Appendix I. Modification of the original profiler, skin irritation/corrosion inclusion rules by BfR.

|  |  |  |
| --- | --- | --- |
| **Category Name** | **Original Definition in literature\*** | **Modification** |
|  | C:\Users\Atsu\AppData\Local\Temp\OASIS\7272\{F4A016CB-5842-4DD2-B196-7B2CB680FF62}\SkinIrritationCorrosionInclusionRules.zip\(Hydro)Peroxides_files\image001.gif

|  |
| --- |
| R1 = alkyl chainR = H or alkyl chain  |

 | The original profiler can cover only peroxides in which both Rs are alkyl. We modified it to allow hydro peroxides in which R or R1 is H. |
| Acyl halides | C:\Users\Atsu\AppData\Local\Temp\OASIS\5832\{CF1AEFA9-86D6-452F-991A-65BFD6817AA7}\SkinIrritationCorrosionInclusionRules.zip\Acyl halides_files\image001.gif

|  |
| --- |
| X = halogenR = alkyl, arylalkyl or aryl group |

 | The original profiler does not cover acyl halides in which R has different functional groups (e.g., –OH). We modified it to allow R linked to any other atom. |
| Aliphatic acids and (Met)acrylic acids |

|  |
| --- |
| C:\Users\Atsu\AppData\Local\Temp\OASIS\5832\{CF1AEFA9-86D6-452F-991A-65BFD6817AA7}\SkinIrritationCorrosionInclusionRules.zip\Aliphatic acids and Metacrilic acids_files\image001.gifC:\Users\Atsu\AppData\Local\Temp\OASIS\5832\{CF1AEFA9-86D6-452F-991A-65BFD6817AA7}\SkinIrritationCorrosionInclusionRules.zip\Aliphatic acids and Metacrilic acids_files\image002.gifR ≤ C8 aliphatic chain and no other subgroupsR = H or CH3 |

 | In the definition, H is not included in R. However, we modified it to add H in R. |
| Aliphatic halogenated saturated acids | C:\Users\Atsu\AppData\Local\Temp\OASIS\5832\{CF1AEFA9-86D6-452F-991A-65BFD6817AA7}\SkinIrritationCorrosionInclusionRules.zip\Aliphatic halogenated saturated acids_files\image001.gif

|  |
| --- |
| R=aliphatic chainHal =Cl, Br |

 | We modified the original profiler to allow R linked to any other atom.  |
| Aliphatic iso(thio)cyanates |

|  |
| --- |
| C:\Users\Atsu\AppData\Local\Temp\OASIS\4544\{14C21D87-B447-4BD4-A4CD-B588E7D81031}\SkinIrritationCorrosionInclusionRules.zip\Aliphatic iso (thio)cyanates_files\image001.gifC:\Users\Atsu\AppData\Local\Temp\OASIS\4544\{14C21D87-B447-4BD4-A4CD-B588E7D81031}\SkinIrritationCorrosionInclusionRules.zip\Aliphatic iso (thio)cyanates_files\image002.gif1. Isocyanates2. IsothiocyanateR = alkyl (aliphatic chain)Some isocyanates/isothiocyanates hydrolyse rapidly when getting in contact with water; the resulting metabolite may cause only mild skin irritation. |

 | We modified the original profiler to cover not only primary iso(thio)cyanates but also secondary and tertiary iso(thio)cyanates. We also modified it to allow R linked to any other atom. |
| Allyl halides,sulfonates | C:\Users\Atsu\AppData\Local\Temp\OASIS\4544\{14C21D87-B447-4BD4-A4CD-B588E7D81031}\SkinIrritationCorrosionInclusionRules.zip\Allyl halides,sulfonates_files\image001.gif

|  |
| --- |
| X = Cl,Br or F or sulfon (OSO2-−RIV )R, R',R",R"' = H, alkyl, arylalkyl or aryl groupRIV = alkyl, arylalkyl or aryl group |

 | We modified the original profiler to allow R, R', R", R''' linked to any other atom. |
| Alpha-carbamoyl halogen compounds (α-halo-carbamoyl) | C:\Users\Atsu\AppData\Local\Temp\OASIS\10224\{F64711B5-88FF-460E-8483-0980C628F704}\SkinIrritationCorrosionInclusionRules.zip\Alpha -carbamoyl halogen compounds ( a-halo carbamoyl)_files\image001.gif

|  |
| --- |
| R= alkyl, arylR1 = O, S |

 | We modified the original profiler to allow R linked to any other atom.  |
| Alpha-halogenated aldehydes/ketones or thioaldehydes/thio-ketones | C:\Users\Atsu\AppData\Local\Temp\OASIS\10224\{F64711B5-88FF-460E-8483-0980C628F704}\SkinIrritationCorrosionInclusionRules.zip\Alpha-halogenated aldehydes ketones or thioaldehydes thio-ketones_files\image001.gif

|  |
| --- |
| R, R’ = H, alkyl, arylalkyl or aryl groupR" = O, S |

 | We modified the original profiler to allow R, R' linked to any other atom.  |
| Aromatic amines | C:\Users\Atsu\AppData\Local\Temp\OASIS\11000\{C2A9CAE8-C5E4-44CB-9C34-CC9EEE7B001C}\SkinIrritationCorrosionInclusionRules.zip\Aromatic amines_files\image001.gif

|  |
| --- |
| R and R1 = H or aliphatic chainR2 = any |

 | The original profiler does not cover tertiary amines. We modified it to cover tertiary amines. |
| Aziridines  | C:\Users\Atsu\AppData\Local\Temp\OASIS\11000\{C2A9CAE8-C5E4-44CB-9C34-CC9EEE7B001C}\SkinIrritationCorrosionInclusionRules.zip\Aziridines_files\image001.gif

|  |
| --- |
| R = H or alkyl |

 | The original profiler can cover only aziridines in which both Rs are alkyl. We modified it to allow H as R. |
| Benzyl halides | C:\Users\Atsu\AppData\Local\Temp\OASIS\11000\{C2A9CAE8-C5E4-44CB-9C34-CC9EEE7B001C}\SkinIrritationCorrosionInclusionRules.zip\Benzyl halides_files\image001.gif

|  |
| --- |
| R = alkyl, arylalkyl or arylX = halo (F, Cl, Br, I) or -OSO2Compounds with good leaving group at alpha position of an aromatic bond belong to this group. |

 | In the definition, H is not included in R. However, we modified it to add H in R. |
| Disulfides  | C:\Users\Atsu\AppData\Local\Temp\OASIS\11000\{C2A9CAE8-C5E4-44CB-9C34-CC9EEE7B001C}\SkinIrritationCorrosionInclusionRules.zip\Disulfides_files\image001.gif

|  |
| --- |
| R= alkyl |

 | We modified the original profiler to allow R linked to any other atom.  |
| Epoxides (=oxiranes) | C:\Users\Atsu\AppData\Local\Temp\OASIS\7292\{3DDD2DB9-DD18-477B-989C-769BC9C9D956}\SkinIrritationCorrosionInclusionRules.zip\Epoxides(=oxiranes)_files\image001.gif

|  |
| --- |
| R, R', R'', R''' = H, alkyl, arylalkyl or aryl group |

 | We modified the original profiler to allow R, R', R", R''' linked to any other atom. |
| Esters including acrylic and methacrylic esters | C:\Users\Atsu\AppData\Local\Temp\OASIS\7292\{3DDD2DB9-DD18-477B-989C-769BC9C9D956}\SkinIrritationCorrosionInclusionRules.zip\Esters including acrylic and methacrylic esters__files\image001.gif | The original profiler does not cover esters in which R has different functional groups (e.g. –OH). We modified it to allow R linked to any other atom. |
| Halogenated alkanes | C:\Users\Atsu\AppData\Local\Temp\OASIS\7292\{3DDD2DB9-DD18-477B-989C-769BC9C9D956}\SkinIrritationCorrosionInclusionRules.zip\Halogenated alkanes_files\image001.gif

|  |
| --- |
| R = aliphatic Hal = F, Cl, Br |

 | We modified the original profiler to allow R linked to any other atom.  |
| Lactones  | C:\Users\Atsu\AppData\Local\Temp\OASIS\628\{AC0D3E36-61F9-4B09-B4AA-CEB9CF6F32DF}\SkinIrritationCorrosionInclusionRules.zip\Lactones_files\image001.gif

|  |
| --- |
| R, R1 = H, alkyl, arylalkyl or aryl group |

 | We modified the original profiler to allow ring with other functional groups. |
| Organic silicon halides |

|  |
| --- |
| C:\Users\Atsu\AppData\Local\Temp\OASIS\628\{AC0D3E36-61F9-4B09-B4AA-CEB9CF6F32DF}\SkinIrritationCorrosionInclusionRules.zip\Organic silicon halides_files\image001.gifR, R1, R2 can be any kind of groupsHal = F, Cl, Br or I |

 | We modified the original profiler to cover di- and tri- halogens. |
| Primary and secondary aliphatic amines | C:\Users\Atsu\AppData\Local\Temp\OASIS\10792\{E726224F-2195-4FD0-9BBF-6730534AF968}\SkinIrritationCorrosionInclusionRules.zip\Primary and secondary aliphatic amines_files\image001.gif

|  |
| --- |
| Primary, secondary R and R1 = H and /or aliphatic chain or non-aromatic ring |

 | The original profiler does not cover primary and secondary amines in which R has different functional groups. We modified it to cover these chemicals (e.g., diamine). |
| Silicon ether (alkoxysilanes) | C:\Users\Atsu\AppData\Local\Temp\OASIS\10792\{E726224F-2195-4FD0-9BBF-6730534AF968}\SkinIrritationCorrosionInclusionRules.zip\Silicon ether(alkoxysilanes)_files\image001.gif

|  |
| --- |
| R can be any kind of groupSome alkoxysilanes hydrolyse rapidly when getting in contact with water, the resulting metabolite may cause only mild skin irritation. |

 | We modified the original profiler to allow R linked to any other atom. We also included methoxysilane into this category. |
| Silicon ethers (alkoxysilanes) with alpha keton groups | C:\Users\Atsu\AppData\Local\Temp\OASIS\10792\{E726224F-2195-4FD0-9BBF-6730534AF968}\SkinIrritationCorrosionInclusionRules.zip\Silicon ethers(alkoxysilanes) with alpha keton groups_files\image001.gif

|  |
| --- |
| R and R1 can be any kind of group |

 | We modified the original profiler to allow R linked to any other atom. |
| Substituted dihalogen-benzoic acids | C:\Users\Atsu\AppData\Local\Temp\OASIS\9176\{BA7A0612-858B-43B8-B1B0-7585D3F37A57}\SkinIrritationCorrosionInclusionRules.zip\Substituted dihalogen-benzoic acids_files\image001.gifR1-3 = Halogen (F, Cl, Br or I) or alkyl (aliphatic chain) | The original one does not cover cases in which R1, R2 or R3 is a halogen. We modified it to cover these chemicals. |

\* Etje Hulzebos, John D. Walker, Ingrid Gerner, and Kerstin Schlegel, Use of structural alerts to develop rules for identifying chemical substances with skin irritation or skin corrosion potential, QSAR Comb. Sci. 24 (2005) pp. 332-342