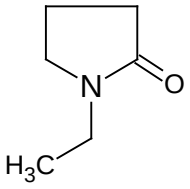
Derivation of HBM guide values* **FACTSHEET** NEP			
Substance	**N-Ethyl-2-pyrrolidone (NEP)**		
Parameter	**Value / Descriptor**	**Dimension**	**Comments**
HBM Guide value			
Guide value II (HBM II - Health hazard value)	children: 25 adults: 40	mg/l	urine, sum of 5-HNEP and 2-HESI
Guide value I (HBM I - Precautionary value)	children: 10 adults:15	mg/l	urine, sum of 5-HNEP and 2-HESI
Year of issue	2015		
Status	final		
General Information			
CAS No.	2687-91-4		
IUPAC name	1-Ethylpyrrolidin-2-one		
Molar mass	113.2	g/mol	
HBM-parameter	∑5-HNEP + 2-HESI		substance specific metabolites
Molar mass	129.2/143.2 → mean:136.2	g/mol	mean molar mass of 5-HNEP + 2-HESI
Database (TDI or key study)			
Key study: Author(s) (Year)	Kaspers et al (2006)		
Species	rat		
Route/type of study	oral		subchronic feeding study
Study length (Exposure duration)	90 d		
Critical endpoint/ effect	reduced grasp intensity		
POD_{HBM-II}	**250**	**mg/(kg bw x d)**	**BMD10**
POD_{HBM-I}	**90**	**mg/(kg bw x d)**	**BMDL05**
Assessment factors			**used by HBM Commission**
Severity of effect	-		
Adjusted exposure duration factor (time scaling)	n. a.		Oral study
Adjusted study length factor	2		subchronic → chronic
Route-to-route extrapolation factor	n. a.		
Adjusted absorption factor	n. a.		
Interspecies factor	4		allometric
	2.5		dynamic
Intraspecies factor	10		general population
Sensitive population factor	1		
Total assessment factor (TAF)	**200**		
Kinetik terms			
Fue(96h)	5-HNEP: 28.9 %, 2-HESI : 21.6 %		fraction of dose excreted in urine, molar basis (total, within 96h)

	sum: 50.5 % → 0.505		
Proportion molar mass metabolites to molar mass NEP	136.2/113.2 → 1,2		5-HNEP: 129.2; 2-HESI: 143.2 g/mol (mean metabolites: 136.2 g/mol); NEP: 113.2 g/mol
Urine volume	0.02 0.03	L/(kg bw x d) L/(kg bw x d)	adults children
Result (Calculation)			
POD/TAF	250/200 → 1.25 90/200 → 0.45	mg/(kg bw x d)	basis for HBM-II value derivation basis for HBM-I value derivation
Kinetic extrapolation and HBM value calculation for children	1.25 x 0.505 x 1.2 : 0.03 = 25.25 → 25 0.45 x 0.505 x 1.2 : 0,03 = 9.09 → 10	mg/L	rounded value: HBM-II HBM-I
Kinetic extrapolation and calculated HBM values for adults	1.25 x 0.505 x 1.2 : 0.02 = 37.88 → 40 0.45 x 0.505 x 1.2 : 0.02 = 13.64 → 15	mg/L	rounded value: HBM-II HBM-I
Management			
The values apply to children or adults, respectively. If the HBM value is exceeded first a check-up will be necessary. For measurements above the HBM-II value there is cause for concern for pregnant women. Air measurements to determine the source of exposure can be useful. Also a history of skin absorption should be considered and the use of cleaning and maintenance products and building products should be inquired			

*) Grundsatzpapier for the derivation of HBM guide values. Bundesgesundheitsbl Gesundheitsforsch Gesundheitsschutz 57(1):138-147 http://link.springer.com/article/10.1007/s00103-013-1867-2

Rationale:

N-Ethyl-2-pyrrolidone (NEP), a polar aprotic solvent, is used in many applications as substitute for the structural analogue N-methyl-2-pyrrolidone (NMP), e. g. for surface coatings, in cleaning agents and paint strippers. Monitoring studies indicate that individuals within the general public, without occupational exposure, may be exposed to NEP to an extent, which is comparable to NMP. As NMP, NEP presents a potential health hazard due to its developmental toxicity and teratogenicity. Exposure to NEP can be quantified by the determination of the excretion of its urinary metabolites 5-Hydroxy-N-ethyl-2-pyrrolidone (5-HNEP) and 2-Hydroxy-N-ethylsuccinimide (2-HESI). For the derivation of HBM values, the Human Biomonitoring Commission (HBM commission) evaluated different toxicological endpoints and finally decided on the BMDL05 and the BMD10 for the endpoint “reduced grasp intensity” of a subchronic feeding study with rats as point of departure (POD) for further procedural steps. The resulting HBM-I and HBM-II values for the sum of the metabolites 5-HNEP and 2-HESI in the urine of children are 10 resp. 25 mg/l and in the urine of adults are 15 resp. 40 mg/l. If the HBM values are exceeded, a check-up will be necessary at first. Measurements above the HBM II value give cause for concern, especially for pregnant women. Air measurements to determine the source of exposure can be useful. The possibility of skin absorption from use of cleaning agents and paint strippers should also be traced. As NEP und NMP have similar toxicological effects, a potential mixed exposure to both substances has to be taken into account.