J Occup Health 2014; 56: 393–398

Journal of Occupational Health

*Brief Report*

# Solvent Use in Private Research Laboratories in Japan: Comparison with the Use in Public Research Laboratories and on Production Floors in Industries

Takaaki HANADA, Ai ZAITSU, Satoshi KOJIMA, Hirohiko UKAI, Yasuhiro NAGASAWA, Shiro TAKADA, Takuya KAWAKAMI, Fumiko OHASHI and Masayuki IKEDA

Kyoto Industrial Health Association, Japan

**Abstract: Solvent Use in Private Research Laboratories in Japan: Comparison with the Use in Public Research Laboratories and on Production Floors in Industries: Takaaki HANADA, *et al*. Kyoto Industrial Health Association—Background and Objectives:** Solvents used in production facility-affiliated private laboratories have been seldomly reported. This study was initiated to specify solvent use characteristics in private laboratories in comparison with the use in public research laboratories and on production floors. Elucidation of the applicability of conclusions from a public laboratory survey to private institutions is not only of scientific interest but also of practical importance. **Materials:** A survey on use of 47 legally stipulated organic solvents was conducted. The results were compiled for April 2011 to March 2013. Through sorting, data were available for 479 unit workplaces in private laboratories. Similar sorting for April 2012 to March 2013 was conducted for public research laboratories (e.g., national universities) and production floors (in private enterprises) to obtain 621 and 937 cases, respectively. Sampling of workroom air followed by capillary gas-chromatographic analyses for solvents was conducted in accordance with regulatory requirements. **Results:** More than one solvent was usually detected in the air of private laboratories. With regard to solvent types, acetone, methyl alcohol, chloroform and hexane were prevalently used in private laboratories, and this was similar to the case of public laboratories. Prevalent use of ethyl acetate was unique to private laboratories. Toluene use was less common both in private and public laboratories. The prevalence of administrative control class 1 (i.e., an adequately controlled environment) was higher in laboratories (both private and public) than production floors. **Conclusions:** Solvent use patterns are similar in private and public laboratories, except that the use of mixtures of solvents is substantially more popular in private laboratories than in public laboratories.
(J Occup Health 2014; 56: 393–398)

**Key words:** Organic solvents, Private research laboratories, Production floor, Public research laboratories

*Received Mar 31, 2014; Accepted Jun 3, 2014*
*Published online in J-STAGE Jul 25, 2014*
*Correspondence to: M. Ikeda, Kyoto Industrial Health Association (Main Office), 67 Nishinokyo-Kitatsuboicho, Nakagyo-ku, Kyoto 604-8472, Japan*

The use of organic solvents (referred to as solvents thereafter) is widespread not only on production floors in enterprises but also in public and private laboratories for testing, development and research. It may be the case that the practice of solvent use varies depending on the objectives of the laboratories. Thus, solvent use in laboratories affiliated with production facilities of enterprises may be more oriented, for example, to the testing of products and different from the use on the production floors[1–3]. It is further possible that the solvent use may not be similar between laboratories in industrial settings and those in public research facilities such as national or public universities[4–6]. Nevertheless, essentially no reports are available on solvent use in enterprise-run research facilities, although health effects of solvent use in laboratories have been reported, as to be detailed later.

The present survey was initiated to investigate the types and use patterns (i.e, single or mixed) of solvents used in laboratories in private enterprises in comparison with those in public research laboratories and production floors.

## Materials and Methods

*Survey of solvent use in private laboratories*

In the two-fiscal year period of April 2011 to March 2013, about 2000 unit workplaces utilizing solvents were surveyed in Kyoto prefecture and its surrounding areas in Japan, and the results were compiled as a database[7, 8]. When testing and research laboratories were selected (after regulation-defined classification of

activities, such as "testing and research"), 481 laboratories were identified (defined as unit workplaces according to the definition by regulations and guidelines[9–12]). Of the 481 laboratories, >90% of laboratories belonged to manufacturing companies, and the remaining belonged to independent enterprises (including medical facilities such as hospitals), respectively. For comparison purposes, the survey database for the period of April 2012 to March 2013 (i.e., one fiscal year) was sorted for cases of production floors (i.e., those other than laboratories) in private enterprises. In practice, 945 cases were available. Sorting of the same database for public research laboratories (e.g., those in national universities) gave 613 cases.

*Solvents analyzed in workroom air*

In practice, 47 types of solvents (7 solvents in Group 1 and 40 solvents in Group 2) were considered in accordance with regulations. The methods of sampling (with Tedlar bags) and analyses (by capillary gaschromatography) were as previously detailed elsewhere[1–3, 6]. Group 3 solvents were not taken into account, as they are natural solvent mixtures and do not fit with the gaschromatographic identification[11, 13].

*Statistical analyses*

The $\chi^2$-test was applied as necessary.

## Results

*Number of solvents in one unit workplace*

The distribution histograms are shown in Fig. 1. With regard to the number of solvents detected in one unit workplace, more than one solvent was detected per laboratory room in most of the private laboratories [Fig. 1 (A)], which was in a sharp contrast to the cases of public laboratories [Fig. 1 (B)] where a single solvent was detected in most cases. The mode was 3 for the former, whereas it was 1 for the latter. When statistical evaluation by the $\chi^2$-test was conducted for the difference in prevalence of single-solvent workplaces (in contrast to multiple solvent workplaces), the prevalence was significantly lower ($p<0.01$) for private laboratories than for public laboratories. The difference between private laboratories and production floors was also significant ($p<0.01$).

*Number of staff or workers in one unit workplace*

When the number of staff or workers in a unit workplace in private laboratories was depicted in a histogram [Fig. 2 (A)] in comparison with those in the other two groups [Fig. 2 (B) and (C)], it was interesting to note that the distribution was more or less similar in the three groups in the sense that the mode was 1 in all of three cases followed by gradual decreases as the number of subjects increased. This

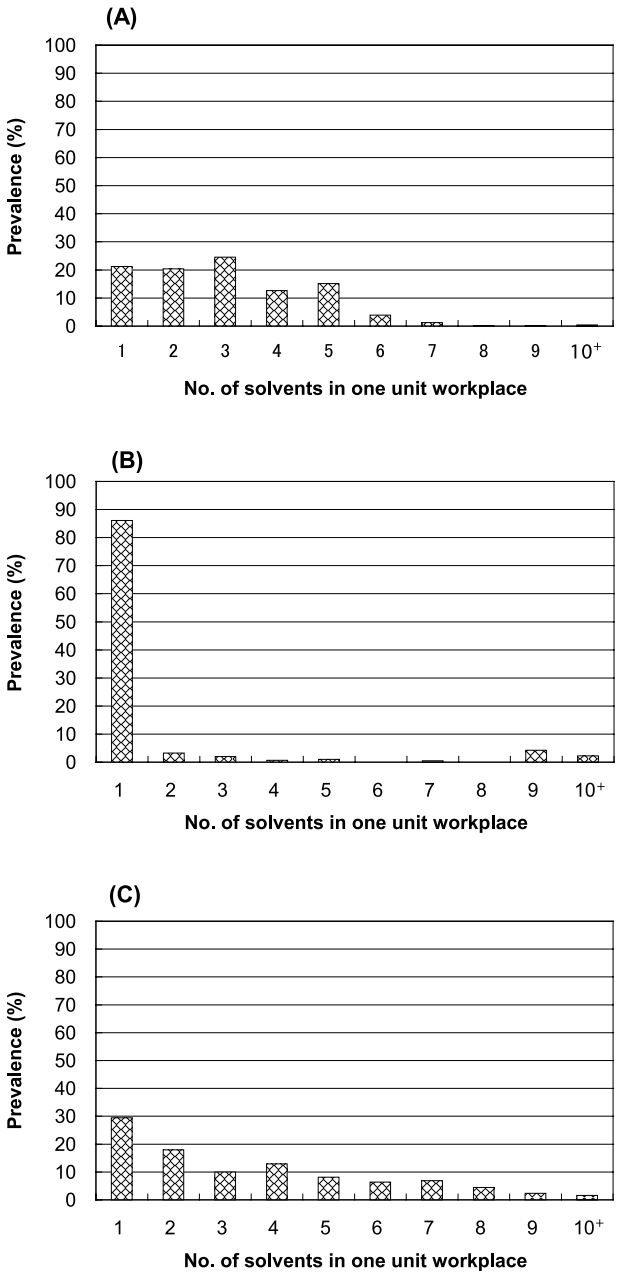


**Fig. 1.** Number of solvents in workroom air of laboratories and production floors
(A) Private laboratories. (B) Public laboratories. (C) Production floors. Note that the distribution does not follow a normal distribution. The median was 3 solvents in (A), 1 solvent in (B) and 3 solvents in (C).

was rather contrary to expectations based on the different distributions in solvent numbers [Fig. 1 (A), (B) and (C)]. Nevertheless, the prevalence of unit workplaces with one staff member or worker was significantly lower ($p<0.01$ by the $\chi^2$-test) in private laboratories than in public laboratories. There was no significant difference ($p>0.10$) between private laboratories and production floors.

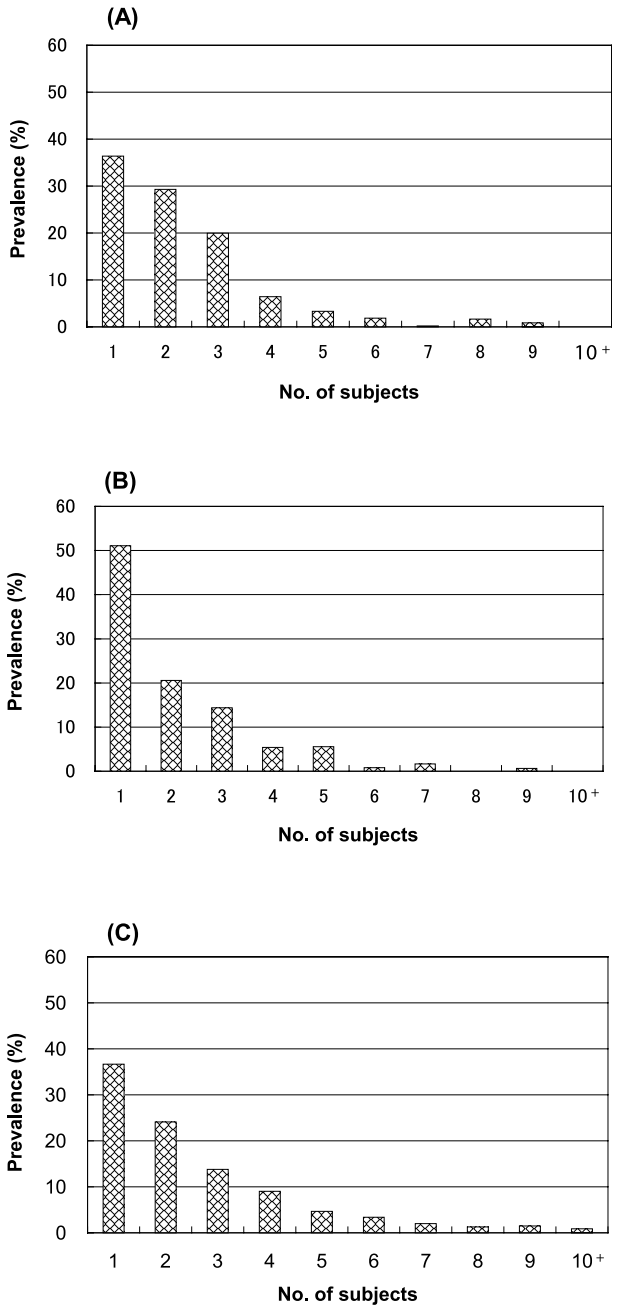


**Fig. 2.** Number of staff or workers in laboratories and on production floors
(A) Private laboratories. (B) Public laboratories. (C) Production floors. Note that the distributions are markedly skewed. The median was 2 persons in (A), 1 person in (B) and 2 persons in (C).

*Most common solvents*

The top 15 most common solvents are shown in Table 1 for private laboratories, in comparison with those for public laboratories and for production floors. The most remarkable difference was the high prevalence of acetone and methyl alcohol, which was commonly found both in private (51 and 42% respectively) and in public laboratories (33 and 26%). Whereas methyl alcohol was also commonly used (34%) on production floors, use of acetone was less prevalent (22%). In a sharp contrast, use of toluene was quite prevalent on production floors (48%), but this multipurpose solvent[1–3] was less frequently detected in private laboratories (20%) and even less so in public laboratories (10%). The same was also the case for isopropyl alcohol, which showed a low prevalence in private and public laboratories (27 and 12% respectively) in contrast to its high prevalence (42%) on production floors. The prevalence for chloroform was high in both types of research laboratories (18% and 18%) but quite low (out of the top 15 solvents) in production floors. Similarly, use of hexane was prevalent in private (34%) and public laboratories (14%) but less so on production floors (5%). Ethyl acetate was frequently used in private laboratories (39%) and on production floors (33%) but not often in public laboratories (11%).

*Comparison of workroom conditions*

When compared in terms of administrative control classes (ACCs[11]), the distribution of classes for private laboratories was as follows: 98.3, 1.3, and 0.4% for ACC 1, 2, and 3, respectively. Those for public laboratories and production floors were 99.3, 0.4, 0.3%, and 83.8, 10.2 and 6.0%, respectively. The $\chi^2$-test revealed that the prevalence of ACC 1 did not show significant difference between the two types of laboratories ($p>0.10$), but there was a significant difference in prevalence between production floors and either of the two types of laboratories ($p<0.01$ for both). It appeared that workroom conditions were better for both private and public laboratories than for production floors.

## Discussion

To the best of the authors' knowledge, the present study is the first systematic report on the solvent use in private research laboratories. It was made clear that the pattern of solvent use in private laboratories was similar to that in public laboratories in terms of the popular use of acetone and methyl alcohol. Relatively prevalent use of chloroform and hexane was also common to these two groups of laboratories. In contrast, toluene and isopropyl alcohol were less commonly used in private laboratories, whereas these two solvents were most commonly used on production floors (Table 1). More than one solvent was often detected in private laboratories, whereas single-solvent use was unique to public laboratories (Fig. 1), which may suggest that the risk of simultaneous exposure to multiple solvents is higher in private laboratories than

**Table 1.** Top 15 most frequently detected solvents in workroom air

| Ranking | Private laboratories | | | Public laboratories | | | Production floors | | |
|---|---|---|---|---|---|---|---|---|---|
| | Solvent | No.[a] | %[a] | Solvent | No.[a] | %[a] | Solvent | No.[a] | %[a] |
| | No. of unit workplaces | 481 | | No. of unit workplaces | 613 | | No. of unit workplaces | 945 | |
| 1 | Acetone | 246 | 51.1 | Acetone | 200 | 32.6 | Toluene | 457 | 48.4 |
| 2 | Methyl alcohol | 201 | 41.8 | Methyl alcohol | 158 | 25.8 | Isopropyl alcohol | 401 | 42.4 |
| 3 | Ethyl acetate | 189 | 39.3 | Chloroform | 113 | 18.4 | Methyl alcohol | 325 | 34.4 |
| 4 | Hexane | 162 | 33.7 | Hexane | 88 | 14.4 | Ethyl acetate | 307 | 32.5 |
| 5 | Isopropyl alcohol | 128 | 26.6 | Isopropyl alcohol | 73 | 11.9 | Xylenes | 279 | 29.5 |
| 6 | Toluene | 98 | 20.4 | Ethyl acetate | 69 | 11.3 | n-Butyl acetate | 259 | 27.4 |
| 7 | Chloroform | 87 | 18.1 | Toluene | 64 | 10.4 | Methyl ethyl ketone | 250 | 26.5 |
| 8 | Tetrahydrofuran | 66 | 13.7 | Dichloromethane | 62 | 10.1 | Acetone | 206 | 21.8 |
| 9 | Methyl ethyl ketone | 47 | 9.8 | Xylenes | 45 | 7.3 | Methyl isobutyl ketone | 183 | 19.4 |
| 10 | O-Dichlorobenzene | 42 | 8.7 | Tetrahydrofuran | 44 | 7.2 | 1-Butyl alcohol | 100 | 10.6 |
| 11 | Ethyl ether | 28 | 5.8 | Ethyl ether | 34 | 5.5 | Cyclohexanone | 86 | 9.1 |
| 12 | Dichloromethane | 27 | 5.6 | N,N-Dimethyl formamide | 28 | 4.6 | EG[b] monobutyl ether | 76 | 8.0 |
| 13 | n-Butyl acetate | 25 | 5.2 | 1,2-Dichloroethane | 26 | 4.2 | Isobutyl alcohol | 64 | 6.8 |
| 14 | N,N-Dimethyl formamide | 24 | 5.0 | 2-Butyl alcohol | 10 | 1.6 | Hexane | 46 | 4.9 |
| 15 | Methyl isobutyl ketone | 20 | 4.2 | 1,4-Dioxane | 6 | 1.0 | Isobutyl acetate | 45 | 4.8 |
| | Total number of solvents detected | 1,458 | | Total number of solvents detected | 1,051 | | Total number of solvents detected | 3,276 | |

[a] Numbers of cases detected. Percentages for numbers taking the number of unit wotkplaces as the denominator. [b] EG stands for ethylene glycol.

in public laboratories, although the workroom environments were generally better than those of production floors; the proportion of ACC 1 (i.e., adequately controlled environment[11]) was higher in laboratories than on production floors. It is known that such better work environments were achieved by extensive use of exhaust chambers in public laboratories[6], and the same situation appeared to have been achieved also in private laboratories.

Increasing attention has been focused on the safety of the laboratory environment. Based on a literature survey, information from 13 selected publications[4, 5, 14–24] on types of solvents and possible health effects on laboratory staff and personnel has been summarized in Table 2. The health effects reported are various from neuromuscular Raynaud's phenomenon[21] to reproductive disturbances such as miscarriage and abortion[4, 23]. The description of the laboratories involved are generally brief and insufficient in most cases (with two exceptional cases[14, 18]) to make a clear identification of whether the laboratory studied was a research-oriented one[4] or testing and development sections of production facilities. Detailed descriptions of solvents involved were provided in earlier reports[4, 14], but simpler descriptions were provided in later reports. Information related to exposure prevalence by solvent types was available only in limited cases[4, 14]. Nevertheless, the use of chloroform may require attention[4, 14, 15, 23] because this solvent is commonly used in laboratories but only on rare occasions on production floors (Table 1). The descriptions of solvent application in histology laboratories would be expected to be simple[16, 17, 21, 22] because xylenes, toluene or the combination of them would be the only solvents used in this field of study[6]. Overall, therefore, it was not possible to examine if the observations as summarized in Table 1 could be confirmed through a literature survey.

There are several limitations in the present study. The study was based on sampling of laboratory air and analyses of solvent vapor concentrations, and no other relevant data were available. For example, the amounts of solvents or solvent mixtures used in the laboratories remained unknown. The use of exhaust chambers was considered to be adequate. This observation was, however, based on expert judgments at the time of visits to the laboratories, and no quantitative data on installation and operation were available, although the fact that more than 98% of the laboratories were classified as ACC 1 supports this evaluation.

In conclusion, private laboratories (mostly as testing and development sections affiliated with production facilities) share characteristics in common with public (research-oriented) laboratories in terms of the prevalent use of acetone, methyl alcohol, chloroform and hexane, and limited use of toluene and isopropyl alcohol. In the laboratory air, more than two solvents were often detected in private laboratories,

**Table 2.** Selected reports on solvent exposure and health effects in laboratories

| Year of publication | Reference No. | Type of laboratory | Organic solvents (* Non-solvent chemical) | Health effects |
|---|---|---|---|---|
| 1984 | 4 | University laboratory | Benzene, chloroform, dichloroethane, dichloromethane, ether, ethyl alcohol, formaldehyde*, methyl alcohol, petroleum ether, phenol*, propylene oxide*, toluene, xylenes, etc. | Slight insignificant increase in miscarriage rate |
| 1994 | 14 | Not specified | Acetone, acetonitrile, benzene, carbon tetrachloride, chloroform, cyclohexane, ethyl alcohol, ether, ethyl acetate, formaldehyde*, heptane, isopropyl alcohol, methyl alcohol, dichloromethane, petroleum benzine, toluene, 1,1,1-trichloroethane, trichloroethylene, white spirit, xylenes | Increase in spontaneous abortion rate |
| 2001 | 15 | Biomedical | Acetone, benzene, chloroform, ethyl ether, phenol* | Delay in pregnancy |
| 2002 | 16 | Pathology and anatomy | Formaldehyde*, hexane, methyl ethyl ketone, toluene | Cytogenetic damage in buccal cells |
| 2003 | 17 | Hospital laboratory | Ethyl alcohol, toluene | Neurobehavioral functions |
| 2006 | 18 | Not specified | Organic solvents (not specified) | No high risk of reproductive failures |
| 2006 | 19 | Medical | Not specified | Elevated olfactory functions |
| 2008 | 20 | Chemical | Acetone, acetonitrile, benzene, dichloromethane, ethyl acetate, ethyl alcohol, hexane | Increased mutagenicity in urine |
| 2008 | 5 | University laboratory | Various including acetone, chloroform, methyl alcohol | Not stated |
| 2011 | 21 | Histology, cytoogy. and transfusion | Acetone, chlorinated solvents, toluene, xylene, | Raynaud's phenomenon |
| 2011 | 22 | Histopathology | Formaldehyde*, xylenes | Not clear |
| 2012 | 23 | Pharmaceutical | Chloroform, hexane, formaldehyde*, phenol* | Possibility of spontaneous abortion |
| 2012 | 24 | Pharmaceutical | Toluene, xylenes, formaldehyde* | Increase in systolic blood pressure |

whereas only one solvent vapor was detected in the majority of public laboratories. Despite such differences in solvent use patterns, the work environments in laboratories (irrespective of private or public) were maintained generally adequately, being better than the conditions on production floors.

*Acknowledgments*: Thanks are due to the administration and our fellow staff at Kyoto Industrial Health Association for their interest in and support to this work.

*Conflicts of interest*: The authors declare that they have no conflicts of interest.

## References

1) Ukai H, Inui S, Takada S, et al. Types of solvents used in small- to medium-scale industries in Japan; a nationwide field survey. Int Arch Occup Environ Health 1997; 70: 385–92.
2) Samoto S, Fukui Y, Ukai H, et al. Field srvey on types of solvents used in enterprises of various sizes. Int Arch Occup Environ Health 2006; 79: 558–67.
3) Nagasawa Y, Ukai H, Okamoto S, et al. Organic solvent use in enterprises in Japan. Ind Health 2011; 49: 534–41.
4) Axelsson G, Lütz C, Rylander R. Exposure to solvents and outcome of pregnancy in university laboratory employees. Brit J Ind Med 1984; 41:

305–12.
5) Takada S, Okamoto S, Yamada C, et al. Chemical exposure in research laboratories in a university. Ind Health 2008; 46: 166–73.
6) Nagasawa Y, Samoto H, Ukai H, et al. Organic solvent use in large research institutions in Japan. Environ Health Prev Med 2013; 18: 341–8.
7) Kyoto Industrial Health Association. Annual Report 2011. Kyoto Industrial Health Association, Kyoto, 2012 (in Japanese).
8) Kyoto Industrial Health Association. Annual Report 2012. Kyoto Industrial Health Association, Kyoto, 2013 (in Japanese).
9) Ministry of Health, Labour and Welfare, Japan. Ordinance for Preventions of Solvent Poisonings (2006 version; Ordinance No. 1). Ministry of Health, Labour and Welfare, Tokyo, 2006 (in Japanese).
10) Ministry of Health, Labour and Welfare, Japan. Working Environment Measurement Standards (Ministry of Health, Labour and Welfare Notification No. 44). Ministry of Health, Labour and Welfare, Tokyo, 2006 (in Japanese).
11) Ministry of Health, Labour and Welfare, Japan. Working Environment Evaluation Standards (Ministry of Health, Labour and Welfare Notification No. 50). Ministry of Health, Labour and Welfare, Tokyo, 2006 (in Japanese).
12) Japan Association for Working Environment Measurement. Working Environment Measurement System in Japan (3rd ed.) Japan Association for Working Environment Measurement, Tokyo, 1996.
13) Ministry of Health, Labour and Welfare, Japan. Enforcement Order of Occupational Safety and Health Law (2009 version; Cabinet Order No. 295). Ministry of Health, Labour and Welfare, Tokyo, 2009 (in Japanese).
14) Taskinen H, Kyyrönen, Hemminki K, Hoikkala M, Lajunen K, Lindbohm M-L. Laboratory work and pregnancy outcome. J Occup Med 1994; 36: 311–9.
15) Wennborg H, Bodin L, Vainio H, Axelsson G. Solvent use and time to pregnancy among female personnel in biomedical laboratories in Sweden. Occup Environ Med 2013; 58: 225–31.
16) Burgaz S, Erdem O, Çakmak G, Erdem N, Karakaya A, Karakata AE. Cytogenetic analysis of buccal cells from shoe-workers and pathology and anatomy laboratory workers exposed to n-hexane, toluene, methyl ethyl ketone and formaldehyde. Biomarkers 2002; 7: 151–61.
17) Herpin G, Cauchard GC, Vouriot A, et al. Neurotox Res 2003; 13: 185–96.
18) Zhu JL, Knudsen LE, Andersen A-MN, Hjollund NH, Olsen J. Laboratory work and pregnancy outcomes; a study within the National Birth Cohort in Denmark. Occup Environ Med 2006; 63: 53–8.
19) Zibrowski EM, Robertson J. Olfactory sensitivity in medical laboratory workers occupationally exposed to organic solvent mixtures. Occup Med 2006; 56: 51–4.
20) Varella SD, Rampazo RA, Varanda EA. Urinary mutagenicity in chemical laboratory workers exposed to solvents. J Occup Health 2008: 50: 415–22.
21) Purdie GL, Purdie DJ, Harrison AA. Raynaud's phenomenon in medical laboratory workers who work with solvents. J Rheumatol 2011; 38: 1940–6.
22) Gunsun TH, Smith HR, Vinciullo C. Assessment and management of chemical exposure in the Mohs laboratory. Dermatol Surg 2011; 37: 1–9.
23) Attarchi MS, Ashouri M, Labbafinejad Y, Mohammadi S. Assessment of time to pregnancy and spontaneous abortion status following occupational exposure to organic solvents mixture. Int Arch Occup Environ Health 2012; 85: 295–303.
24) Mohammadi S, Golabadi M, Labbafinejad Y, Pishgahhadian F, Attarchi M. Effects of exposure to mixed organic solvents on blood pressure in non-smoking women in a pharmaceutical company. Arch Hig Rada Toksikol 2012; 63: 161–9.