

1 Prioritised substance group: Aprotic solvents - NOT UPDATED

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1.1 Policy-related questions

1. What is the current external exposure of the workers in EU to reprotoxic aprotic solvents and do they exceed Guidance values (reference values), where they are available? What data gaps exist?
2. What is the current internal exposure of the workers in EU to reprotoxic aprotic solvents, especially with respect to female workers at reproductive age, and do they exceed Guidance values (reference and HBM values), where they are available? What data gaps exist?
3. Are there geographical differences and differences caused by industrial sector in the exposure of workers in EU to reprotoxic aprotic solvents?
4. What is the current exposure of the general EU population to reprotoxic aprotic solvents, especially with respect to females at reproductive age as well as mothers and their young children, and do they exceed Guidance values (reference and HBM values), where they are available? What data gaps exist?
5. What are the environmental concentrations of reprotoxic aprotic solvents in different environmental media and what is their geographical distribution and time trend in EU, and can they contribute to the overall exposure of the general population? What data gaps exist?
6. What are the indoor air and dust concentrations of reprotoxic aprotic solvents?
7. What is the content of reprotoxic aprotic solvents in widely used commodities (cosmetics, washing & cleaning products, paints, textiles, leather, etc.)?
8. How the exposure of general population to reprotoxic aprotic solvents is correlated with lifestyle and consumption patterns, what is the main exposure route?
9. Are there differences in exposure of the general EU population to regulated and non-regulated reprotoxic aprotic solvents (banned use in cosmetics)?
10. Are there differences in exposure of the workers in EU in relation to regulated and non-regulated reprotoxic aprotic solvents after the restriction for NMP will enter into force after 9 May 2020?
11. What are differences in profiles of reprotoxic aprotic solvents observed in exposure assessment regarding occupational environment and in relation to general public taking into account spatial and temporal distribution?
12. What are the mixture effects of aprotic solvents as a whole in relation to human exposure and how it can be estimated?
13. What are the best indicator`s substances (markers) to identify hazardous exposures to aprotic solvents as a whole?
14. What are the analytical options available with respect to aprotic solvents (gas chromatography-mass spectrometry versus liquid chromatography-tandem mass

spectrometry for biological matrices, other methods in addition, methods for environmental media)?

15. What are the levels of reprotoxic aprotic solvents and associated health effects in vulnerable population groups, namely, mothers and their young children?
16. Are there other potentially hazardous aprotic solvents apart from the four reprotoxic aprotic solvents in question?
17. What is the state - of - the – art regarding chemical safety`s legislation on reprotoxic aprotic solvents in question and other potentially hazardous aprotic solvents identified?
18. Can reference values be established for any reprotoxic aprotic solvent in the case they are missing?
19. Can biomarkers of health effects be developed?

1.2 Research Activities to be undertaken

Table 1 Research activities research activities to be carried out to answer the policy questions for aprotic solvents

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
1, 2, 3, 4, 5, 6, 7, 8, 10	NMP	<p>Toxicological information.</p> <p>Established biomarkers of exposure and HBM values. Analytical methods in place. Notion on the most significant exposure route.</p> <p>Some information on external and internal exposure in the occupational environment.</p>	<p>Very general knowledge about releases to environment – the related information should be gathered.</p> <p>No information on contamination of different environmental media – published information must be searched and environmental monitoring should be arranged in different geographical locations within EU.</p> <p>No information on content in widely used consumers` products – investigations should be arranged.</p> <p>Information on indoor pollution is lacking – special investigations should be arranged.</p> <p>Lacking information on exposure in the general population - published information must be searched and biomonitoring shall be arranged, especially in relation to vulnerable population groups, namely, females at reproductive age, mothers and their young children. Spatial (geographical) and temporal distribution shall be followed-up.</p> <p>No systematic investigations on exposure levels caused by different industrial sectors and geographical locations within EU – such information should be gathered by additional literature search.</p> <p>Information on REACH restriction success is lacking – such investigations shall be done after the transitional period.</p> <p>Association between exposure of general population and lifestyle and consumption patterns is unclear – special investigations shall be arranged.</p>

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
1, 2, 3, 4, 5, 6, 7, 8, 9	DMF	<p>Toxicological information.</p> <p>Established biomarkers of exposure and HBM values. Analytical methods in place. Notion on the most significant exposure route.</p> <p>Some information on external and internal exposure in the occupational environment.</p>	<p>Very general knowledge about releases to environment – the related information should be gathered.</p> <p>No information on contamination of different environmental media – published information must be searched and environmental monitoring should be arranged in different geographical locations within EU.</p> <p>No information on content in widely used consumers` products – investigations should be arranged.</p> <p>Information on indoor pollution is lacking – special investigations should be arranged.</p> <p>Lacking information on exposure in the general population - published information must be searched and biomonitoring shall be arranged, especially in relation to vulnerable population groups, namely, females at reproductive age, mothers and their young children. Spatial (geographical) and temporal distribution shall be followed-up.</p> <p>No systematic investigations on exposure levels caused by different industrial sectors and geographical locations within EU – such information should be gathered by additional literature search.</p> <p>Information on success in relation to prohibition in cosmetic products is unclear - such investigations shall be done.</p> <p>Association between exposure of general population and lifestyle and consumption patterns is unclear – special investigations shall be arranged.</p>
1, 2, 3, 4, 5, 6, 7, 8, 9	DMAC	<p>Toxicological information.</p> <p>Established biomarkers of exposure and HBM values. Analytical methods in place. Notion on the most significant exposure route.</p> <p>Limited information on external and internal exposure in the occupational environment.</p>	<p>Very general knowledge about releases to environment – the related information should be gathered.</p> <p>No information on contamination of different environmental media – published information must be searched and environmental monitoring should be arranged in different geographical locations within EU.</p> <p>No information on content in widely used consumers` products – investigations should be arranged.</p> <p>Information on indoor pollution is lacking – special investigations should be arranged.</p> <p>Lacking information on exposure in the general population - published information must be searched and biomonitoring shall be arranged, especially in relation to vulnerable population groups, namely, females at reproductive age, mothers and their young children. Spatial (geographical) and temporal distribution shall be followed-up.</p> <p>No systematic investigations on exposure levels caused by different industrial sectors and geographical locations within EU – such information should be gathered by additional literature search.</p> <p>Information on success in relation to prohibition in cosmetic products is unclear - such investigations shall be done.</p> <p>Association between exposure of general population and lifestyle and consumption patterns is unclear – special investigations shall be arranged.</p>

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
1, 2, 3, 4, 5, 6, 7, 8	NEP	Toxicological information. Established biomarkers of exposure and HBM values. Analytical methods in place. Notion on the most significant exposure route.	<p>Very general knowledge about releases to environment – the related information should be gathered.</p> <p>No information on contamination of different environmental media – published information must be searched and environmental monitoring should be arranged in different geographical locations within EU.</p> <p>No information on content in widely used consumers` products – investigations should be arranged.</p> <p>Information on indoor pollution is lacking – special investigations should be arranged.</p> <p>Lacking information on exposure in the general population and in the occupational environment - published information must be searched and biomonitoring shall be arranged, especially in relation to vulnerable population groups, namely, females at reproductive age, mothers and their young children. Spatial (geographical) and temporal distribution shall be followed-up.</p> <p>No systematic investigations on exposure levels caused by different industrial sectors and geographical locations within EU – such information should be gathered by additional literature search.</p> <p>Association between exposure of general population and lifestyle and consumption patterns is unclear – special investigations shall be arranged.</p>
11, 12, 13, 14, 15, 17, 18, 19	NMP, DMF, DMAC, NEP	Toxicological information. Established biomarkers of exposure and some HBM values. Analytical methods in place. Restricted external and internal exposure information in the occupational environment is in place.	<p>Differences in profiles of reprotoxic aprotic solvents in relation to exposure and mixture effect is unclear – special investigations shall be done, possibilities to come to one common indicator substance (biomarker) should be assessed.</p> <p>No knowledge on biomarkers of health effects – special investigations shall be arranged.</p> <p>Contradictory information on applicability of different analytical methods – available methods shall be assessed, possibility and necessity to develop new methods should be assessed, and interlaboratory validation exercises shall be arranged.</p> <p>Association between exposure of vulnerable population groups and related health effects is unclear – special investigations shall be arranged.</p> <p>No reference values including HBM values for all reprotoxic aprotic solvents – the missing reference values shall be developed.</p>
16, 17	Other aprotic solvents	-	Lacking knowledge on possible other hazardous aprotic solvents– additional screening should be done and potential other priority aprotic solvents should be identified, their legal status should be investigated.