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# 2-Butanone – Addendum for re-evaluation of the BAT value

## Assessment Values in Biological Material – Translation of the German version from 2014

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**Keywords:**

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| | |
|---|---|
| **BAT value (2013)** | **2 mg 2-butanone/l urine**<br>Sampling time: end of exposure or end of shift |
| **MAK value (1961)** | **200 ml/m³ ≙ 600 mg/m³** |
| Absorption through the skin (1996) | H |
| Carcinogenicity | – |

In 1988 the biological tolerance value (BAT value) for 2-butanone [78-93-3] (methyl ethyl ketone) was established at 5 mg 2-butanone/l urine at the end of exposure or end of shift (translated in Angerer 1995). The derivation was based on data available for the relationship between external and internal exposure, taking into consideration the MAK value (maximum workplace concentration) of 200 ml/m³ as reference value for the setting of the BAT value. The MAK value for 2-butanone was last confirmed in 2000 (Greim 2000). Its evaluation was based on the irritation to eyes, nose and throat, which had been reported at exposure concentrations of 100 to 200 ml/m³ without clear dose-response relationship. Exposure levels of 300 ml/m³ and more, however, were clearly not tolerated. Except for the known neurotoxicity which occurs only in combination with n-hexane and comparable γ-diketone formers, no systemic toxicity was described.

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## Re-evaluation

The BAT value for 2-butanone was mainly established on the basis of three field studies, which provided exact data for the parameters of the regression equations for the relationship between 2-butanone concentrations in the air and those in urine (Ghittori et al. 1987; Miyasaka et al. 1982; Perbellini et al. 1984). In these three studies the calculated average concentrations in urine correlating with an inhalation exposure to 200 ml 2-butanone/m³ are between 2.1 and 5.3 mg/l (see Table 1). The two lower values corresponded to the analytical values obtained in investigations by Angerer et al. (1985), which were, however, determined mainly in persons wearing respiratory protection. Recalling that these values are average values for collectives exposed to ambient air concentrations at the level of the limit value, a BAT value of 5 mg 2-butanone/l urine was set as ceiling value.

**Tab. 1** Parameters reported from field studies on the correlations between 2-butanone in air and the resulting concentration of 2-butanone in urine

| $C_{air}$ [ml/m³] | $C_{urine}$ for an exposure at the level of the MAK value (200 ml/m³ ≙ 600 mg/m³) [mg/l] | Equation $C_{urine} = \beta \times C_{air} + offset$ | References |
|---|---|---|---|
| < 100[a)] | 5.3 | $C_{urine}$ [µg/l] = 26.3 × $C_{air}$ [ml/m³] + 53.0 | Miyasaka et al. (1982) |
| ≤ 92 | 2.1 | $C_{urine}$ [µg/l] = 3.2 × $C_{air}$ [µg/l] + 196 | Perbellini et al. (1984) |
| ≤ 330[a)] | 2.2 | $C_{urine}$ [mg/l] = 0.0032 × $C_{air}$ [mg/m³] + 0.32 | Ghittori et al. (1987) |
| ≤ 268 | 2.5 | $C_{urine}$ [mg/l] = 0.004 × $C_{air}$ [mg/m³] + 0.118 | Imbriani et al. (1989) |
| ≤ 356 | 1.4 | $C_{urine}$ [mg/l] = 0.00389 × $C_{air}$ [ml/m³] + 0.656 | Jang et al. (1993) |
| ≤ 224 | 5.2 | $C_{urine}$ [mg/l] = 0.026 × $C_{air}$ [ml/m³] – 0.056 | Yoshikawa et al. (1995) |
| ≤ 6 | 6.7 | $C_{urine}$ [µg/l] = 33.4 × $C_{air}$ [ml/m³] + 36.8 | Kawai et al. (2003) |

[a)] not given, estimated from figure

Since the last evaluation of the BAT value several new field studies have been conducted allowing the derivation of exposure-concentration relationships (see Table 1; reviews by Gobba et al. 1997; Imbriani and Ghittori 2005). In the overall view of the published studies a clear dichotomy is found with regard to the derived values equivalent to the MAK value: the values in the Japanese studies (Kawai et al. 2003; Miyasaka et al. 1982; Yoshikawa et al. 1995) are, at 5.2 to 6.7 mg 2-butanone/l, almost twice as high as those in the Italian studies (Ghittori et al. 1987; Imbriani et al. 1989; Perbellini et al. 1984). The unusual high value in the study by Kawai et al. (2003) can be attributed to the fact that the values were extrapolated from a comparably wide scattering point cloud in the low-dose range. The slope of the regression line in the study by Ghittori et al. (1987) on the other hand is potentially calculated too low. The Korean study (Jang et al. 1993), which by far results in the lowest estimate, is only of limited use for the evaluation due to the low number of only 14 test persons. Due to obvious mistakes made when converting different dimensions, the correlation given in the study by Ong et al. (1991) is not further taken into consideration here.

In addition to the above-mentioned field studies, the results of chamber exposure studies are available in which, with two exceptions, the excretion of 2-butanone in urine was however either not determined or not reported. Liira et al. (1990 b) investigated the 2-butanone excretion in five male test persons after 4-hour exposure to 200 ml/m³, with and without co-exposure to ethanol. The concentration at the end of the exposure was about 2 mg/l urine and increased to up to two and a half times this value after ethanol exposure. Tomicic et al. (2011) exposed 10 men and 15 women to 100 ml/m³ for six hours under resting conditions and obtained average concentrations of 1.0 mg/l urine (men) and 1.44 mg/l urine (women without hormonal contraception).

Theoretically, as alternative parameters, 2-butanone concentrations in alveolar air and in blood as well as the determination of 2-butanone metabolites (3-hydroxy-2-butanone, 2,3-butanediol) in urine could be considered (Brown et al. 1987; Brugnone et al. 1983; Liira et al. 1988, 1990 a; Perbellini et al. 1984). However, available data are insufficient and, at present, there is no apparent advantage in the use of these parameters over the determination of unchanged 2-butanone in urine.

The BAT value is thus established on the basis of the results from the field studies on the excretion of 2-butanone in urine. The conspicuous discrepancy between the Asian and the Italian studies can be first and foremost explained by the different activity of the oxidizing enzyme cytochrome P450 2E1 (Bolt et al. 2003). Differences in analytical methods and operating procedures (high/low dermal absorption) are in principle also possible explanations. For this reason, the European studies are preferred for the derivation of the BAT value. The results of the European field studies have been confirmed by the results of the chamber studies by Liira et al. (1990 b) and Tomicic et al. (2011).

The **BAT value** is therefore established at

**2 mg 2-butanone/l urine.**

Sampling should be carried out at the end of exposure or end of shift.

# Notes

## Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (https://www.dfg.de/en/dfg_profile/statutory_bodies/senate/health_hazards/conflicts_interest/index.html) ensure that the content and conclusions of the publication are strictly science-based.

# References

Angerer J (1995) 2-Butanone. BAT Value Documentation, 1990. In: Lehnert G, Greim H (eds) Biological Exposure Values for Occupational Toxicants and Carcinogens, vol 2. VCH, Weinheim, 43–50. Also available from DOI: 10.1002/3527600418.bb7893e0002

Angerer J, Kassebart V, Wolf D, Behling K, Lehnert G (1985) Kombinierte Lösungsmittelexpositionen bei Beizarbeiten. In: Bolt HM, Piekarski C, Rutenfranz J (eds) Dokumentationsband über die 25. Jahrestagung der Deutschen Gesellschaft für Arbeitsmedizin und Umweltmedizin. Gentner Verlag, Stuttgart, 461–465

Bolt HM, Roos PH, Thier R (2003) The cytochrome P-450 isoenzyme CYP2E1 in the biological processing of industrial chemicals: consequences for occupational and environmental medicine. Int Arch Occup Environ Health 76(3): 174–185. DOI: 10.1007/s00420-002-0407-4

Brown WD, Setzer JV, Dick RB, Phipps FC, Lowry LK (1987) Body burden profiles of single and mixed solvent exposures. J Occup Med 29(11): 877–883

Brugnone F, Perbellini L, Apostoli P, Caretta D, Cocheo V (1983) Environmental and biological monitoring of occupational methylethyl ketone exposure. Dev Toxicol Environ Sci 11: 571–574

Ghittori S, Imbriani M, Pezzagno G, Capodaglio E (1987) The urinary concentration of solvents as a biological indicator of exposure: proposal for the biological equivalent exposure limit for nine solvents. Am Ind Hyg Assoc J 48(9): 786–790

Gobba F, Ghittori S, Imbriani M, Maestri L, Capodaglio E, Cavalleri A (1997) The urinary excretion of solvents and gases for the biological monitoring of occupational exposure: a review. Sci Total Environ 199(1-2): 3–12. DOI: 10.1016/S0048-9697(97)05476-4

Greim H (ed) (2000) 2-Butanon. In: Gesundheitsschädliche Arbeitsstoffe, Toxikologisch-arbeitsmedizinische Begründung von MAK-Werten. 30th issue. Wiley-VCH, Weinheim. Also available from DOI: 10.1002/3527600418.mb7893d0030

Imbriani M, Ghittori S (2005) Gases and organic solvents in urine as biomarkers of occupational exposure: a review. Int Arch Occup Environ Health 78(1): 1–19. DOI: 10.1007/s00420-004-0544-z

Imbriani M, Ghittori S, Pezzagno G, Capodaglio E (1989) Methyl ethyl ketone (MEK) in urine as biological index of exposure. G Ital Med Lav 11(6): 255–261

Jang J-Y, Kang S-K, Chung HK (1993) Biological exposure indices of organic solvents for Korean workers. Int Arch Occup Environ Health 65(1 Suppl): 219–222. DOI: 10.1007/BF00381345

Kawai T, Zhang Z-W, Takeuchi A, Miyama Y, Sakamoto K, Higashikawa K, Ikeda M (2003) Methyl isobutyl ketone and methyl ethyl ketone in urine as biological markers of occupational exposure to these solvents at low levels. Int Arch Occup Environ Health 76(1): 17–23. DOI: 10.1007/s00420-002-0374-9

Liira J, Riihimäki V, Pfäffli P (1988) Kinetics of methyl ethyl ketone in man: absorption, distribution and elimination in inhalation exposure. Int Arch Occup Environ Health 60(3): 195–200. DOI: 10.1007/BF00378697

Liira J, Johanson G, Riihimäki V (1990 a) Dose-dependent kinetics of inhaled methylethylketone in man. Toxicol Lett 50(2-3): 195–201. DOI: 10.1016/0378-4274(90)90011-a

Liira J, Riihimäki V, Engström K (1990 b) Effects of ethanol on the kinetics of methyl ethyl ketone in man. Br J Ind Med 47(5): 325–330. DOI: 10.1136/oem.47.5.325

Miyasaka M, Kumai M, Koizumi A, Watanabe T, Kurasako K, Sato K, Ikeda M (1982) Biological monitoring of occupational exposure to methyl ethyl ketone by means of urinalysis for methyl ethyl ketone itself. Int Arch Occup Environ Health 50(2): 131–137. DOI: 10.1007/BF00378075

Ong CN, Sia GL, Ong HY, Phoon WH, Tan KT (1991) Biological monitoring of occupational exposure to methyl ethyl ketone. Int Arch Occup Environ Health 63(5): 319–324. DOI: 10.1007/BF00381581

Perbellini L, Brugnone F, Mozzo P, Cocheo V, Caretta D (1984) Methyl ethyl ketone exposure in industrial workers. Uptake and kinetics. Int Arch Occup Environ Health 54(1): 73–81. DOI: 10.1007/BF00378730

Tomicic C, Berode M, Oppliger A, Castella V, Leyvraz F, Praz-Christinaz S-M, Danuser B (2011) Sex differences in urinary levels of several biological indicators of exposure: a human volunteer study. Toxicol Lett 202(3): 218–225. DOI: 10.1016/j.toxlet.2011.01.032

Yoshikawa M, Kawamoto T, Murata K, Arashidani K, Katoh T, Kodama Y (1995) Biological monitoring of occupational exposure to methyl ethyl ketone in Japanese workers. Arch Environ Contam Toxicol 29(1): 135–139. DOI: 10.1007/BF00213098