAg is used reported is electronics/displays
 - (Inkjet-type) Spraying possible to coat surfaces

[68]

Occupational Exposure Update of Exposure Scenarios

Silver Work Group &
Nano Task Force
Joint Meeting

Brussels

4 September 2013

Daniel Vetter
EBRC Consulting
Hannover, Germany

Update requirements (I/II)

- Update of IUCLID section 3.5 (life cycle description)
 - Some descriptors became obsolete
 - Some specific combinations of descriptors are no longer possible
 - Strict differentiation of “use” and “service life”
- Explicit reflection of cleaning/maintenance and removal of residuals
 - Inclusion of specific workplace
 - Inclusion of explanatory text for the methodology used for the assessment of this workplace in introduction

70

Update requirements (II/II)

- Amendments reflecting developments in terminology/good occupational hygiene practice
- Inclusion of additional uses/exposure modifiers
 - Inclusion of additional physical forms
 - Reflection of additional uses
- Inclusion of nano-Ag considerations (see below)
 - Additional workplace for powder production (vapour deposition)
 - Additional workplace for powder handling (more restrictive RPE)
 - Inclusion of read-across concept for exposure data based on dustiness

71

Applicability of ES to nano-Ag (I/VI)

- Scope of report
 - Identify relevant workplaces
 - Check applicability of exposure assessment for these workplaces
 - Include the relevance of efficiency assumptions of applied RMMs
 - Propose a way forward where required
- Uses assumed relevant for nano-Ag based on physical form
 - Manufacture, refining and recycling of silver metal (9.1)
 - Re-melting and alloying (9.2)
 - Production of batteries (9.3)
 - Electronics, contact materials and electroplating (9.4)
 - Production, preparation, use of chemicals, preparations or catalysts (9.5)
 - Professional uses of silver containing preparations (excluding alloys) (9.8)

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Applicability of ES to nano-Ag (II/VI)

Use / Exposure Scenario	Workplace	Physical form	Data basis
Manufacture, refining and recycling (9.1)	Hot processes	solid/molten	measured data
	Wet processes	solution	measured data
	Production and handling of powders	powder	measured data
	Classifying and sifting of powders	powder	measured data
Re-melting and alloying (9.2)	Production and handling of powders	powder	analog. data
Production of batteries (9.3)	Raw material handling	powder	analog. data
	Sintering	powder	analog. data
Electronics, contact materials and electroplating (9.4)	Raw material handling	powder, cryst/gran, massive	analog. data
	Processes in closed systems	powder, cryst/gran, massive	MEASE
	Mechanical treatment	massive, powder	analog. data
	Hot processes	molten	analog. data
	Wet process	wetted powder, solution	analog. data
	Production and handling of powders	powder	analog. data
Production, preparation and use of chemicals, preparations or catalysts (9.5)	Powder handling	powder	analog. data
	Wet process	solution	analog. data
	Spraying	solution	MEASE
Professional use of preparations (9.8)	Handling prep. at ambient temperature	solution	MEASE
	Handling prep. at high energy conditions	solution	MEASE

Applicability of ES to nano-Ag (III/VI)

- Applicability of ES to be assessed on the basis of the individual assessment method used
 - Monitoring data obtained in relevant (non-nano-Ag) workplaces
 - Analogous data (data from similar workplaces)
 - Modelled data (obtained from exposure assessment tool MEASE)
- Occupational exposure is determined by
 - Substance intrinsic emission potential (e.g. dustiness)
 - Process intrinsic emission potential (e.g. pressure, temperature)
 - Implemented risk management measures (e.g. LEV, RPE)
- Assessment to consider exposure factors and data sources

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Applicability of ES to nano-Ag (IV/VI)

- Efficiency of implemented RMMs
 - LEV: literature suggests significantly higher efficiencies for smaller particles (including nano-range) ✓
 - Enclosure: literature suggests to check efficiency of enclosures, however airtightness suggests same efficiency ✓ to be confirmed...
 - RPE: literature leaves some doubts on same efficiency, however:
 - results refer to high breathing rates ✓
 - APFs for RPE in ES given on worst case basis assumed to compensate ✓
- Process intrinsic emission potential in relevant processes
 - Same level of kinetic energy ✓ interaction with particle size?
 - Thermal energy effects overwritten by enclosure ✓
 - Pressure not relevant, wet conditions only positive impact ✓

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Applicability of ES to nano-Ag (V/VI)

- Substance intrinsic emission potential
 - Suspensions/solutions: same as for non-nano-Ag ✓
 - Damp powders: lower than for dry non-nano-Ag ✓
 - Dry powders: max. factor of 3 higher than for dry non-nano-Ag ✗ + only n=1...
- Applicability of assessment based on measured/analogous data
 - Efficiencies of RMMs are not assumed to be significantly lower
 - Higher dustiness could be accounted for by a correction factor
 - To be based on additional dustiness tests
 - Influence of coatings to be considered in dustiness testing
 - Extrapolation to be confirmed by (some) monitoring data
- Applicability of modelled assessment
 - To be confirmed for closed processes and spray applications by monitoring

76

Applicability of ES to nano-Ag (VI/VI)

- o Consequences and proposed strategy
 - o Short term (i.e. for October update)
 - o Powder handling workplaces: more restrictive RPE selected based on revised assessment (dustiness factor) in separate workplace
 - o Spraying of nano-Ag suspensions/solutions: more restrictive RPE in separate workplace
 - o Enclosure: Inclusion of specific workplace for vapour deposition in ES for manufacture
 - o Mid term (potentially for October update)
 - o Confirmation of dustiness results >>> Requires solution re confidentiality!
 - o Investigating influence of coating on dustiness
 - o Mid – long term (announcement in October update)
 - o Strategy to be developed by considering feasibility and practicality issues
 - o Conduct of monitoring campaign for inhalation exposure

77

Strategy for dustiness testing

- o Dustiness testing should investigate into
 - o Influence of particle size
 - o Influence of wetting (if applicable)
 - o Influence of coatings
- o Current EBRC proposal potentially based on incomplete and/or biased information
- o Conclusive strategy currently hindered by
 - o Confidentiality issues
 - o Missing overview on market in terms of specifications and shares
 - o Suggestion to enable bilateral communication between EBRC and companies → i.e. disclosure of company names and contact persons related to provided nano-Ag specifications

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15. Waste exposure scenario: final draft for discussion/approval by Ag WG

[79]



Exposure scenario building and environmental release estimation for the waste life stage of the manufacture and use of silver, silver compounds and nano silver

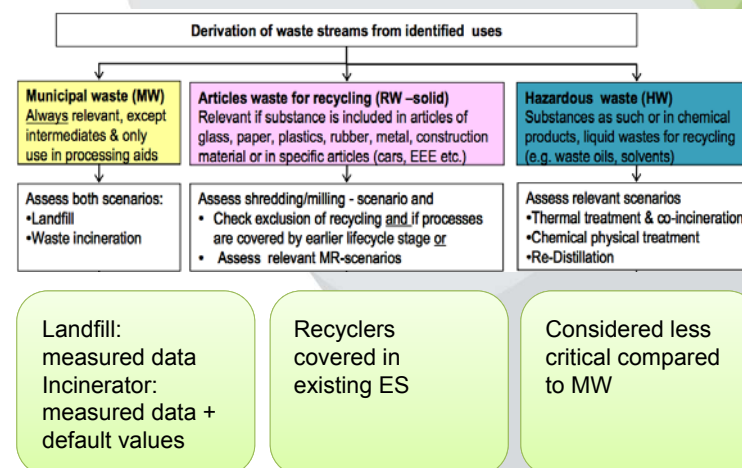
Marnix Vangheluwe, Maxime Eliat-Eliat and Isabelle Vercaigne

Brussels
4th September 2013

► Obligations M/I REACH regulation

- Provide general information in the technical dossier on **types, amounts and composition** of waste occurring on **manufacture and use** of the substance their identified uses
- **Take the waste life cycle stage into account** when undertaking the appropriate exposure and risks assessments embedded **in the exposure scenario** for their identified uses

► Scope of the assessment



► Concentration of Ag in municipal waste

Country	Concentration Ag In mg Ag/ kg dry MW	Method of analysis	Comment
The Netherlands	1.3 to < 1.43	Direct waste analysis	Some types of waste were removed from the analysis: non-ferro fractions, batteries, cleaning products, cartridges, fireworks, ... = UNDERESTIMATION
United Kingdom	0.16 to 16.34 Average: 1.8	Direct waste analysis	
Switzerland	7.5	Indirect waste analysis	MW without separately collected paper, glass and metals
Europe (except RO, PL, BG, EL, IE)	0 to 15	Not reported	
Europe	7.1	Calculated value	
USA	< 3 to 7	Combustible waste only	

► Municipal waste

- Emissions from municipal waste landfills have been assessed using measured data -> **NO RISKS for municipal waste landfills**
- Emissions from municipal waste incinerators have been assessed using a combination of measured data and default values from the guidance -> **NO RISKS for municipal waste incineration**

► Hazardous waste

85

- Ca. 40 questionnaires received
- A refined F_{waste} could be calculated
– F_{waste} = 0%
- Almost all silver in waste is recycled, close to zero silver goes to a hazardous waste treatment site -> **NO RISKS for hazardous waste**
- Information from the questionnaires are used for qualitative description of the different waste types in the report

► Waste types, amounts and treatment for manufacture of silver

86

Waste from	Type of waste	Suitable waste code	Amount (t/y)	Composition	Waste treatment process/ recycling	Information source
Manufacture	Sludge from on-site WWTP	06 05 02*	Range: 0 – 7500 t/y. Median: 250 t/y	Range: < 0.001 – 99.9 % Ag. Median: 0.03 % Ag.	Internal or external recycling	In house questionnaire 2012
	Flue gas dust	10 06 06* 10 07 03 10 07 04 10 07 05	Range: 0 – 55 t/y. Median: 6 t/y	Range: 0.3 – 75 % Ag. Median: 7.5 % Ag.	Internal or external recycling	
	Slags	10 07 01	Range: 0 – 150,000 t/y. Median: 25 t/y	Range: 0.002 – 10 % Ag. Median: 1 % Ag.	Internal or external recycling	
	Sludge from hydrometallurgical processes	10 07 05 11 01 09*	Range: 0 – 20,000 t/y. Median: 24 t/y	Range: 0.01 – 84 % Ag. Median: 1.8 % Ag.	Internal or external recycling	
	Packaging material	15 01 10*	Range: 0 – 18 t/y. Median: 3.5 t/y	Range: 0.1 – 31 % Ag. Median: 3.8 % Ag.	Internal or external recycling	
	Other wastes: slimes, leach residues, drosses, solid wastes, precipitates, salts, adsorbents, spoilt products, soaps, refractories ...	08 01 11 08 03 12* 10 07 02 15 02 02* 16 03 03* 16 11 04	Range: 0 – 3500 t/y.	Range: < 1 – 85 % Ag.	Internal or external recycling	

► Information to report in the ES

87

Conditions and measures related to external treatment of waste for disposal

Hazardous wastes from onsite risk management measures and solid or liquid wastes from production, use and cleaning processes should be disposed of separately to hazardous waste incineration plants or hazardous waste landfills as hazardous waste. Releases to the floor, water and soil are to be prevented. If the silver content of the waste is elevated enough, internal or external recovery/recycling might be considered.

Fraction of daily/annual use expected in waste: 0%

Appropriate waste codes: 06 05 02*, 08 01 11, 08 03 12*, 09 01 01*, 09 01 03*, 09 01 04*, 09 01 05*, 09 01 06*, 09 01 13*, 10 06 06*, 10 07 02, 10 07 03, 10 07 04, 10 07 05, 11 01 09*, 15 01 10*, 15 02 02*, 16 01 18, 16 03 03*, 16 08 01, 16 11 04

Suitable disposal: Hazardous waste produced during the manufacture and downstream use is sent to a recycler only marginal amounts are sent to a landfill or an incinerator. Waste containing silver is recycled for almost a 100%

A detailed assessment has been performed on modelled and measured data and is reported in the Waste report (ARCHE, 2013)



16. Prioritisation of technical items according to Dossier update needs and available PMC Secretariat resources



[89]

Need to agree on priorities!

Technical item	Time (technical)	Time (management)	Needed for dossier update/rank	Proposed ranking
Speciation/BLM freshwater	+++++	+++	No/4	3
Oyster embryo test	+++	++	No/3	2
Marine SSD	++++	+++	No/3	2
Activated sludge test	++	++	Yes/1	1
Soil test at CSIRO	+++	++	Yes/1	1
PNECsoil review	++++	+++	Yes/1	1
Soil SSD	+++	++	Yes/1	2
Further soil research at CSIRO	+++++	+++	No/4	3
DNEL review	++++	+++	Yes/1	1
Read-across strategy	++++	+	Yes/1	1
Dustiness tests	+++	++	Ideally/2	1
Exposure monitoring	++++	++	Not possible/3	2
IUCLID 5/CSR update	++++	++++	Yes/1	1
ES update	++++	+++	Yes/1	1

[90]

Summary of priorities

1. Required items for 2013 dossier update

- Oct 2013 meeting
 - Activated sludge test
 - Soil tests at CSIRO
 - Soil SSD
 - PNECsoil review
 - DNEL review
 - Read-across strategy
- Dec 2013 meeting
 - IUCLID 5/CSR update
 - ES update
 - Confirm budget requirements for 2014 + onwards projects

2. 'Nice to have' items for 2013 dossier update

- Dustiness tests AgNP
- Oyster embryo test
- Marine SSD

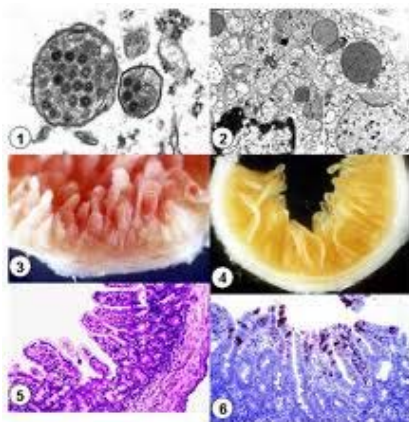
3. Longer-term projects

- Exposure monitoring
- DNEL review (after publication of NTP study)
- BLM freshwater
- Further soil research at CSIRO

[91]

III. Administrative items

[92]



17. Status of characterization data generation: tour de table

[93]

Characterisation data (1)

- Minutes and annexes of 17 & 18 July Ag WG conference calls were circulated on 22 Jul with a list of questions
- One question (question e)) invited PMC Members to report on status of characterisation data generation
- 5/33 responses received + 3 companies had also responded to previous similar requests
- Total of 5 companies have (started to) generate(d) the recommended characterisation information as per responses (4 on nanoAg, 1 on Ag)
- Summary of nanoAg information collected → cf. next slide

[94]

Characterisation data (2)

- Types of materials reported:
 - Powders
 - Suspensions
- Suspension media reported:
 - Water and solvent
 - Daxad
 - Triton X-405
- « Wetting agents » reported:
 - Cardura
 - Carbitol acetate
 - Ethyl acetate
 - Terpineol
 - Toluene
- Coatings reported:
 - Uncoated
 - Non-toxic organic coating to prevent agglomeration
 - Carbohydrate
 - Fatty acid
- Range of sizes (D10) reported: 10-100 nm (larger particles also reported, with D10 up to ~ 400 nm)
- Morphologies reported:
 - (irregular) spherical
 - plate/platelet
- Range of surface areas reported:
 - Spherical: 0,001-16 m²/g
 - Plate/platelets: 0,125-2,5 m²/g

**Content of this slide proposed
as basis to complete ID Card and
phys-chem section of joint Ag
Dossier.**

**Anything incorrect, missing, or
too broad?**

[95]

18. Preparation of meeting with RIVM



[96]

18.1. Feed-back from RIVM including proposed Agenda (received on 2 Sep)

Agenda informal meeting

1. Welcome
2. Introduction
3. Process of substance evaluation (procedures / time lines)
4. Initial ground for concern
5. Registrants view of the dossier (update) and research work (progress)
6. Discussion
7. AoB

RIVM
RIVM
RIVM
RIVM
PMC
PMC

RIVM Participants:

Dr. Betty Hakkert, coordinator Substance Evaluation Bureau REACH
Dr. Petra van Kesteren, human toxicologist, VSP
Dr. Eric Bleeker, eco toxicologist, VSP
Dr. Susan Wijnhoven, human toxicologist, VSP
Drs. Rob Jongeneel, human toxicologist, VSP
Ing. Maarten Nederveen, secretary Substance Evaluation Bureau REACH

PMC Participants:

Dr. Klaus Rothenbacher, PMC (PMC science manager)
Caroline Braibant, PMC (PMC secretary general)
Dr. Rodger Battersby, EBRC (consultant to PMC, mammalian tox.)
Daniela Cholakova, Aurubis (LR)
Peter Simpson, WCA environment, UK (consultant to PMC, ecotox.)

[97]

18.2. Outcome of preparatory meeting with PMC delegation and Eurométaux

Exchanges and tips/remarks on Agenda

- 'Informal' meeting
- RIVM opens meeting, followed by presentation by and discussion with PMC on dossier update and general research work
- Agenda (implicitly) includes items proposed by PMC
- Agenda seems open, three hours, on a Friday afternoon ☺

Exchanges and tips/remarks on participants

- RIVM:
 - B. Hakkert coordinating
 - Other participants new/unknown so far
 - More human toxicology expertise than ecotox
- PMC:
 - Well balanced
 - Fulfills legal, representation and technical needs, with no risk of contradiction

[98]

18.3. Agreement on key messages and relevant documents to be circulated to RIVM

Key messages:

- Difference with SAS in that Ag covers various forms and sizes, is not a closed case, work in progress
- SAS however likely to be a good model of Ag Evaluation procedure – continue exchanges and prepare accordingly
- Dossier weaknesses/hot topics are (as for SAS case):
 - **Characterisation** insufficiently precise (especially on coatings) and not matching characteristics provided in supporting literature
 - Members to complete ASAP; direct contact with consultants recommended; bottle neck
 - **Patchy dataset** on Human Health
 - Should be strengthened with NTP study once published
 - **Effect of particle vs. ion**
 - Precautionary approach for ENV and awaiting NTP study for HH
 - No reference to any **consumer use of nanoAg** (e.g. textiles) – consider options:
 1. Leave out
 2. Try to obtain data and report in dossier

Recommended background documents:

- None
- If slides are allowed, proposed to present (and leave with NL) slides addressing the following topics (draft outline):
 - Background/Scope
 - Characterisation
 - Gap filling read-across/category approaches
 - Use coverage in Dossier
 - Anticipated content/timing of Dossier update

Next steps:

- Draft slideset skeleton by 5 Sep
- Draft slideset by 12 Sep
- Final draft and conf call of participants by 18 Sep
- Meeting with RIVM on 20 Sep

[99]



19. Discussion and agreement on recommended approach towards reviewing the Ag Dossier update

[100]

Ag WG 18 Jul conf call

- Is a review useful? **Yes**
- Should it be formal or informal? Preferably **informal** to allow it to happen in the available timeframe
- When should the review start? Sufficient time before the Dossier update submission timeframe, i.e. potentially on an interim version of the Ag Dossier in **Oct 2013**
- Should it be reviewed by one or more readers? Ideally **more than one**
- Who should review the Dossier?
 - Internally it was suggested for **company experts** to continue their review while BASF (new Member of PMC, not involved in Ag project before) and the **new PMC Manager** (starting on 2 Sep, REACH knowledgeable but not necessarily knowledgeable on metal-specific issues) have a thorough reading of the Dossier and revert with your questions and comments
 - Externally it was suggested to request **Eurométaux** (V. Verougstraete and H. Waeterschoot) as well as other consultants like ARCHE to review the Dossier. Furthermore, it was recommended to look for **additional possibilities**.

[101]

Since 18 Jul...

- Renaud Nicolay on board
- Eurométaux confirmed willingness to review and proposes to share as follows (~ 1 day each):
 - Violaine Verougstraete: HH
 - Hugo Waeterschoot: ENV
- Eurométaux also recommend to ask additional reviewer to check on specific items picked up during Eurométaux' review
 - ARCHE willing to address ENV items
 - HH:
- Timing of review by R. Nicolay and Eurométaux: end Oct-1st wk Nov
- Timing of additional review: mid Nov-3rd wk Nov
- Timing of Ag registrants' review: end Oct-3rd wk Nov

[102]



20. PMC response to EU public consultation relating to REACH annexes and nanomaterials: discussion and approval of version for submission by 13 Sep 2013

[103]

- PM and Zn only two active Members on nanos in Eurométaux
- PMC's proposed draft response shared by Eurométaux as proposed NFM industry's response
- Draft response circulated with background documents
 - Mainly in favour of option 5 (Tailored information requirements and clear regulatory provisions)
 - Very much aligned with CEFIC's draft response
- Any comment before submission of response by 13 Sep?

[104]

21. Typical profiles of Ag and Ag compounds: feed-back from Ag WG for inclusion in IUCLID 5 files



[105]

- Minutes and annexes of 17 & 18 July Ag WG conference calls were circulated on 22 Jul with a list of questions
- One question (question c)) invited PMC Members to report on typical impure profiles among registered Ag and Ag compounds
- 6/33 responses received, with following profiles reported:
 - Ag:
 - Impure Profile 1 Ag > 98,5 which contains > 0,1% Pd, Pb, and Cu
 - Impure Profile 2 Ag > 99,9 which may contain > 0,1% As
 - AgNO₃:
 - Impure Profile 1 contains 6% of Cu
 - AgCl:
 - Impure Profile 1 of AgCl 93-97 which may contain > 0,1% HAuCl₄, H₂PtCl₆, and H₂PdCl₄
 - Impure Profile 2 of AgCl 98,5-99,5% which may contain > 0,1% PdCl₂, FeCl₂, CuCl₂, and PbCl₂
- Any other?
- Next step: derive classification and report in joint dossiers

[106]

IV. General

[107]

22. Transport classifications and translation of short ES for (relevant) Ag and Ag compounds in scope



[108]

- Transport classifications: Ag WG agreed to derive these for all Ag substances and include in PMC inventory for common reference/harmonised use
- Translation of short ES:
 - Cf. question d) of list of questions circulated with minutes of 17 & 18 Jul 2013 Ag WG cc
 - 6/33 responses received + previous input indicate following languages are of interest:
 - French (1)
 - German (3)
 - Italian (1)
 - Polish (1)
 - Spanish (1)
 - Any other? Should all the above be pursued?
- Will be launched after Dossier update is submitted and all final classifications have been derived + contact of translating agencies have been collected (one provided already) → ADD TO 'TO DO LIST'

[109]

23. AOB, next meetings and closing remarks



[110]

- AOB?
- Next meetings:
 - Originally:
 - Brussels, 23 Oct – 10:30-16:30
 - Brussels, 3 Dec – 10:30-16:30
 - **New proposal:**
 - Brussels, 19 Nov – 10:30-16:30
 - Early Dec, follow-up cc, date tbd by Ag WG

THANK you!

[111]