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Case Report

흡입노출에 의한 만성・발암성시험 대상물질 및 우선순위 선정 연구

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Selection of Candidate Materials and their Prioritization for Chronic Inhalation and Carcinogenicity Test

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ABSTRACT

Objectives: There is requirement to select candidate materials for chronic inhalation/carcinogenicity testing, so we would like to set the priority of candidate materials.

Methods and Results: We recommend the priorities for candidate materials based on the chemicals stipulated in the Occupational Safety and Health Act(OSHAct) and the Toxic Chemicals Control Act(TCCA) in Korea.

Conclusions: We presented candidate chemicals consisting of solids(powders), gases and liquids(Such as organic solvents) with priorities.

Key words: candidate materials, carcinogenic, chronic, inhalation

I. 서 론

암은 인류 역사의 시작과 함께 같이 존재해 온 질병으로, 현재 암은 대부분의 국가에서 순환기 질병 중 가장 높은 비중을 차지하는 사망 원인이 되고 있지만 확실한 치료효과를 기대할 수 있는 암 치료제는 아직도 개발되지 못한 실정이다(Fayed, 2014). 2005년 통계청이 발표한 사망원인 통계결과 중 주목되는 부분은 우리나라의 전체 사망자 중 1/4 가량이 암으로 숨질 정도로 암 사망률이 높고, 매일 162명이 암으로 목숨을 잃는다는 점은 정부가 좀 더 적극적으로 암 대책에 나서야 할 것임을 반증하고 있다(Statistics Korea, 2012). 중앙 암 등록본부에서는 우리나라의 모든 암 등록자료를 통합하여 국가 암 발생 DB를 구축하였으며, 동 DB는 중앙 암 등록자료, 지역 암 등록자료, 암종별 등록자료, 암 통계생산을 위한 보완조사 자료 및 통계청 암 사망자료를 포함, 이 자료를 이용하여 매년 암발생률을 산출하고 있다(Jung et al., 2014). 암 발생의 원인으로는 식습관(35%)과 흡연(30%)이 가장 큰 비중을 차지하였고, 감염(9%), 유전(5%), 직업(4%), 음주(3%) 등의 순으로, 음식 및 생활습관이 80% 이상을 차지하고 있다. 또한, 모반도체회사 근로자들의 백혈병 발병과 1급 발암물질인 석면검출 등의 논란을 계기로 최근 '직

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업성 암'에 대한 관심이 높아지고 있으며, 특히 개인의 직업력에 의한 직업성 암은 주로 30~40대의 젊은 연령에서 발생하고, 남자에 많으며, 발암물질의 작용을 받는 부위(Target organ), 즉 호발부위가 있어 한 부위에 다발적으로 생긴 암이 말기에 이를수록 여러 장기에 전이되는 경향이 있다. 직업력에 관련하여 노출기간과 잠복기가 존재하는데 방사선 노출에 의한 백혈병은 4~6년, 석면에 의한 악성중피종은 잠복기가 40년이나 된다(Ahn et al., 2010). 직업성 암에서 상대적으로 많이 발생하는 폐암의 원인으로 주목받는 작업환경 중의 발암물질은 자동차 배기가스의 벤조피렌, 니트로피렌, 쓰레기 소각장의 다이옥신 등 다양하다. 기타 방사선, 자외선 등의 물리적 인자와 유전적 인자, 적극적이고 경쟁심이 많아 평소 혈압이 높고 스트레스에의 면역력이 약한 사람들에서 암이 발생할 확률이 높은 것으로 알려져 있다. 특히 스트레스나 과식 등의 개인성향 및 담배, 자외선, 대기오염물질들로 인해 우리 몸에서 생성될 수 있는 활성산소는 암 발생의 직접적인 원인으로 대두되고 있다(Weinstei, 1991). 1970년대 이후 우리나라의 산업화와 함께 많은 화학물질의 사용이 증가되고 있으며, 결과적으로 이는 1980년대 이후의 중금속 중독, 유기용제 중독 및 직업성 암과 같은 독성 화학물질에 의한 직업성 질환의 증가로 나타났다. 대부분의 경우 1990년 이후 정부, 사업주, 근로자나 노동조합 등에서 작업환경 개선 등에 노력한 결과 진폐증과 같은 직업성 질환은 빠른 속도로 감소되었다. 직업성 암은 현재 발암물질의 사용을 제한, 금지하고 있지만 그 잠재적 영향(잠복기)이 길어 아직은 증가되고 있는 실정이다(Kang & Kim, 2010).

근로복지공단에서 운영하는 산업재해보상보험의 산업재해 보상 현황을 분석해 보면, 직업성 질환의 특성을 알 수 있다. 전체 직업성 질병의 1%는 암이었고, 그 원인이 되는 유해요인은 화학물질과 중금속 등이었다. 이는 우리나라의 근로자들에서 발생하는 직업성 암의 예방을 위해 관리정책이 필요함을 나타냈다(Ahn et al., 2010). 그러나 우리나라는 아직까지 이런 예상만큼 많은 직업성 암이 보고되고 있지 않다. 현재까지 직업성 암은 석면 노출, 크롬, 배기가스, 코크스 및 실리카 노출로 인한 폐암, 벤젠 또는 유기용제 노출로 인한 백혈병 및 벤지딘 염의 노출로 인한 방광암이 보고되었다. 긴 잠복기로 인해 직업성 암은 일반적으로 퇴직 이후에 발견되는 것이 사실이므로 특별한 주의가 필요하게 된다(Kang et al., 2001). 전체 암의 약 2~8%는 직업에 의한 것으로 생각되고 있으며, 특정 화학물질과 같은 직업 및 환경과 암과의 관계는 석면, 실리카, 목분진, 매연, 다환방향족탄화수소(벤조피렌), 중금속(비소, 크롬, 니켈), 방향족 아민(4-아미노비페닐, 벤지딘), 유기용제(벤젠, 염화비닐), 방사선/라돈 등의 실내오염물질(포름알데히드, 흡연) 등은 폐, 피부, 방광, 중피종이나 백혈병 등 특정 암의 발생과 관련된다(Yang, 2011). 상대적으로 암이 많이 발생하는 기관은 남성에서 폐, 간, 방광 및 피부였고, 여성에서는 간, 폐, 피부 및 방광이었다. 폐와 관련된 두 개의 직업적 사례들이 있었고, 직업성 암은 가까운 미래에 더욱 증가될 것으로 예측되므로 이를 검사하기 위한 노력들이 계속되어야 한다(Bae et al., 1999).

우리나라에서 중공업 및 화학공업은 1970년대 이후 빠른 성장을 이루어 왔고, 첫 번째 직업성 암은 1993년에 보고된 석면에 의한 중피종이었다. 안전보건공단 산업안전보건연구원은 1992년부터 직업성 암에 대한 역학조사를 수행해 왔으며, 이 조사에는 중피종, 폐암, 백혈병, 비호지킨성 림프종 및 방광암이 있었다. 1994년에 우리나라에서 발암물질에 노출된 근로자의 비율을 조사한 결과, 작업장에서 발암물질에 노출된 근로자의 현황에 대한 자세한 정보를 얻을 수 있었으며, 근로자 보상 및 복지서비스(COMWEL) 전자 DB에 의하면 가장 일반적인 암은 소화기계 암이었다. 한편 가장 높은 승인율을 보인 암은 호흡기 암, 림프 또는 조혈기계 암이었다(Kim et al., 2010). 업종별로는 제조업이 가장 많았지만, 승인율은 광업 및 채석업이 가장 높았다(Lee et al., 2011). COMWEL의 요청으로 산업안전보건연구원은 1992년부터 근로자의 업무연관성에 대한 폐암의 가장 흔한 원인인 석면, 6가 크롬, 다환방향족탄화수소(PAHs) 및 결정형 실리카에 대한 조사를 하였으며, 석면 노출은 모든 악성 중피종 사례들과 관련이 있었다. 다른 종류의 호흡기 암은 후두암, 비강암 및 인두암 등이었다(Kang et al., 2001). 신규화학물질을

감안하면 우리나라에서 직업성 암의 발생은 미래에 더욱 증가될 것이다. 많은 요인들이 암 발생을 주도할 것이며, 직업성, 유전적 및 생식적 요인들이 관련될 것이다.

현대의 화학물질 중독은 사고성 급성중독에서 만성중독으로 변화하고 있고, 직업별 발생 양상이 고농도・급성중독에 의한 재래형에서 저농도・만성중독으로 변화하고 있다. 화학물질 유해성 확인을 위해서는 급성독성 및 만성독성 등 유해성을 종합적으로 평가하는 것이 필수이나 만성독성평가 설비는 부재한 실정이다. 특히 만성독성에 의한 직업병 발병은 이미 많은 근로자들이 장기간 노출로 인하여 건강장해를 입은 후에야 인지할 수 있으므로, 사용 전 만성독성에 대한 정보는 선진 화학물질관리를 위한 핵심요소라고 할 수 있다. 만성 직업성 질환은 사전에 예측되어야 실질적인 예방이 가능하고, 이황화탄소, 망간, 석면 등에 의한 직업성 암 등이 실제 질병이 발생한 후에서야 경각심을 갖게 되었으며, 이로 인한 사회적 비용이 증가했을 뿐만 아니라 근로자와 그 가족의 큰 고통이 수반되었다. 그러므로 만성독성 질환의 예방을 위해서는 현재 우리나라에서 유통되는 화학물질에서 주요 만성독성/발암성이 발생할 가능성이 있는 대상 화학물질을 사전에 선정하여 구체적인 예방활동을 선행하는 것이 무엇보다 시급히 요구되고 있다. 이러한 사전예방적인 대책은 수립하기 위해서는 과학적 근거가 필요하며, 그 근거의 가장 기본적인 것이 만성독성/발암성 시험이라 할 수 있다(Han, 2009).

이런 시대 상황에 맞추어, 산업안전보건연구원에서는 산업화학물질의 흡입독성시험 자료 생산을 위한 GLP(Good Laboratory Practice) 만성흡입독성 및 발암성시험 분야의 구축을 추진 중에 있으며, 실험동물을 이용 만성 흡입독성시험을 통하여 저 농도, 장기노출 근로자의 인체에 미치는 유해성을 예측하고 건강장해 원인규명 자료 및 독성시험을 통한 물질의 유해성분류 및 노출기준설정의 기초자료를 제공하고, 저농도 장기노출에 대한 직업성 암 예방 근로자 건강장해 예방하기 위해, 저 농도 만성 흡입노출 화학물질에 대한 유해성 평가 인프라를 구축하고 있으며, 이의 법적 추진근거는 산업안전보건법 제39조(유해인자의 관리 등) 및 산업안전보건법 시행규칙 제81조(유해인자의 분류・관리) 이다(MoEL, 2014a; 2014b; 2013). 만성발암성시험시설 건물신축 및 흡입설비 도입은 본격적으로 시험시설 신축 및 관련 설비 도입이 시작되는 시점부터 준공되기까지 전담인력으로 운영될 계획이고, 만성센터 신축 및 흡입설비 도입 관련하여 분야별로 업무 분담을 하고 있다. 또한 GLP 인증을 위한 검증(Validation)을 실시하는데, 건축설계에 따라 시설의 건축추진 및 흡입챔버 등의 시험설비 도입과 GLP시험시설에 합당하게 신축될 수 있도록 검증을 통한 신뢰성 확보를 목표로 하고 있으며, 흡입노출, 동물사육, 병리검사, 신뢰성보증 등 관련 전문 인력 확보를 위한 중・장기 발전계획을 수립하고 있다.

본 연구에서는 위와 같은 목적으로 진행하는 산업안전보건연구원의 사업에 도움이 되고자 흡입노출에 의한 만성・발암성시험이 꼭 필요한 적시성 및 적합성을 고려한 시험대상 후보물질 목록을 그 우선순위와 함께 제안함으로써 동 시험의 원활한 수행에 기여하고자 하였다.

Ⅱ. 연구 방법

본 흡입노출에 의한 만성・발암성시험 대상 후보물질 선정 및 우선순위의 결정은 아래의 방법으로 수행하였다.

1) 모집단의 설정 : 당초 본 연구과제의 세부추진계획에서, 동 대상물질의 선정 작업을 위한 1차 모집단은 산업안전보건법상 관리대상물질을 포함한 기존 화학물질 35,000여종과 1999년부터 2013년까지의 사업주가 고용노동부에 그 유해성・위험성을 조사하여 제출한 신규화학물질 6,000여종으로 계획하였으나, 40,000종이 넘는 화학물질에 대한 정보를 각각 검색하고 분석하기에는 현실적으로 1년이라는 연구기간이 부족하였다. 따라서 위 모집단 데이터베이스(DB)에서, 아래의 인터넷 정보 사이트를 참고하여 발암성이 예측되는 물질들을 우선적으로 DB 추출하여 모집단으로 활용하였다.

(1) Carcinogenic Potency DB : 화학물질의 잠재적 발암성을 예측하여 정보를 제공하는 사이

(2) Comparative Toxicogenomics Database : 독성유

전체 정보를 기초로 발암관련 유전자의 발현과 관련된 화학물질 정보를 제공하는 사이

(3) 미국환경청(United States Environmental Protection Agency; EPA) ACToR : EPA에서 제공하는 전산 독성연구 프로그램 정보로서, QSAR과 같은 화학물질의 독성영향 예측 정보를 제공하는 사이트

2) 위의 화학물질 유해성 관련 인터넷 정보 사이트에서 검색된 화학물질(기존화학물질 중 2,482종) 및 신규화학물질 중 CAS 번호가 부여된 단일물질(중합체 제외)을 모집단으로 활용하였다.

3) 위 모집단의 화학물질들을 중심으로,

- KOSHANET MSDS등을 이용하여 각 기관(IARC, NTP, ACGIH, EU 등)의 발암성구분을 입력
- NTP Database Search를 이용하여 GLP만성 · 발암성시험 report가 있는지 검색
- Chemical Carcinogenesis Research Information System(CCRIS)을 이용 그 밖의(Non-GLP등) 만성 · 발암성시험 report가 있는지 검색
- CCRIS에서 Tumor inhibition/promotion studies 결과가 있는지 검색
- 흡입노출을 통한 만성 · 발암성시험 report가 없는 물질에 대해 "O"표시
- 흡입노출을 통한 GLP만성 · 발암성시험 report가 이미 있으므로 시험이 절대로 필요하지 않은 물질은 "XX"표시
- 기타의 물질은 “△” 표시
- oral route에서 carcinogenicity positive 여부 검색
- KOSHANET MSDS 정보에서 TopKat computed probability of mutagenicity 검색
- KOSHANET MSDS 정보에서 생식세포변이원성 Category 검색
- 증기압은 4 mmHg 이상, 비중은 1.5 미만의 발생(Generation) 가능한 물질을 선택
- 유럽화학물질청(ECHA)의 만성/발암성시험 자료 여부 확인
- ECHA의 유통량 확인(유통량 밴드 1,000톤 이상)
- OECD SIDS report 및 Japan challenge program 결과와 상호 비교

4) 우선순위의 결정 : 위의 방법으로 자료 및 정보 검색한 내용을 Excel 프로그램으로 입력하고, 정렬하여, 연구결과물로서의 DB 파일로 정리하였으며, 시험대상 후보물질로 선정을 위해 아래의 기준으로 그 우선순위를 부여하였으며, 그 우선순위를 점수화하지는 않았다.

- OECD SIDS와 같은 국제적인 협력을 통해 각 회원국에 배당된 화학물질 유해성 평가 프로그램에서 아직 평가되지 않은 물질
- OECD SIDS Occupational Exposure 정보 반영
- ECHA에서 그 발암성을 결정하는데 있어 근거자료가 없어서 확실한 결론을 내지 못하고 있는 물질
- ECHA에서 그 발암성을 결정하는 있어 근거자료가 부족하여 확실한 결론을 내리지 못하고 있는 물질
- ECHA의 유통량 확인(유통량 밴드 1,000톤 이상)에서 그 유통량이 많은 물질
- Japan Challenge 프로그램에서 유해성을 평가하지 않은 물질
- 위 물질 중 만성독성, 발암성 및 유전독성이 예측되는 물질

본 사례보고에서는 흡입노출을 통한 만성독성 및 발암성시험 대상 후보물질을 제시하기 위하여 위에서 제시한 절차로 물질 정보, 구분 및 고찰을 통해 우선순위를 포함한 대상 후보물질을 제시하는데 있어 EURAM scoring 등의 점수화 방법을 사용하지는 않았고, 선정 및 그 우선순위에 대한 근거자료들 만을 제시하였다.

Ⅲ. 연구 결과

1. 만성 · 발암성시험 대상물질의 선정

흡입노출을 통한 만성독성 및 발암성시험 대상 후보물질을 제시하기 위하여, 위 연구방법에서 제시한 절차로 물질 정보, 구분 및 고찰을 통해 우선순위를 포함한 대상 후보물질을 아래 Table 1~3과 같이 선정하였으며, 고체(분말), 기체(가스 포함) 및 액체(유기용제 등)로 구분하여 제시하였으며, 선정 및 우선순위의 근거(Grounds of selection)를 제시하였다.

Table 1. Candidate chemicals with chronic inhalation and carcinogenicity test(Solid phase)

Chemical name	CAS No	Priority	Grounds of selection
Pyrithione zinc	13463-41-7	1	· Carcinogenicity classification - No Data · EPA ACToR - Ha, Cr, Ca, G · Specific gravity 1.782 · Stomach Noeoplams related · ECHA tonnage band 1,000 - 10,000 tpa · ECHA report GLP: SD rat-oral: gavage -There were no dose related or significantly increased incidences of tumours · no Pre-GLP: rat-oral: feed-No adverse effect was apparent · GLP: Crl:Cd-1(SD_BR(VAF plus) rat - oral: gavage · GLP: CD-1 mouse-dermal- Histopathology: No effects on tumour incidence. · OECD SIDS N/A · Japan Challenge N/A · Acute toxicity(Inhalation: Dust/Mist) : Class 2 · TLV - No Data
Zinc(as fume)	7440-66-6	2	· Carcinogenicity classification - No Data · App. E(Chem for In-Depth Evalu) of NTP report vol 12 · EPA ACToR Ha, Cr, Ca, G · ECHA tonnage band 1,000,000 - 10,000,000 tpa · ECHA data lacking · OECD SIDS sponsored by the Netherlands(1995) · Japan Challenge N/A · There is also no clear experimental or epidemiological evidence for a direct carcinogenic action of zinc. · Occupational Exposure related · Vapor pressure 0.1 ㎪(487℃), Specific gravity 7.14 · TLV - No Data
Triclosan	3380-34-5	3	· Carcinogenicity classification - No Data · App. E(Chem for In-Depth Evalu) of NTP report vol 12 · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 6.45e-07 mmHg · Hepatocellular Carcinoma 관련 · ECHA tonnage band 1,000 - 10,000 tpa · GLP: SD rat - oral: feed - There were no treatment-related tumours · GLP: Bio F1D Alexander Syrian hamster - oral: feed - There was no evidence · non-GLP: CD-1 mouse - dermal - The results showed that triclosan was not carcinogenic to the mice · non-GLP: Albino mice - oral: feed · GLP: CD-1 mouse - oral: feed - · OECD SIDS sponsored by Australia(2003) · Occupational Exposure related · TLV - No Data
Sodium chlorite	7758-19-2	4	· IARC group 3 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Specific gravity 2.47 · Germ cell mutagenicity Class 2 · ECHA tonnage band 1,000 - 10,000 tpa · GLP no data - Fischer 344 rat - oral: drinking water - Tumors developed · GLP no data - Fischer 344 rat - oral: drinking water - No statistically significant differences were observed in the incidences of tumor formation · GLP no data - Sencar mouse - dermal · GLP no data - Sencar mouse - dermal - No skin tumors developed · GLP no data - B6C3F1 mouse - oral: drinking water - These results indicated no clear evidence of a carcinogenic potential · GLP no data - B6C3F1 mouse - oral: drinking water - Long-term in vivo carcinogenicity tests · SIDS sponsored by BIAC(2006) · Occupational Exposure related

Chemical name	CAS No	Priority	Grounds of selection
			· Japan Challenge N/A · Acute toxicity(Inhalation: Dust/Mist) : Class 2 · TLV - No Data
Resorcinol	108-46-3	5	· IARC group 3, ACGIH A4 · has NTP GLP carcinogencity report · has TOXNET-CCRIS carcinogencity report · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 0.0002 mmHg, Specific gravity 1.2717 · ECHA tonnage band 10,000 - 100,000 tpa · GLP: Fischer 344 rat - oral: gavage - Result(Carcinogenicity): Negative · GLP: B6C3F1 mouse - oral: gavage - Result(Carcinogenicity): Negative · SIDS sponsored by Japan(2002) · Occupational Exposure related · has report in Japan Challenge program · TWA(ROK) : 10 ppm 45 ㎎/㎥ STEL(ROK) : 20 ppm 90 ㎎/㎥ · ACGIH TWA 10 ppm STEL 20 ppm
Sodium benzoate	532-32-1	6	· Carcinogenicity classification - No Data · App. E(Chem for In-Depth Evalu) of NTP report vol 12 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 3.67e-09 mmHg, Specific gravity 1.44 · ECHA tonnage band 10,000 - 100,000 tpa · GLP no data - Fischer 344 rat - oral: feed - not carcinogenic · GLP no data - Swiss mouse - oral: drinking water - not carcinogenic · SIDS sponsored by The Netherland(2000) · has report in Japan Challenge program · TLV - No Data
Sodium Dodecyl Sulfate	151-21-3	7	· Carcinogenicity classification - No Data · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 0.00000000000047 ㎜Hg, Specific gravity >1.1 · Germ cell mutagenicity Class 2 · Hepatocellular Carcinoma related · ECHA tonnage band 1,000 - 10,000 tpa · Non-GLP: Colworth Wistar rat - oral: feed - The material was not tumorigenic · Non-GLP: Osborne-Mendel rat - oral: feed - There was no increase in tumor rates. · SIDS sponsored by Germany(1991) · Occupational Exposure related · has report in Japan Challenge program · TLV - No Data
Benzoyl peroxide	94-36-0	8	· IARC group 3, ACGIH A4 · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 7.06e-05 mmHg, Specific gravity 1.334 · Skin Neoplasms related · ECHA tonnage band 1,000 - 10,000 tpa · GLP no data - Sencar mouse - dermal - Benzoyl peroxide was inactive on the skin as a complete carcinogen · non-GLP: Albino mouse and rat - oral: feed - didn't elicit any signf of carcinogenic activity in mice and rats. · GLP - B6C3F1/CrIBR mouse - dermal - no histologic findings indicative of oncogenicity · GLP no data - Used(Hr) stock albino mouse - dermal - · GLP no data - Normal human bronchial epithelial cell - · GLP no data - hr Oslo strain and SENCAR mouse - dermal - No induction of carcinoma · GLP no data - Syrian golden hamster - skin(Painting of the hamster buccal pouch) - · GLP no data - Pathogen-free Syrian golden hamster - dermal - able to promote the formation of dermally located Melanotic tumors. · GLP no data - Sencar mouse - dermal - Benzoyl peroxide enhanced the progression

Chemical name	CAS No	Priority	Grounds of selection
			of preexisting papillomas · GLP no data - mouse - dermal - · Swiss Albino mouse - dermal - · GLP no data - Sencar mouse - dermal - a mouse skin promoter but was inactive as a complete carcinogen or as a tumor initiator. · GLP no data - Sencar mouse - dermal - a potent promoter and has possible carcinogenic action. · Rat, mice, human - dermal - no evidence to support development of skin cancer in humans · SIDS sponsored by Korea(1999) · Occupational Exposure related · has report in Japan Challenge program · TWA(ROK) : 5 ㎎/㎥ · ACGIH TWA 5 mg/㎥

Ha: Hazards, Cr: Chronic, Ca: Carcinogenic, G: Genotoxic
tpa: ton per annually
TLV:Threshol Limit Value, TWA: Time-Weighted Average, STEL: Short-term exposure limit

Table 2. Candidate chemicals with chronic inhalation and carcinogenicity test(Gas phase)

Chemical name	CAS No	Priority	Grounds of selection
Butane	106-97-8	1	· EU CLP Carc. 1A · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure ≥5, Specific gravity 0.6 · Germ cell mutagenicity Class 1B · ECHA tonnage band 1,000,000 - 10,000,000 tpa · OECD SIDS N/A · has report in Japan Challenge program · TWA(ROK) : 800 ppm 1900 ㎎/㎥ · ACGIH TWA 1000 ppm
Propane	74-98-6	2	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure ≥5, Specific gravity 0.5853(At -45℃) · ECHA tonnage band 1,000,000 - 10,000,000 tpa · OECD SIDS N/A · has report in Japan Challenge program · TLV - No Data
Dimethyl ether	115-10-6	3	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 4450 mmHg, Specific gravity 0.61 · ECHA tonnage band 10,000 - 100,000 tpa · GLP - Crl:CD(R)(SD)BR rat - inhalation: vapour - whole body - No neoplastic lesions were observed · OECD SIDS N/A · has report in Japan Challenge program · TLV - No Data
Chloromethane; Methyl chloride	74-87-3	4	It was excluded because this chemical was already performed in Japan Bioassay Center.
2-Butene	107-01-7	5	· Carcinogenicity classification - No Data · EPA ACToR Ha, Cr, Ca, G · Vapor pressure ≥5 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by The Netherlands(1990) · Occupational Exposure possible

Chemical name	CAS No	Priority	Grounds of selection
			· has report in Japan Challenge program · TLV - No Data
Butylene; But-1-ene	106-98-9	6	· Carcinogenicity classification - No Data · Vapor pressure ≥5 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by The Netherlands(2000) · Occupational Exposure possible · has report in Japan Challenge program · TLV - No Data
Methylamine	74-89-5	7	It was excluded because this chemical was already performed in Japan Bioassay Center.
1,1-Difluoroethane	75-37-6	8	· ACGIH A4 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure ≥5, Specific gravity 0.896 · ECHA tonnage band 1,000 - 10,000 tpa · GLP - Crl:CD®Br rat - inhalation: vapour - whole body - was not carcinogenic · TLV - No Data

Ha: Hazards, Cr: Chronic, Ca: Carcinogenic, G: Genotoxic
tpa: ton per annually
TLV:Threshol Limit Value, TWA: Time-Weighted Average, STEL: Short-term exposure limit

Table 3. Candidate chemicals with chronic inhalation and carcinogenicity test(Liquid phase)

Chemical Name	CAS No	Priority	Grounds of selection
Dimethyl disulfide	624-92-0	1	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 28.7 mmHg, Specific gravity 1.06 · ECHA tonnage band 10,000 - 100,000 tpa · OECD SIDS N/A · Japan Challenge N/A · Acute toxicity(Inhalation: Vapor) : Class 3 · ACGIH TWA 0.5 ppm
Isoamyl acetate	123-92-2	2	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 5.6 mmHg, Specific gravity 0.87 · ECHA tonnage band 1,000 - 10,000 tpa · No GLP - Wistar rat - subcutaneous - No spontaneous malign tumours were observed in the control animals.10 had malign neoplasms(Liver cell sarcoma, 2 hepatocellular carcinoma, 1 spleen carcinoma, 1 glandular stomach carcinoma and 2 myeloid leukemia; 10 benign tumours were also observed) after s.c. treatment. · No GLP - Wistar rat - oral: gavage - No spontaneous malign tumours were observed in the control animals. 4 malign tumours were observed after oral treatment: 1 myeloid leukemia, 2 liver cell carcinoma and 1 gastroesophageal vestibule carcinoma(3 benign tumors were also observed). · No GLP - Wistar rat - oral: gavage - These data and their interpretation should be regarded together in a weight of evidence approach to evaluate a possible carcinogenic effect of isopentyl acetate. · GLP no data - These data should be regarded together in a weight of evidence approach to evaluate possible cancerogenic effects of isopentyl acetate. · No GLP - Wistar rat - subcutaneous - These data and their interpretation should be regarded together in a weight of evidence approach to evaluate a possible carcinogenic effect isopentyl acetate. · SHOWED LIVER CARCINOMAS & SARCOMAS, SPLEEN SARCOMAS, & PROVENTRICULAR CARCINOMAS & MYELOID LEUKEMIA. · OECD SIDS N/A

Chemical name	CAS No	Priority	Grounds of selection
			· Japan Challenge N/A · TWA(ROK) : 50 ppm 260 ㎎/㎥ STEL : 100 ppm 520 ㎎/㎥ · ACGIH TWA 50 ppm STEL 100 ppm
Isopropyl ether	108-20-3	3	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 149 mmHg, Specific gravity 0.7 · ECHA tonnage band 1,000 - 10,000 tpa · GLP - SD rat - oral: gavage - limited usefulness for the purpose of identifying a potential carcinogenic effect of diisopropyl ether as it provides no convincing evidence for such an effect. · OECD SIDS N/A · Japan Challenge N/A · TWA(ROK) : 250 ppm 1025 ㎎/㎥ STEL : 310 ppm 1320 ㎎/㎥ · ACGIH TWA 250 ppm STEL 310 ppm
4-Methylmorpholine	109-02-4	4	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Ca, G · Vapor pressure 13.2 mmHg, Specific gravity 0.92 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA lack of carcinogenicity data · OECD SIDS N/A · Japan Challenge N/A · TLV - No Data
5-Methyl-2-hexanone	110-12-3	5	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 5.77 mmHg, Specific gravity 0.89 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA carcinogenicity report - No data · OECD SIDS N/A · Japan Challenge N/A · Acute toxicity(Inhalation: Vapor) : Class 4 · TWA(ROK) : 50 ppm 240 ㎎/㎥ · ACGIH TWA 50 ppm
Piperidine	110-89-4	6	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 32.1 mmHg, Specific gravity 0.862 · ECHA tonnage band 1,000 - 10,000 tpa · GLP no data - ddy mouse - implantation in urinary bladder - may have caused the significantly higher incidence of bladder cancer than that in control Group A(P <0.001). · GLP no data - Fischer 344 rat - intraperitoneal - Piperidine was negative in this test system. · No GLP - Strain A mouse - intraperitoneal - Compared to the control with 0.22 lung tumours per mouse, piperidine was entirely negative. · No GLP - SIV 50 rat - oral: feed - A limited examination of the organs revealed no increased tumour incidence. · No GLP - mouse - implantation - Carcinoma were observed. · No GLP - SD rat - oral: drinking water - No specific tumors from N-nitrosopiperidine were observed. · No GLP - MRC rat - oral: drinking water - No significant difference between untreated or nitrite treated animals and treated groups(Piperidine, piperidine plus nitrite) was observed in number of tumour bearing animals and in types of tumours. Common(Spontaneous) tumours observed in treated and control rats were mainly pituitary adenomas and tumours of breast, uterus or testis. · OECD SIDS N/A · Japan Challenge N/A

Chemical name	CAS No	Priority	Grounds of selection
			· Acute toxicity(Inhalation: Vapor) : Class 3 · TLV - No Data
Trimethyl orthoformate	149-73-5	7	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 81.4 mmHg, Specific gravity 0.97 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA lack of carcinogenicity data · OECD SIDS N/A · Japan Challenge N/A · TLV - No Data
Ether	60-29-7	8	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 538 mmHg, Specific gravity 0.7 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA lack of carcinogenicity data · OECD SIDS N/A · Japan Challenge N/A · TWA(ROK) : 400 ppm 1200 ㎎/㎥ STEL : 500 ppm 1500 ㎎/㎥ · ACGIH TWA 400 ppm STEL 500 ppm
2-Chloropropane	75-29-6	9	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 515 mmHg, Specific gravity 0.8617 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA lack of carcinogenicity data · OECD SIDS N/A · Japan Challenge N/A · TLV - No Data
1,2-Diaminopropane	78-90-0	10	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 10.6 mmHg, Specific gravity 0.9 · ECHA tonnage band 1,000 - 10,000 tpa · GLP no data - C3H mouse - dermal - The results indicate no evidence for cutaneous oncogenicity when EDA was applied to the skin of mice for their lifetime. · OECD SIDS N/A · Japan Challenge N/A · TLV - No Data
Methyl chloroacetate	96-34-4	11	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 7.63 mmHg, Specific gravity 1.2 · ECHA tonnage band 1,000 - 10,000 tpa · GLP no data - Strain A mouse - intraperitoneal - Methyl chloroacetate was not tumorigenic by pulmonary adenoma bioassay. · OECD SIDS N/A · Japan Challenge N/A · Acute toxicity(Inhalation: Vapor) : Class 2 · TLV - No Data
tert-Butyl methacrylate	585-07-9	12	· Carcinogenicity classification - No Data · Haz-Map No Data · EPA ACToR Ha, Ca, G · Vapor pressure >5, Specific gravity 0.88 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA lack of carcinogenicity data · OECD SIDS N/A

Chemical name	CAS No	Priority	Grounds of selection
			· has report in Japan Challenge program · TLV - No Data
tert-Butylalcohol	75-65-0	13	· ACGIH A4 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 42 mmHg, Specific gravity 0.8 · ECHA tonnage band 1,000,000 - 10,000,000 tpa · OECD SIDS N/A · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 4 · TWA(ROK) : 100 ppm 300 ㎎/㎥ STEL : 150 ppm 450 ㎎/㎥ · ACGIH TWA 100 ppm
Chlorobenzene	108-90-7	14	· ACGIH A3 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 12 ㎜Hg, Specific gravity 1.1058 · Germ cell mutagenicity : Class 2 · Hepatocellular Carcinoma related · ECHA tonnage band 10,000 - 100,000 tpa · GLP no data - Equivocal evidence for carcinogenicity for chlorobenzene. · GLP no data - Fischer 344 rat - oral: gavage - chlorobenzene administration increased the occurence of neoplastic nodules of the liver in high dose(120 mg/kg/day) male F344/N rats, providing some but not clear evidence of carcinogenicity. Carcinogenic effects of chlorobenzene were not observed in female F344/N rats. · GLP no data - SD rat - intraperitoneal - · GLP no data - oral: gavage - the cancer results are equivocuos for male rats, but negative for female rats and mice belonging to both species. · GLP no data - rats, mice, hamsters, non-human primates, dogs - Chlorobenzene is evaluated as positive as carcinogenic in rat liver. · GLP no data - Fischer-344/N(F344 rats), B6C3F1(Mouse) - oral: gavage - neoplastic nodules in male rats have been observed. · GLP no data - No evidence of carcinogenicity of monochlorobenzene in animals and limited evidence for genotoxicity. · GLP no data - B6C3F1 mouse - oral: gavage - No site-specific tumors or non-neoplastic pathology occurred · OECD SIDS N/A · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 4 · Carcinogenicity : Class 2 · TWA(ROK) : 10 ppm 46 ㎎/㎥ STEL : 20 ppm 94 ㎎/㎥ · ACGIH TWA 10 ppm
Cyclohexylamine	108-91-8	15	· ACGIH A4 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 10.1 mmHg, Specific gravity 0.86 · Germ cell mutagenicity : Class 1B · ECHA tonnage band 10,000 - 100,000 tpa · GLP no data - FDRL rat - oral: feed - the substance was evalutated not to be carcinogenic. · No-GLP - Wistar rat - oral: feed - Cyclohexylamine hydrochloride did not show any carcinogenic potential. · GLP - no data - ASH-CS1 mouse - oral: feed - the incidence of tumors up to and including 3000 ppm(Approx. 400 mg/kg bw/day) cyclohexylamine hydrochloride. · No GLP - rat(Albino) - oral: feed - no tumours were detected. · GLP no data - Human WI 38, Rodent BHK 21 mammalian cells - in vitro test - no cell transformation activity was observed · No-GLP - Swiss mouse - oral: feed - No differences in tumor incidences between treated and control animals · No-GLP - Beagle dog - oral: capsule - no carcinogenic effect · No-GLP - Charles River rat - oral: feed - 1 invasive transitional cell carcinoma

Chemical name	CAS No	Priority	Grounds of selection
			of the bladder(Grade 2) was observed; no invasion of the muscular wall, no metastatic lesions. · No - GLP - SD rat-oral: feed - no tumours. · OECD SIDS N/A · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TWA(ROK) : 10 ppm 40 ㎎/㎥ · ACGIH TWA 10 ppm
Pyridine	110-86-1	16	· IARC group 3, ACGIH A3 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 20.8 mmHg, Specific gravity 0.98 · ECHA tonnage band 1,000 - 10,000 tpa · GLP - Fischer 344 rat - oral: drinking water · GLP - Wistar rat - oral: drinking water - The incidence of testicular adenoma in rats exposed to 400 ppm was significantly increased compared to controls. There is equivocal evidence of carcinogenicity in the male Wistar rat based on interstitial cell neoplasm of the testis. · GLP - B6C3F1 mouse - oral: drinking water - Hepatocellular neoplasms, including hepatoblastomas, in exposed male and female mice were increased in a dose-related manner. Incidences of hepatocellular adenoma were significantly increased relative to controls in 250 ppm males and females and 1000 ppm males. Incidences of hepatocellular carcinoma and hepatoblastoma were significantly increased relative to controls in all exposed groups of males and females except for the incidence of hepatoblastoma in 125 ppm females. Incidences of hepatocellular adenoma, hepatocellular carcinoma or hepatoblastoma were significantly increased in all exposed male groups and in 250 and 500 ppm females relative to controls. There was clear evidence of carcinogenic activity in mice, based on hepatocellular carcinoma and hepatoblastoma. · GLP - Fischer 344 rat - oral: drinking water - Incidences of renal tubule adenoma and renal tubule adenoma plus carcinoma in high dose males were significantly increased compared to controls. The severity of nephropathy in males increased slightly with exposure concentration. Incidences of mononuclear cell leukemia in female rats were significantly increased in the 200 and 400 ppm groups compared to controls. There was some evidence of carcinogenic activity in male F344 rats based on a finding of increased renal tubule neoplasms. · GLP no data - not restricted to any one route of exposure - There is limited evidence in experimental animals for the carcinogenicity of pyridine. Pyridine is not classifiable as to its carcinogenicity to humans(Group 3). · OECD SIDS N/A · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 4 · TWA(ROK) : 2 ppm 6 ㎎/㎥ · ACGIH TWA 5 ppm
1,3-Dioxolane	646-06-0	17	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 70 mmHg, Specific gravity 1.06 · Germ cell mutagenicity : Class 2 · ECHA tonnage band 1,000+ tpa · No GLP - Albino rat - oral: drinking water - The audit of the draft chronic study with Dioxolane in rats concluded that the study contains accurate toxicological information concerning the effects of Dioxolane administered to the drinking water. An increase in tumour incidence was not reported. · OECD SIDS N/A · has report in Japan Challenge program · ACGIH TWA 20 ppm
Amylene	513-35-9	18	· Carcinogenicity classification - No Data · Haz-Map data available

Chemical name	CAS No	Priority	Grounds of selection
			· EPA ACToR Ha, Cr, Ca, G · Vapor pressure 468 mmHg, Specific gravity 0.6623 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA Carc. 2 H351: Suspected of causing cancer. · SIDS sponsored by United States(2000) · Occupational Exposure possible · Japan Challenge N/A · TLV - No Data
sec-Butyl alcohol	78-92-2	19	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 18.3 mmHg, Specific gravity 0.81 · ECHA tonnage band 100,000 - 1,000,000 tpa · ECHA data lacking · SIDS sponsored by United States(1991) · Occupational Exposure possible · has report in Japan Challenge program · TWA(ROK) : 100 ppm 305 ㎎/㎥ STEL : 150 ppm 455 ㎎/㎥ · ACGIH TWA 100 ppm
Isopropyl acetate	108-21-4	20	It was excluded because this chemical was already performed in Japan Bioassay Center.
Methylcyclohexane	108-87-2	21	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 46 mmHg, Specific gravity 0.8 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA data lacking · SIDS sponsored by Japan(2011) · Japan Challenge N/A · TWA(ROK) : 400 ppm 1600 ㎎/㎥ · ACGIH TWA 400 ppm
Di-tert-butyl peroxide	110-05-4	22	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 25.1 mmHg, Specific gravity 0.8 · Germ cell mutagenicity : Class 2 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA data lacking · SIDS sponsored by United States(2000) · Japan Challenge N/A · TLV - No Data
Propionaldehyde	123-38-6	23	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 317 mmHg, Specific gravity 0.8 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA data lacking · SIDS sponsored by United States(1990) · Japan Challenge N/A · ACGIH TWA 20 ppm
Trichlorovinyl silane	75-94-5	24	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 65.9 mmHg, Specific gravity 1.27 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA data lacking · SIDS sponsored by United States(2002) · Occupational Exposure possible

Chemical name	CAS No	Priority	Grounds of selection
			· Japan Challenge N/A · TLV - No Data
Heptane	142-82-5	25	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 46 mmHg, Specific gravity 0.68 · ECHA tonnage band 1,000+ tpa · ECHA data lacking · SIDS sponsored by United States(2001) · Occupational Exposure related · Japan Challenge N/A · TWA(ROK) : 400 ppm 1600 ㎎/㎥ STEL : 500 ppm 2000 ㎎/㎥ · ACGIH TWA 400 ppm STEL 500 ppm
Isooctane	540-84-1	26	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 49.3 mmHg, Specific gravity 0.69 · ECHA tonnage band 1,000+ tpa · ECHA lack of carcinogenicity data · SIDS sponsored by United States(2001) · Occupational Exposure related · Japan Challenge N/A · TLV - No Data
Methyldichlorosilane	75-54-7	27	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 429 mmHg, Specific gravity 1.1 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by United States(2013) · Occupational Exposure related · Japan Challenge N/A · TLV - No Data
Dimethyldichlorosilane	75-78-5	28	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 144 mmHg, Specific gravity 1.07 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by United States(2003) · Occupational Exposure related · Japan Challenge N/A · Acute toxicity(Inhalation: Gas) : Class 3 · TLV - No Data
tert-Amyl methyl ether	994-05-8	29	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 75 mmHg, Specific gravity 0.77 · ECHA tonnage band 100,000 - 1,000,000 tpa · GLP no data - SD rat - oral: gavage - When all malignant tumours frequencies were compared no differences were seen between the TAME-treated and controls. The following tumours were reported in creased incidences, although most of them did not have statistical significance. · SIDS sponsored by Finland(2000) · Japan Challenge N/A · ACGIH TWA 20 ppm
Isopropylamine	75-31-0	30	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 580 mmHg, Specific gravity 0.694

Chemical name	CAS No	Priority	Grounds of selection
			· ECHA tonnage band 10,000+ tpa · SIDS sponsored by United States(2001) · Occupational Exposure related · Japan Challenge N/A · Acute toxicity(Inhalation: Vapor) : Class 4 · TWA(ROK) : 5 ppm 12 ㎎/㎥ STEL : 10 ppm 24 ㎎/㎥ · ACGIH TWA 5 ppm
Dibutyl ether	142-96-1	31	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 6.01 mmHg, Specific gravity 0.7684 · ECHA tonnage band 1,000 - 10,000 tpa · SIDS sponsored by Germany(2003) · Occupational Exposure related · Japan Challenge N/A · TLV - No Data
1,3-Pentadiene	504-60-9	32	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 405 mmHg, Specific gravity 0.6952 · ECHA tonnage band 1,000 - 10,000 tpa · SIDS sponsored by United States(1990) · A related isomer, isoprene did not appear to be carcinogenic in rats at an inhalation dose up to 7000 ppm. · Japan Challenge N/A · TLV - No Data
Ethyl mercaptan	75-08-1	33	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 529 mmHg, Specific gravity 0.839 · ECHA tonnage band 1,000 - 10,000 tpa · SIDS sponsored by United States(2003) · Japan Challenge N/A · Acute toxicity(Inhalation: Vapor) : Class 4 · TWA(ROK) : 0.5 ppm 1 ㎎/㎥ · ACGIH TWA 0.5 ppm
Dimethyl sulfide	75-18-3	34	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 502 mmHg, Specific gravity 0.85 · ECHA tonnage band 1,000 - 10,000 tpa · SIDS sponsored by United States(2004) · Occupational Exposure related · Japan Challenge N/A · ACGIH TWA 10 ppm
t-Butyl mercaptan	75-66-1	35	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 181 mmHg, Specific gravity 0.79426 · ECHA tonnage band 1,000 - 10,000 tpa · SIDS sponsored by United States(2003) · Japan Challenge N/A · TLV - No Data
N,N-Dimethylethylamine	598-56-1	36	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 352 mmHg, Specific gravity 0.675

Chemical name	CAS No	Priority	Grounds of selection
			· ECHA tonnage band 1,000+ tpa · SIDS sponsored by United States(2001) · Occupational Exposure possible · Japan Challenge N/A · Acute toxicity(Inhalation: Gas) : Class 4 · TLV - No Data
Ethyl acetate	141-78-6	37	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressire 93.2 mmHg, Specific gravity 0.9 · ECHA tonnage band 100,000 - 1,000,000 tpa · ECHA lack of carcinogenicity data · No GLP - A/He mouse - intraperitoneal - Ethyl acetate did not produce an increase in mouse lung tumours compared with controls. · SIDS sponsored by United States(1995) · Occupational Exposure related · has report in Japan Challenge program · TWA(ROK) : 400 ppm 1400 ㎎/㎥ · ACGIH TWA 400 ppm
Formic acid	64-18-6	38	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 42.6 mmHg, Specific gravity 1.22 · ECHA tonnage band 100,000 - 1,000,000 tpa · GLP - Crl:HanWist(Glx:BRL)BR rat - oral: feed - There was no evidence of a tumorigenic effect in the stomach or any other tissue. · GLP - Crl:CD-1(ICR)BR mouse - oral: feed - The potassium diformate was not carcinogenic. · SIDS sponsored by United States(2003) · No GLP - Swiss mouse - dermal - negative · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 4 · TWA(ROK) : 5 ppm 9 ㎎/㎥ · ACGIH TWA 5 ppm STEL 10 ppm
1-Butanol(Butyl alcohol)	71-36-3	39	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 6 mmHg, Specific gravity 0.81 · Colonic Neoplasms related · ECHA tonnage band 100,000 - 1,000,000 tpa · ECHA lack of carcinogenicity data · SIDS sponsored by United States(1993) · Occupational Exposure related · has report in Japan Challenge program · TWA(ROK) : 20 ppm 60 ㎎/㎥ · ACGIH TWA 20 ppm
Methyltrichlorosilane	75-79-6	40	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 167 mmHg, Specific gravity 1.3 · ECHA tonnage band 100,000 - 1,000,000 tpa · ECHA lack of carcinogenicity data · SIDS sponsored by United States(2003) · Occupational Exposure related · has report in Japan Challenge program · TLV - No Data
tert-Butylhydroperoxide	75-91-2	41	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G

Chemical name	CAS No	Priority	Grounds of selection
			· Vapor pressure 5.46 mmHg, Specific gravity 0.93 · Germ cell mutagenicity : Class 2 · Prostatic Neoplasms related · ECHA tonnage band 100,000 - 1,000,000 tpa · No-GLP - ddN mouse - dermal - TBHP increased the occurrence of skin tumours in mice initiated with 4-nitroquinolone 1-oxide. · No-GLP - ICR/Ha Swiss mice - dermal - TBHP was not a skin carcinogen under the conditions of this test. · SIDS sponsored by The Netherlands(1997) · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TLV - No Data
Methyl ethyl ketone	78-93-3	42	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 90.6 mmHg, Specific gravity 0.8 · ECHA tonnage band 100,000 - 1,000,000 tpa · ECHA lack of carcinogenicity data · SIDS sponsored by United States(1991) · Occupational Exposure related · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TLV - No Data
Methyl acetate	79-20-9	43	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 216 mmHg, Specific gravity 0.93 · ECHA tonnage band 100,000 - 1,000,000 tpa · GLP no data - rats and mice - inhalation - Methyl acetat is considered as not carcinogenic. · SIDS sponsored by Germany(1993) · Occupational Exposure related · has report in Japan Challenge program · TWA(ROK) : 200 ppm 610 ㎎/㎥ STEL : 250 ppm 760 ㎎/㎥ · ACGIH TWA 200 ppm STEL 250 ppm
Pentene, 2,4,4-trimethyl-	25167-70-8	44	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Ca, G · Vapor pressure 44.7 mmHg, Specific gravity 0.7 · ECHA tonnage band 10,000 - 100,000 tpa · ECHA lack of carcinogenicity data · SIDS sponsored by Germany(1995) · Occupational Exposure related · has report in Japan Challenge program · TLV - No Data
n-Propanol	71-23-8	45	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 21 mmHg, Specific gravity 0.8 · ECHA tonnage band 10,000 - 100,000 tpa · ECHA lack of carcinogenicity data · SIDS sponsored by Germany(1995) · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TWA(ROK) : 200 ppm 500 ㎎/㎥ STEL : 250 ppm 625 ㎎/㎥ · ACGIH TWA 100 ppm
Trimethylchlorosilane	75-77-4	46	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G

Chemical name	CAS No	Priority	Grounds of selection
			· Vapor pressure 234 mmHg, Specific gravity 0.856 · ECHA tonnage band 10,000 - 100,000 tpa · ECHA lack of carcinogenicity data · SIDS sponsored by United States(1990) · Occupational Exposure related · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TLV - No Data
Isobutyl alcohol	78-83-1	47	It was excluded because this chemical was already performed in Japan Bioassay Center.
Methyl cellosolve	109-86-4	48	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 9.5 mmHg, Specific gravity 0.9647 · Prostatic Neoplasms related · ECHA tonnage band 1,000 - 10,000 tpa · ECHA lack of carcinogenicity data · SIDS sponsored by United States(2006) · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TWA(ROK) : 5 ppm 16 ㎎/㎥ · ACGIH TWA 5 ppm
Allyl methacrylate	96-05-9	49	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 5.77 mmHg, Specific gravity 0.927 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA lack of carcinogenicity data · SIDS sponsored by United States(2001) · Occupational Exposure related · has report in Japan Challenge program · TLV - No Data
Hexamethyldisilazane	999-97-3	50	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 13.8 mmHg, Specific gravity 0.7742 · ECHA tonnage band 1,000 - 10,000 tpa · ECHA lack of carcinogenicity data · SIDS sponsored by United States(2002) · Occupational Exposure possible · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TLV - No Data
4-Xylene	106-42-3	51	· ACGIH A4 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 8.84 mmHg, Specific gravity 0.86 · ECHA tonnage band 1,000,000 - 10,000,000 tpa · SIDS sponsored by Hungary, United States(2003) · Occupational Exposure related · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 4 · TWA(ROK) : 100 ppm 435 ㎎/㎥ STEL : 150 ppm 655 ㎎/㎥ · ACGIH TWA 100 ppm STEL 150 ppm
Cyclohexanone	108-94-1	52	· IARC group 3, ACGIH A3 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 500 ㎩(20℃) 5 mmHg, Specific gravity 0.95 · Germ cell mutagenicity : Class 2

Chemical name	CAS No	Priority	Grounds of selection
			· ECHA tonnage band 1,000,000 - 10,000,000 tpa · GLP no data - Fischer 344 rat - oral: drinking water - The evidence for carcinogenic activity of cyclohexanone is marginal and the effect, if any, is weak. · SIDS sponsored by Canada(1991) · Occupational Exposure related · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TWA(ROK) : 25 ppm 100 ㎎/㎥ STEL : 50 ppm 200 ㎎/㎥ Skin · ACGIH TWA 20 ppm STEL 50 ppm(Skin)
Cyclohexane	110-82-7	53	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 96.9 mmHg, Specific gravity 0.8 · ECHA tonnage band 1,000,000 - 10,000,000 tpa · GLP no data - Swiss mouse - dermal - The results indicated that cyclohexane is a weak complete tumour promoter on the mouse skin. · SIDS sponsored by France(1993) · has report in Japan Challenge program · TWA(ROK) : 200 ppm 700 ㎎/㎥ · ACGIH TWA 100 ppm
p-Xylene	106-42-3	54	It was deleted because this chemical was duplicated in the above list.
Acetic Acid	64-19-7	55	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 15.7 mmHg, Specific gravity 1.0492 · Lung Neoplasms related · ECHA tonnage band 1,000,000 - 10,000,000 tpa · No-GLP - CD-1 mouse - dermal - did not show any carcinogenic potential. However, with a dosing regimen that did not lead to excessive toxicity, acetic acid exhibited weak promotor activity in mice initiated with ß-PL or DMBA.. · No GLP - outbred white rat - oral - gavage(Intraoesophogeal) - to rats for 8 months did not induce tumours in the oesophagus and forestomach, although hyperplasia was present in all animals. Acetic acid by the same regimen increased the incidence of oesophageal/stomach tumour formation in rats also dosed with a known gastric carcinogen, presumably as a consequence of local hyperplasia. · SIDS sponsored by Czech Republic, Slovak Republic(2004) · has report in Japan Challenge program · TWA(ROK) : 10 ppm 25 ㎎/㎥ STEL : 15 ppm 37 ㎎/㎥ · ACGIH TWA 10 ppm STEL 15 ppm
Acetone	67-64-1	56	· ACGIH A4 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 232 mmHg, Specific gravity 0.8 · ECHA tonnage band 1,000,000 - 10,000,000 tpa · No-GLP - ICR mouse - dermal - There were no indications for a carcinogenic potential after dermal application of acetone. · GLP no data - CD-1 mouse - dermal - Acetone was capable of inhibiting tumor formation when used in a mouse two-stage initiation-promotion experiment. · No GLP - several strains(Sencar, CF1, C3H/HeJ, ICR/Ha Swiss, hr/hr Oslo) mouse - dermal - In summary, there are no indications of an elevated tumor incidence in acetone-treated vehicle control groups demonstrating a lack of a carcinogenic potential of acetone itself. · SIDS sponsored by United States(1995) · has report in Japan Challenge program · TWA(ROK) : 500 ppm 1188 ㎎/㎥ STEL : 750 ppm 1782 ㎎/㎥ · ACGIH TWA 500 ppm STEL 750 ppm
Acetic anhydride	108-24-7	57	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G

Chemical name	CAS No	Priority	Grounds of selection
			· Vapor pressure 4 mmHg, Specific gravity 1.08 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by Canada(1991) · Occupational Exposure related · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TWA(ROK) : C 5 ppm C 20 ㎎/㎥ · ACGIH TWA 5 ppm
1-Octene	111-66-0	58	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 17.4 mmHg, Specific gravity 0.7149 · Germ cell mutagenicity : Class 2 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by United States(1991) · Occupational Exposure related · has report in Japan Challenge program · TLV - No Data
n-Butyl acetate	123-86-4	59	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 11.5 mmHg, Specific gravity 0.88 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by United States(1995) · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 3 · TWA(ROK) : 150 ppm 710 ㎎/㎥ STEL : 200 ppm 950 ㎎/㎥ · ACGIH TWA 150 ppm STEL 200 ppm
o-Xylene	95-47-6	60	· ACGIH A4 · Haz-Map - No Data · Vapor pressure >5, Specific gravity 0.88 · ECHA tonnage band 100,000 - 1,000,000 tpa · GLP no data - F344/N rat - oral: gavage - There was no evidence of treatment -related carcinogenicity. · GLP no data - B6C3F1 mouse - oral: gavage - There was no evidence of treatment-related carcinogenicity following gavage administration of mixed xylenes to male and female B6C3F1 mice. · SIDS sponsored by Hungary, United States(2003) · Occupational Exposure related · has report in Japan Challenge program · TWA(ROK) : 100 ppm 435 ㎎/㎥ STEL : 150 ppm 655 ㎎/㎥ · ACGIH TWA 100 ppm STEL 150 ppm
m-Xylene	108-38-3	61	· ACGIH A4 · Haz-Map - No Data · Vapor pressure >5, Specific gravity 0.86 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by Hungary, United States(2003) · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 4 · TWA(ROK) : 100 ppm 435 ㎎/㎥ STEL : 150 ppm 655 ㎎/㎥ · ACGIH TWA 100 ppm STEL 150 ppm
1-Hexene	592-41-6	62	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 184 mmHg, Specifc gravity 0.7 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by United States(1991) · Occupational Exposure related · has report in Japan Challenge program

Chemical name	CAS No	Priority	Grounds of selection
			· ACGIH TWA 50 ppm
Isopentane	78-78-4	63	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 689 mmHg, Specific gravity 0.6 · ECHA tonnage band 100,000 - 1,000,000 tpa · SIDS sponsored by United States(2001) · has report in Japan Challenge program · ACGIH TWA 600 ppm
Allyl alcohol	107-18-6	64	· ACGIH A4 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 26.1 mmHg, Specific gravity 0.9 · ECHA tonnage band 10,000 - 100,000 tpa · GLP no data - Fischer 344 rat - Rats treated via drinking water. Hamsters dosed orally, by gavage - This study is unreliable, no evidence of carcinogenic activity. · GLP no data - SD rat - oral: gavage - it is likely that allyl alcohol would not be carcinogenic. · SIDS sponsored by Japan(2002) · Occupational Exposure related · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 2 · TWA(ROK) : 0.5 ppm 1.2 ㎎/㎥ STEL : 4 ppm 10 ㎎/㎥ · ACGIH TWA 0.5 ppm
Glyoxal	107-22-2	65	It was excluded because this chemical was already performed in Japan Bioassay Center.
Isobutyl acetate	110-19-0	66	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 17.8 mmHg, Specific gravity 0.8712 · ECHA tonnage band 10,000 - 100,000 tpa · SIDS sponsored by United States(2000) · Occupational Exposure related · has report in Japan Challenge program · TWA(ROK) : 150 ppm 700 ㎎/㎥ STEL : 187 ppm 875 ㎎/㎥ · ACGIH TWA 150 ppm
Cyclopentane	287-92-3	67	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 318 mmHg, Specific gravity 0.8 · ECHA tonnage band 10,000 - 100,000 tpa · SIDS sponsored by United States(2001) · has report in Japan Challenge program · TWA(ROK) : 600 ppm 1720 ㎎/㎥ · ACGIH TWA 600 ppm
1,2-Dichloropropane	78-87-5	68	It was excluded because this chemical was already performed in Japan Bioassay Center.
Ethylenediamine	107-15-3	69	· ACGIH A4 · has carcinogenicity report in TOXNET-CCRIS · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 12 mmHg, Specific gravity 0.9 · ECHA tonnage band 10,000+ tpa · SIDS sponsored by United States(2000) · has report in Japan Challenge program · TWA(ROK) : 10 ppm 25 ㎎/㎥ · ACGIH TWA 10 ppm

Chemical name	CAS No	Priority	Grounds of selection
Methylacrylonitrile	126-98-7	70	· Carcinogenicity classification - No Data · has carcinogenicity report in NTP-GLP · has carcinogenicity report in TOXNET-CCRIS · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 71 mmHg, Specific gravity 0.8 · ECHA tonnage band 1,000 - 10,000 tpa · GLP - Fischer 344 rat - oral: gavage - there was no evidence of carcinogenic activity of methacrylonitrile in male or female F344/N rats administered 3, 10, or 30 mg/kg. In male and female rats, methacrylonitrile administration caused significant increases in the incidences of non-neoplastic lesions of the nose and liver. · GLP - B6C3F1 mouse - oral: gavage - Under the conditions of these 2-year gavage studies, there was no evidence of carcinogenic activity of methacrylonitrile in male or female B6C3F1 mice · SIDS sponsored by Japan(1999) · Occupational Exposure related · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 2 · TWA(ROK) : 1 ppm 3 ㎎/㎥ · ACGIH TWA 1 ppm
Peracetic acid	79-21-0	71	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 14.5 mmHg, Specific gravity 1.2 · Germ cell mutagenicity : Class 2 · ECHA tonnage band 1,000 - 10,000 tpa · No GLP - ICR mouse - dermal - act as tumour promotor, the higher incidence of skin tumours found when PAA was administered alone is ascribed to its irritating/corrosive properties which is comparable to the effects of acetic acid and thus, not unique to PAA. sustained irritation will eventually cause tumour formation at the treatment site. · SIDS sponsored by The Netherlands(2003) · Occupational Exposure related · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 1 · TLV - No Data
Cyclopentanone	120-92-3	72	· Carcinogenicity classification - No Data · Haz-Map data available · EPA ACToR Ha, Cr, Ca · Vapor pressure 11.4 mmHg, Specific gravity 0.9487 · ECHA tonnage band 1,000+ tpa · GLP no data - Fischer 344 rat - oral: drinking water - Negative · GLP no data - B6C3F1 mouse - oral: drinking water - Negative · SIDS sponsored by France(2003) · has report in Japan Challenge program · TLV - No Data
Triethylamine	121-44-8	73	· ACGIH A4 · Haz-Map data available · EPA ACToR Ha, Cr, Ca, G · Vapor pressure 54 mmHg, Specific gravity 0.7 · ECHA tonnage band 1,000+ tpa · No GLP - SIV 50 rat - oral: feed - No toxicity or development of tumors was observed. The authors assume that in spite of the large dose, the Nitrosamine production is insuffcient to be tumorigenic. · SIDS sponsored by United States(2001) · Occupational Exposure possible · has report in Japan Challenge program · Acute toxicity(Inhalation: Vapor) : Class 1 · TWA(ROK) : 2 ppm 8.3 ㎎/㎥ STEL : 4 ppm 16.6 ㎎/㎥ · ACGIH TWA 1 ppm STEL 3 ppm

기타 고체상 대상물질의 후보군으로는 미세분진으로서 자동차 배기물질, 유리섬유, 보온제(석면대체물질) 및 초미세입자(나노물질) 등이 제안될 수 있으며, 특히 국내·외에서 사회적으로 이슈가 되고 있는 물질들을 선정의 우선순위로 놓을 수도 있을 것이다. 이런 물질에는 대표적으로 베릴륨(Beryllium)이 있는데, 이 물질은 IARC(International Agency for Research on Cancer) group 1(Beryllium and beryllium compounds), ACGIH A1, NTP K(Beryllium and beryllium compounds), EU CLP 발암성 1B로 분류되어 있어 본 연구의 모집단 설정에서 제외하였다. 하지만 이 물질의 만성 노출로 인한 질병인 베릴륨중독증(Berylliosis; chronic beryllium disease)은 학자들 사이에서 흡입노출로 인한 그 만성발암성 연구의 필요성이 높은 것으로 생각되고 있다.

2. 시험대상물질 선정 절차도 작성

향후 지속적인 만성발암성 시험대상 후보물질의 선정을 일관된 절차로 추진할 수 있도록 그 선정 절차를 일목요연하게 나타낼 수 있는 절차도(Decision tree)를 제시하는 것이 필요하였으며, 아래 Figure 1과 같이 나타냈다. 절차도는 데이터마이닝(Data mining) 분석의 대표적인 분석 방법으로 주어진 데이터를 효과적으로 분류하는데 많이 활용되고 있다.

Ⅳ. 고 찰

본 연구에서는 흡입노출에 의한 만성·발암성시험에서 객관적으로 꼭 필요한 적시성 및 적합성을 고려한 시험대상 후보물질 목록을 그 우선순위와 함께 제안함으로써 동 시험의 원활한 수행에 기여하고자 하였다.

1. 흡입노출에 의한 만성·발암성시험 대상물질의 선정

화학물질의 흡입노출에 의한 만성·발암성시험 대상 후보물질의 선정 및 우선순위의 결정은 모집단 데이

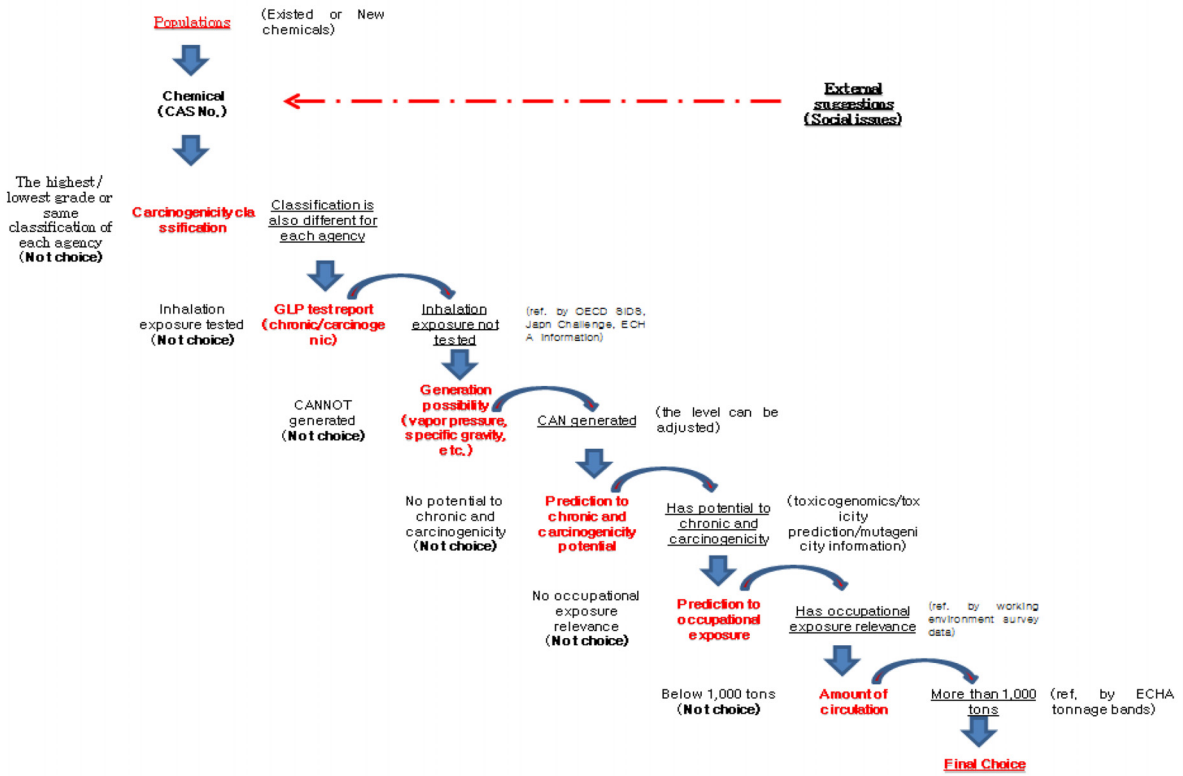

Figure 1. Decision tree for selection of candidate chemicals.

터베이스(DB)에서, 다양한 인터넷 정보 사이트를 참고하여 발암성이 예측되는 물질들을 우선적으로 DB 추출하여 모집단으로 활용하였으며, Carcinogenic Potency DB(화학물질의 잠재적 발암성을 예측하여 정보를 제공하는 사이트), Comparative Toxicogenomics Database(독성유전체 정보를 기초로 발암관련 유전자의 발현과 관련된 화학물질 정보를 제공하는 사이트), EPA ACToR(EPA에서 제공하는 전산 독성연구 프로그램 정보로서, QSAR과 같은 화학물질의 독성영향 예측 정보를 제공하는 사이트) 등을 활용하여 해당 정보를 검색하였고, 이런 화학물질 유해성 관련 인터넷 정보 사이트에서 검색된 화학물질(기존화학물질 중 2,482종) 및 신규화학물질 중 CAS 번호가 부여된 단일물질(중합체 제외)을 모집단으로 활용하였다. 위 모집단의 화학물질들을 중심으로, KOSHANET MSDS등을 이용하여 각 기관(IARC, NTP, ACGIH, EU 등)의 발암성구분을 입력, NTP Database Search를 이용하여 GLP 만성 · 발암성시험 report가 있는지 검색, Chemical Carcinogenesis Research Information System을 이용 그 밖의(Non-GLP등) 만성 · 발암성시험 report가 있는지 검색, CCRIS에서 tumor inhibition/promotion studies 결과가 있는지 검색, oral route에서 carcinogenicity positive 여부 검색, KOSHANET MSDS 정보에서 TopKat Computed probability of mutagenicity 및 생식세포변이원성 category 검색, 증기압은 4 mmHg 이상, 비중은 1.5 미만의 발생(Generation) 가능한 물질을 선택, ECHA의 만성/발암성시험 자료 여부 확인, ECHA의 유통량 확인(유통량 밴드 1,000톤 이상), OECD SIDS report 및 Japan Challenge Program 결과와 상호 비교하였다. 이 방법으로 자료 및 정보 검색한 내용을 Excel 프로그램으로 입력하고, 정렬하여, 연구결과물로서의 DB 파일로 정리하였으며(지면관계상 본 보고에서는 생략하였음), 시험대상 후보물질로 선정을 위해 OECD SIDS와 같은 국제적인 협력을 통해 각 회원국에 배당된 화학물질 유해성 평가 프로그램에서 아직 평가되지 않은 물질, ECHA에서 그 발암성을 결정하는데 있어 근거 자료가 없어서 확실한 결론을 내지 못하고 있는 물질, ECHA에서 그 발암성을 결정하는 있어 근거 자료가 부족하여 확실한 결론을 내리지 못하고 있는 물질, ECHA의 유통량 확인(유통량 밴드 1,000톤 이상)에서 그 유통량이 많은 물질, Japan Challenge 프로그램에서 유해성을 평가하지 않은 물질, 위 물질 중 만성독성, 발암성 및 유전독성이 예측되는 물질의 기준으로 그 우선순위를 부여하였다.

또한, 본 연구에서는 투여경로에 따른 발암성 시험결과의 차이가 있을 수 있음을 감안하여 경구, 경피 등의 기타 경로에서 Carcinogenicity positive/negative 여부를 고찰하였고, 기타 투여경로의 발암성시험에서 Negative 결과를 보인 물질이라도 흡입노출 시의 발암성시험 결과는 다르게 나타날 가능성이 충분히 있고, 각 실험동물 품종 간, 투여 경로 간 독성동태의 차이에 의한 것일 수 있으므로(Lee & Lee, 2004), 시험 후보물질의 선정 시에는 흡입 이외 경로의 발암성시험자료가 있는 물질은 비록 그 결과가 음성이었어도 만성흡입독성/발암성시험의 후보물질로 의미가 있는 것으로 판단하였다.

2. 관련 사업의 향후 추진방안 제언

동 만성흡입독성/발암성시험 사업을 성공적으로 수행하기 위해서 시험대상이 되는 물질들은 발암성뿐만 아니라 생식독성, 발생독성, 유전독성 등 많은 분야에서 인체에 미치는 영향을 다양하게 연구되어야 하고, 산업안전보건법 제40조(화학물질의 유해성 · 위험성 조사)와 관련한 국가적 산업독성물질의 체계적 관리의 차원에서 수행되는 것이 바람직할 것이다.

본 사례보고에서는 흡입노출을 통한 만성독성 및 발암성시험 대상 후보물질을 제시하기 위하여 연구방법에서 제시한 절차로 물질 정보, 구분 및 고찰을 통해 우선순위를 포함한 대상 후보물질을 고체(분말), 기체(가스 포함) 및 액체(유기용제 등)로 구분하여 제시하였으며, 선정 및 우선순위의 근거(Grounds of selection)를 제시하였다. 본 보고에서는 EURAM scoring법 등(Shin et al., 2014)의 점수화를 통한 구체적 우선순위를 산출하는 방법을 사용하지는 않았고, 선정 및 그 우선순위에 대한 근거자료들을 제시하였다. 이런 부분에서 향후 산업안전보건연구원에서는 이 사례보고 내용을 근거로 추가적인 점수화 방법 등을 이용한 우선순위 선정에 관한 추가연구를 계획하고 있다.

근로자, 사업주 및 일반 국민을 대상으로 하는 시험 대상물질 추천방식은 인터넷상에 물질 추천 양식

Table 4. Draft of regulations for the selection of test chemicals in chronic inhalation and carcinogenicity test

Draft of regulations for the selection of test chemicals in chronic inhalation and carcinogenicity test*
Article 1(Purpose)
Article 2(Definitions)
Article 3(Chronic inhalation and carcinogenicity test chemicals selection criteria)
Article 4(Populations of test chemicals)
Article 5(Identification of hazardous materials)
Article 6(Priority sorting)
Article 7(Establishment and configuration of working group)
Article 8(Functions of working group)
Article 9(Meeting of working group)
Article 10(Establishment and configuration of review committee)
Article 11(Functions of review committee)
Article 12(Meeting of review committee)
Article 13(Notice of the committee meeting results)
Article 14(Proposal of the test substance)

*Specific details are not mentioned in this table, because they are trade secret of OSHRI, KOSHA.

등을 공개하며, 이렇게 추천된 물질들은 실무위원회에 의해 시험대상물질로서의 타당성을 검토하고, 타당성이 검토된 물질들은 인터넷 등의 대중 매체에 공개하여 시험대상물질로서의 의견 수렴을 거치는 것도 검토해 볼 수 있을 것이다. 이런 과정을 거친 물질들은 외부 자문위원회 등을 거쳐 독성자료 검토를 통해 시험대상물질들의 우선순위를 결정하게 되며, 최종적으로 시험대상물질을 확정하고 선정된 물질들의 시험을 수행하는 방식으로 하는 것이 바람직하다고 판단된다. 따라서 향후 본 만성흡입독성/발암성시험 대상물질의 지속적인 선정을 위해서는 고용노동부 고시 동등 수준의 국가기준 마련을 위해 아래 Table 4와 같이 만성・발암성시험 대상물질 선정 기준 제정(안)을 제안하였다.

Ⅴ. 결 론

본 연구에서는 산업안전보건연구원에서 만성흡입독성시험시설 신축 이후 수행하게 되는 화학물질 흡입노출에 의한 만성흡입독성 및 발암성 시험의 대상 후보물질 제시가 요구되어 수행하였다. 산업안전보건법상 관리대상물질 및 화학물질관리법상 기존화학물질, 신규화학물질 등 국내 유통화학물질 목록 전반을 대상으로 만성발암성 시험여부를 조사하였고, 동 시험이 필요한 물질에 대한 우선순위를 제안하였다. 시험대상 후보물질 제시를 위하여 물질 정보 검색, 구분 및 고찰을 통해 우선순위를 포함한 대상 후보물질을 선정하였으며, 고체(분말), 기체(가스 포함) 및 액체(유기용제 등)로 구분하여 제시하였다.

화학물질의 저농도 장기노출에 의한 사업장 근로자의 건강장해 예방을 위하여 신규 설치되는 만성흡입독성시험시설에서 수행할 만성흡입독성시험 및 발암성시험을 위해 국제적으로 타당성이 있으며, 시의성 있는 시험대상물질의 우선순위를 정하여 동 시험의 원활한 수행을 통해 화학물질로 인한 직업성 질환을 효과적으로 예방하는데 기여할 것으로 생각된다.

References

Ahn YS, Won JU, Park RM. Cancer morbidity of foundry workers in Korea. J Korean Med Sci 2010;25:1 733-1741

Bae GR, Lim HS, Kim D. Occupational relationship of cancer patients diagnosed in two university hospitals. Korean J Epidemiol 1999;21:64-71

Carcinogenic Potency DB [serial online] 2011 [cited 2014 May 30]. Available from: http://toxnet.nlm.nih.gov/cpdb/

Chemical Carcinogenesis Research Information System [serial online] 2013 [cited 2014 May 30]. Available from: http://toxnet.nlm.nih.gov/newtoxnet/ccris.htm

Comparative Toxicogenomics Database [serial online] 2014

[cited 2014 May 30]. Available from: http://ctdbase.org/detail.go?type=chem&acc=D009930&view=disease&slimTerm=Cancer&assnType=inferred

EPA ACToR [serial online] 2014 [cited 2014 May 30]. Available from: http://actor.epa.gov/actor/faces/ACToRHome.jsp

Fayed L. The History of Cancer [serial online] 2009 [cited 2014 February 2]. Available from: http://cancer.about.com/od/historyofcancer/a/cancerhistory.htm

Han KT. Assessment about the construction of chronic inhalation toxicity system. 2009 Research Report of OSHRI, p. 1-18

Jung KW, Won YJ, Kong HJ, Oh CM, Lee DH et al. Cancer Statistics in Korea: Incidence, mortality, survival, and prevalence in 2011. Cancer Res Treat 2014;46(2): 109-123

Kang SK, Ahn YS, Chung HK. Occupational Cancer in Korea in the 1990s. Korean J Occup Environ Med 2001; 13:351-9

Kang SK, Kim EA. Occupational Diseases in Korea. J Korean Med Sci 2010;25:4-12

Kim EA, Lee HE, Kang SK. Occupational burden of cancer in Korea. Saf Health Work 2010;1:61-8

Lee JS, Lee YH. Research on GLP evaluation of toxicokinetic study in the assessment of the carcinogenicity study. 2004 KNTP Report, vol 5, p. 166-204

Lee KS, Lee JH, Lee HJ. A study on the criteria and supply status of information for managing carcinogens in domestic and foreign. J Korean Soc Occup Environ Hyg 2011;21:40-8

Ministry of Employment and Labor(MoEL). Enforcement Decree Of The Occupational Safety And Health Act. 2014a

Ministry of Employment and Labor(MoEL). Enforcement Regulations of the Occupational Safety And Health Act. 2014b

Ministry of Employment and Labor(MoEL). Occupational Safety And Health Act. 2013

National Toxicology Program(NTP). Database Search [serial online] 2014 [cited 2014 May 30]. Available from: http://tools.niehs.nih.gov/ntp_tox/index.cfm

Shin S, Moon HI, Lee KS, Hong MK, Byeon SH. A Chemical Risk Ranking and Scoring Method for the Selection of Harmful Substances to be Specially Controlled in Occupational Environments. Tchounwou PB, ed. International Journal of Environmental Research and Public Health 2014;11(11):12001-12014

Statistics Korea. Causes of Death Statistics in 2011. 2012. pp. 3

Weinstei IB. Cancer prevention: recent progress and future opportunities. Cancer Res 1991;51(Suppl):5080s-5085s

Yang M. A current global view of environmental and occupational cancers. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev 2011;29:223-49