



PMC-Reconsile meeting: Karstedt

Minutes, Brussels, 1 March 2016

ACTIONS	Who?	By when?	Status?
Update ID card including silicon content (range concentration)	Klaus Rothenbacher	2 March 2016	DONE
Check timing for sensitisation study and add it to the minutes	Klaus Rothenbacher	2 March 2016	DONE
Forward NMR spectra under confidentiality agreement to PFA	Klaus Rothenbacher	4 March 2016	
Send updated ID card including silicon range to PFA after agreement from LR	Klaus Rothenbacher	4 March 2016	
Updated draft cooperation agreement as recommended in the minutes below	Denise O'Connor	4 March 2016	
Send to Denise O'Connor new cost sharing formula	France Capon	4 March 2016	DONE
Agreement on ID card	Reconsile-PMC	10 March 2016	
Agreement on cooperation agreement	PMC	15 March 2016	
Provide to PMC timing for the LtU agreement between Cs	Reconsile	15 March 2016	
Agreement on sameness	Reconsile	17 March 2016	
Agreement on cooperation agreement	Reconsile	End of March 2016	



1st draft of actions plan for Karstedt registration	PMC	End of March 2016	
Circulation of the ID card to the SIEF for sameness check	PMC	April 2016	
Switch SFF in REACH-IT from Blue Start to Heraeus after signature of the cooperation agreement	Blue Star and Heraeus	April 2016	
Draft LtU agreement	PMC	TBD	
Organize a discussion between Reconsile and PMC on LLNA draft report (if cooperation agreement is signed)	PMC	August 2016?	

1. Welcome and tour de table

France Capon welcomed the participants and the meeting started by a tour de table and reminder of the anti-trust guidelines. The aim of the meeting is to review the status of the different steps of the preparation of the registration dossier of Karstedt by the Precious Metals and Rhenium Consortium and agree on a way forward.

France Capon announced that Jelle Mertens will take over the responsibility of Klaus Rothenbacher as of End of April 2016.

The minutes will be prepared by PMC and sent out to the group after the meeting. The draft agenda has been approved by the participants.

2. Substance sameness

The ID card of Karstedt has been finalized and an updated version has been circulated in preparation of the meeting. The ID card is meant to check sameness between potential co-registrants within the SIEF.

Most of the comments from Reconsile have been taken into account except the comment related to reporting the silicon concentration range which has been rejected.

Need now to have the confirmation of sameness based on the available information. There is a remaining issues related to interpretation of NMR spectra available at Reconsile level. When this will be clarified, it will be possible to confirm the sameness. Regarding the silicon content, the LR advised to take this out since not needed for the description of the substance. The Si content of the complex cannot be measured directly, only assumptions based on Pt content can be done. Doing all these



calculations, we do not need the silicon content which belongs to the ligand. This composition is sufficient to do the quantification. Peter Fisk disagrees with the interpretation and asks to put the silicon content back in the substance description. Heraeus agreed to report the range of silicon content as proposed by Reconsile.

PFA requests to have access to the NMR spectra for sameness check.

ACTIONS;

- **Immediately, update ID card added silicon content (range concentration) (KR) - done**
- **4 March 2016, forward from PMC to PFA NMR spectra under confidentiality agreement (no consultation to the public nor the companies) (KR, with spectra provided by LR)**
- **10 March 2016: agreement on ID card by Reconsile and PMC (ALL)**
- **17 March 2016: agreement on the sameness of substance (Reconsile)**
- **March 2016: approve of cooperation agreement**
- **April 2016: circulation of the ID cards to the SIEF (PMC)**
- **April 2016: switch in REACH-IT system (BlueStar) after signature of the cooperation agreement.**

3. Sensitization endpoint

Klaus Rothenbacher introduced the topic of sensitization: 5 studies have been received from Reconsile on this endpoint. Studies are contradictory: from skin sensitizer cat 1A to no skin sensitization. Based on available data we cannot take a decision. Test reports received were incomplete missing the description of tested material which is critical for the interpretation of data: the level of impurities might have an impact on the interpretation of the results. The latest information received from Reconsile is that the missing data are not available. It means that we have identified a data gap and PMC have initiated a new test (LLNA) to ensure that we can clarify the endpoint.

PFA comments that the method chosen for skin sensitization (Local Lymph Node Assay) may not be the most suitable one. It might give false positive results for the ligand. Using weight of evidence on the available Reconsile data, within the PMC tox sub-group, it has already been concluded that Karstedt is most likely a skin sensitizer. However, this is not supported by actual epidemiology data. Need to keep a watching brief on the silicon behaviour. If the outcome is negative, issue is resolved but if positive the issue is not.

Will the existing studies be used? This has not been decided by PMC yet. Certainly not as main studies but we will probably dismiss them since no information on the tested article is available. This has to be confirmed.

If cooperation agreement is signed, a discussion could be organized between Reconsile and PMC on the outcome of the study.

Next steps: agreement or need to discuss additional testing depending on the results at tox WG.

Post meeting information: the draft report for the ongoing LLNA study is scheduled by 29th July 2016

ACTIONS:

- **Immediately, check timing for sensitization study (KR) and add in the minutes – done.**



- **If cooperation agreement is signed, a discussion could be organized between Reconsile and PMC on the outcome of the study.**

4. Cooperation agreement

France Capon introduced the issue summarizing the status of the document and clarifying that the cooperation agreement must be focused on the cooperation between PMC and Reconsile and not on data sharing issues (as agreed at the PMC-Reconsile meeting in July 2015).

The following requests from Reconsile have been discussed

- Include costs incurred by all parties in the contract (article IV, draft cooperation agreement)
- Data sharing agreement between PMC and Reconsile (article V, draft cooperation agreement)

In the context of the new Implementing Act on Data Sharing, participants agreed that it would be advisable to keep the data sharing at the level of the companies. PMC understands the interest of Reconsile to have access to the data for potential read-across in the future but this should be handled under a separate and different agreement.

It is therefore confirmed that the discussion is around 3 different agreements:

- Cooperation agreement between Reconsile and PMC members in preparation of the Registration dossier. This agreement must include the terms of the cooperation (including that costs incurred by Reconsile for relevant tests or consultants costs and which are directly of interest for PMC members, will be charged to PMC directly and aggregated with the other costs related to Karstedt dossier) and a reference to a list of actions and responsibilities in the dossier preparation. This list will be developed in the course of March 2016 and updated as soon as needed by written (email exchanges should be sufficient). Article V will not be updated as requested by Reconsile in the latest version of 20 January 2016.
- LoA: the agreement will be available mid-March and sent to Reconsile members by PMC.
- LtU framework

Cooperation agreement: remove all the new additions from Reconsile except the one of the costs incurred by Reconsile members. Reconsile will charge PMC for the work done on Karstedt and which is relevant for the common dossier.

Mechanism in place to demonstrate Reconsile costs? Everything is itemized and detailed by Reconsile.

ACTIONS:

- **4th March: Denise O'Connor will send to PMC an updated cooperation agreement based on above recommendation**
- **4th March: France Capon will send to Denise O'Connor new cost sharing formula as approved by the PMC in December 2016.**
- **15th March 2016: PMC - approval of agreement**
- **End of March: Reconsile - approval of agreement**



- **Overall framework agreement on LtU: PMC will take care of drafting the agreement - Reconsile will confirm in March 2016 by when the data are needed to define the timeline for drafting the license to use.**

5. Conclusions & next steps

Overall agreed timeline is:

- March 2016 finalisation of the sameness discussion and cooperation agreement
- PNEC will be available over Summer and exposure assessment will be conducted
- DNEL will be available around November and exposure assessment will be conducted
- Draft Registration dossier will be available by end of 2016
- Q1 2017 will be dedicated to approval process (e.g.: 2 months for PMC) to ensure that LR can submit the registration dossier by 31 March 2017.

A more detailed timeline with expected period of technical discussions and review will be drafted in the course of March and updated on a regular basis (*cf. supra*).

After the registration, the preamble of the draft cooperation agreement include already the possibility to continue the cooperation. This will be also part of the LoA. The cooperation agreement can still be amended if needed in case of maintenance or other regulatory process.



Participants list

From Reconsile

- Inneke Claes (ReachCentrum)
- Peter Fisk (PFA) (by phone)
- Louise McLaughlin (PFA) (by phone)
- Denise O'Connor (ReachCentrum)
- Sabine Springael (Dow Corning)
- Jean-Michel Stein (BlueStar) (by phone)

From PMC, the participants who confirmed their availabilities the 1st March are:

- Roland Brasch (Heraeus)
- France Capon (PMC)
- Patrice Corbiau (K&L Gates, PMC Legal Counsel)
- Guy Ethier (Umicore and chair of the PMC)
- Jelle Mertens (PMC)
- Klaus Rothenbacher (PMC)
- Nissanka Rajapakse (Johnson Matthey) (by phone)
- Michael Thiel (BASF, Chair of the PGM WG)
- Markus Willeke (Heraeus) (by phone)