HMA
Heads of Medicines Agencies

HOMEOPATHIC MEDICINAL PRODUCT WORKING GROUP

(HMPWG)

3RD LIST OF FIRST SAFE DILUTIONS (FSD)

DISCUSSION IN THE SUBGROUP FSD	31 March 2017
DISCUSSION IN THE HMPWG	26 – 27 June 2017
ADOPTION BY THE HMPWG for public consultation	26 – 27 June 2017
TRANSMISSION TO HMA for release for consultation	07 July 2017
DEADLINE FOR COMMENTS	07 October 2017

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Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Ammonium bromatum **NH_4Br** HAB	Ph. Eur. 3.1.1 (HAB 5a) for solution Ph. Eur. 4.1.1 (HAB 6) for trituration Ph. Eur. 4.1.2 (Ph. Franç.)	NH_4Br: 0.93-1.06 % in D2 Mr 97.9 Relative content Br^- in stock = 81.61 %	Bromide: ADI	400 µg bromide/kg/day → 1200 µg bromide/day (neonate)	Bromide, sodium salt. Summary report. Committee for Veterinary Medicinal Products EMEA/MRL/182/97-Final	10 g D2 = 106 mg raw material = 86.5 mg Br^- → 10 g D4 = 1.06 mg raw material = 865 µg Br^-	**D4**	ADI bromide ($Br^{-)}$ is based on a $NOEL_{human}$ of 4 mg Br^-/kg/d divided by an UF of 10
Atropinum sulfuricum **$C_{34}H_{48}N_2O_{10}S \cdot H_2O$** HAB	Ph. Eur. 3.1.1 (HAB 5a) for solution Ph. Eur. 4.1.1 (HAB 6) for trituration	Atropine sulphate: 9.4-10.6 % in D1 → 10 g D1 = 1.06 g atropine sulphate	LHRD	0.6 µg atropine/day (neonate)	BNF for children 2015 – 2016; BMJ Group, 2015; p. 730	10 g D1 = 1.06 g atropine sulphate → 10 g D8 = 0.106 µg alkaloids	**D8**	Oral dosage for neonate = 0.02-0.04 mg/kg → LHRD = 0.06 mg/3 kg neonate → divided by 100 = 0.6 µg/3 kg neonate/day. As the former used Merck Manual reference for the entry atropine is no longer available, a retrievable source for the LHRD was provided.

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Aurum iodatum **AuI + AuI_3** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Au: 0.32-0.42 % in D2	PDE	2.7 µg Au/kg/day → 8.00 µg Au/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D2 = 42 mg Au → 10 g D6 = 4.2 µg Au	**D6**	Derivation of PDE gold: LOAEL 32.2 mg Au/kg divided by UF (F1-F5 = 12 x 10 x 10 x 1 x 10) → 0.0027 mg Au/kg/d x 3 kg bw neonate → 0.008 mg Au/d = 8.00 µg Au/d Conclusive remark: The PDE of gold is more conservative and thus the relevant one for FSD assessment.
Calcarea carbonica ostrearum **$CaCO_3$** Ph. Franç. see Calcium carbonicum Hahnemanni (HAB)	Ph. Eur. 4.1.2 (Ph. Franç.)	$CaCO_3$: minimum 90 % in stock Mr 100.1 Ca: relative content = 40.04 %	mean intakes per day adequate for the majority of infants of the first half-year of life	200 mg calcium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1000 mg $CaCO_3$ = 400.4 mg Ca → 10 g D2 = 100 mg $CaCO_3$ = 40.04 mg Ca	**D2**	

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Calcarea phosphorica $Ca_3(PO_4)_2$ Ph. Franç. see Calcium phosphoricum (HAB, slightly different stock)	Ph. Eur. 4.1.2 (Ph. Franç.)	$Ca_3(PO_4)_2$: 35.0-40.0 % Ca in stock Mr 310.174 PO_4: relative content = 61.24 % Ca: relative content = 38.76 %	mean intakes per day adequate for the majority of infants of the first half-year of life	100 mg phosphate/day (neonate) 200 mg calcium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1000 mg $Ca_3(PO_4)_2$ = 612.4 mg PO_4 = 387.6 mg Ca → 10 g D2 = 100 mg $Ca_3(PO_4)_2$ = 61.24 mg PO_4 = 38.76 mg Ca	**D2**	
Calcium carbonicum Hahnemanni $CaCO_3$ HAB see Calcarea carbonica ostrearum (Ph. Franç.)	Ph. Eur. 4.1.1 (HAB 6)	$CaCO_3$: 8.4-10.5 % in D1 Mr 100.1 Ca: relative content = 40.04 %	mean intakes per day adequate for the majority of infants of the first half-year of life	200 mg calcium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1050 mg $CaCO_3$ = 420.42 mg Ca → 10 g D2 = 42.04 mg Ca	**D2**	
Calcium phosphoricum $CaHPO_4 \cdot 2H_2O$ HAB see Calcarea phosphorica (Ph. Franç.;	Ph. Eur. 4.1.1 (HAB 6)	$CaHPO_4 \cdot 2H_2O$: 9.3-11.0 % in D1 Mr 172.1 PO_4: relative content = 55.2 % Ca: relative content = 23.29 %	mean intakes per day adequate for the majority of infants of the first half-year of life	100 mg phosphate/day (neonate) 200 mg calcium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1100 mg raw material = 607.2 mg $P0_4$ = 256.2 mg Ca → 10 g D2 = 60.72 mg $P0_4$ =25.62 mg Ca	**D2**	

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
slightly different stock)								
Causticum Hahnemanni HAB	special manufacturing procedure according to monograph HAB	Potassium hydrogen sulfate, Calcium hydroxide see column „Remarks“	mean intakes per day adequate for the majority of infants of the first half-year of life	200 mg calcium/day (neonate) 400 mg potassium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	Solution=D1	**D1**	It is not expected that a measurable amount of potassium or calcium can be detected in the solution = D1.
Chimaphila umbellata HAB	Ph. Eur. 1.1.5 (HAB 3a): D1 = 3 MT + 7 ethanol	whole plant material	TTC	0.15 µg/day (neonate)	HMPWG - Points to consider on non-clinical safety of homeopathic medicinal products of botanical, mineral and chemical origin (2007) Questions and Answers on First Safe Dilutions (2015)	10 g D1 = 1666.67 mg fresh plant material → D9 = 0.016 µg fresh plant material	**D9**	As there are no validated data regarding the content of naphthoquinones in the starting material, the calculation is based on the content of whole plant. However, an assessment on the basis of naphthoquinones is possible if the content of naphthoquinones is de-

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
								termined by a validated method.
Chimaphila umbellata Ph. Franç.	Ph. Eur 1.1.10 (Ph. Franç.)	whole plant material	TTC	0.15 µg/day (neonate)	HMPWG - Points to consider on non-clinical safety of homeopathic medicinal products of botanical, mineral and chemical origin (2007) Questions and Answers on First Safe Dilutions (2015)	10 g MT = 1000 mg dried plant material → 10 g D7 = 0,10 µg dried plant material	**D7**	As there are no validated data regarding the content of naphthoquinones in the starting material, the calculation is based on the content of whole plant. However, an assessment on the basis of naphthoquinones is possible if the content of naphthoquinones is determined by a validated method.
Drosera HAB	Ph. Eur. 1.1.3 (HAB 2a): D1 = 2 MT + 8 ethanol	whole plant material	TTC	0.15 µg/day (neonate)	HMPWG - Points to consider on non-clinical safety of homeopathic medicinal products of botanical, mineral and chemical origin (2007) Questions and Answers on First Safe Dilutions (2015)	10 g MT = 8333.33 mg fresh plant material → 10 g D9 = 0.0167 µg fresh plant material	**D9**	An assessment on the basis of naphtoquinones is possible if the content of naphtoquinones is determined by a validated method.

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Drosera Ph. Franç.	Ph. Eur. 1.1.10 (Ph. Franç.)	whole plant material	TTC	0.15 µg/day (neonate)	HMPWG - Points to consider on non-clinical safety of homeopathic medicinal products of botanical, mineral and chemical origin (2007) Questions and Answers on First Safe Dilutions (2015)	10 g MT = 1000 mg plant material → 10 g D7 = 0.10 µg plant material	**D7**	An assessment on the basis of the naphtoquinones is possible if the content of naphtoquinones is determined by a validated method.
Galenit PbS HAB	Ph. Eur. 4.1.1 (HAB 6)	PbS: 9.0-10.5 % in D1 Mr 239.3 Pb: relative content = 86.59 %	PDE	5 µg/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1050 mg PbS = 909.2 mg Pb → 10 g D7 = 1.05 µg PbS = 0.91 µg Pb	**D7**	Derivation of PDE lead: Oral intake of 5 µg Pb/day translates into a blood level of 1-2 µg Pb/dL established from epidemiological studies for children age 0-7 years (0-82 months); considered applicable to newborns, hence NO further weight adjustment to PDE ICH Q3D necessary.
Galenit PbS HAB	Ph. Eur. 1.1.10 (Ph. Franç.)	PbS: 9.0-10.5 % in D1 Mr 239.3 Pb: relative content = 86.59 %	PDE	5 µg/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g MT = 1050 mg PbS = 909.2 mg Pb → 10 g D6 = 1.05 µg PbS = 0.91 µg Pb	**D6**	Derivation of PDE lead: Oral intake of 5 µg Pb/day translates into a blood level of 1-2 µg Pb/dL established from epidemiological studies for children age 0-7 years (0-82 months); considered applicable to new-

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
								borns, hence NO further weight adjustment to PDE ICH Q3D necessary.
Juglans regia Ph. Franç.	Ph. Eur. 1.1.10 (Ph. Franç.)	Juglone: 0.002-0.008 % total quinone derivatives in MT, expressed as juglone	TTC	0.15 µg/day (neonate)	HMPWG - Points to consider on non-clinical safety of homeopathic medicinal products of botanical, mineral and chemical origin (2007) Questions and Answers on First Safe Dilutions (2015)	10 g MT = 0.8 mg juglone → 10 g D4 = 0.08 µg juglone	**D4**	Due to the information on juglone content given in the monograph of the Ph. Franç., the assessment is based on these data.
Kalium arsenicosum $KAsO_2$ Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	$KAsO_2$: 96.0-101.0 % in stock Mr 146.0 As: relative content = 51.32 %	PDE	0.3 µg As/kg/day → 0.9 µg As/day (neonate) 400 mg potassium/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013) Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1010 mg $KAsO_2$ = 518.33 mg As → 10 g D7 = 0.52 µg As	**D7**	Derivation of PDE arsenic: MRL = 0.0003 mg/kg/d x 3 kg bw neonate → 0.9 µg As/d (no UF). Conclusive remark: The PDE of arsenic is more conservative and thus the relevant one for FSD assessment.
Kalium bromatum KBr HAB	Ph. Eur. 3.1.1 (HAB 5a) for solution Ph. Eur. 4.1.1 (HAB 6) for trituration	KBr: 9.3-10.6 % in D1 Mr 119.0 K: relative content = 32.86 % Br: relative content = 67.14 %	Bromide: ADI Potassium: mean intakes per day adequate for the majority of	1200 µg bromide/day (neonate) 400 mg potassium/day (neonate)	Committee for Veterinary Medicinal Products EMEA (1997) Bromide, sodium salt. Summary report. EMEA/MRL/182/97-Final Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in	10 g D1 = 1060 mg KBr = 711.68 mg Br = 348.32 mg K → 10 g D4 = 1060 µg KBr = 711.68 µg Br = 348.32 µg K	**D4**	Conclusive remark: The ADI of bromide is more conservative and thus the relevant one for FSD assessment.

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
			infants of the first half-year of life		the European Union, EFSA Journal 2013;11(10):3408			
Kalium bromatum **KBr** Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	KBr: 98.5-101.0 % in stock Mr: 119.0 K: relative content = 32.86 % Br: relative content = 67.14 %	Bromide: ADI Potassium: mean intakes per day adequate for the majority of infants of the first half-year of life	1200 µg bromide/day (neonate) 400 mg potassium/day (neonate)	Committee for Veterinary Medicinal Products EMEA (1997) Bromide, sodium salt. Summary report. EMEA/MRL/182/97-Final Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1010 mg KBr = 678.11 mg Br = 331.89 mg K → 10 g D4 = 1010 µg KBr = 678 µg Br = 331.89 µg K	**D4**	Conclusive remark: The ADI of bromide is more conservative and thus the relevant one for FSD assessment.
Kalium carbonicum **K_2CO_3** HAB	Ph. Eur. 3.1.1 (HAB 5a) for solution Ph. Eur. 4.1.1 (HAB 6) for trituration	K_2CO_3: 9.4-10.6 % in D1 (solution) Mr 138.2 K: relative content = 56.58 %	mean intakes per day adequate for the majority of infants of the first half-year of life	400 mg potassium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1060 mg K_2CO_3 = 599.75 mg K → 10 g D2 = 106 mg K_2CO_3 = 59.975 mg K	**D2**	
Kalium carbonicum **K_2CO_3** Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	K_2CO_3: 99.0-101.0 % in stock Mr 138.2 K: relative content = 56.58 %	mean intakes per day adequate for the majority of infants of the first half-year of life	400 mg potassium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1010 mg K_2CO_3 = 571.46 mg K → 10 g D2 = 101 mg K_2CO_3 = 57.15 mg K	**D2**	

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Kalium chloratum **KCl** HAB see Kalium muriaticum (Ph. Franç.)	Ph. Eur. 3.1.1 (HAB 5a) for solution Ph. Eur. 4.1.1 (HAB 6) for trituration	D1: 9.4-10.6 % KCl Mr 74.6 K: relative content = 52.41 % Cl: relative content = 47.59 %	mean intakes per day adequate for the majority of infants of the first half-year of life	300 mg chloride/day (neonate) 400 mg potassium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1060 mg KCl = 504.45 mg Cl = 555.55 mg K → 10 g D2 = 50.45 mg Cl = 55.55 mg K	**D2**	
Kalium muriaticum **KCl** Ph. Franç. see Kalium chloratum (HAB)	Ph. Eur. 4.1.2 (Ph. Franç.)	KCl: 99.0-101.0 % in stock Mr 74.6 K: relative content = 52.41 % Cl: relative content = 47.59 %	mean intakes per day adequate for the majority of infants of the first half-year of life	300 mg chloride/day (neonate) 400 mg potassium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1010 mg KCl = 480.66 mg Cl = 529.34 mg K → 10 g D2 = 48.07 mg Cl = 52.93 mg K	**D2**	
Kalium nitricum **KNO_3** HAB	Ph. Eur. 3.1.1 (HAB 5a) for solution Ph. Eur. 4.1.1 (HAB 6) for trituration	KNO_3: 0.95-1.07 % in D2 Mr 101.1 K: relative content = 38.67 % NO_3: relative content = 61,33 %	NO_3: RfD K: mean intakes per day adequate for the majority of infants of the first half-year of life	1.6 mg nitrate/kg/day → 4.8 mg nitrate/day (neonate) 400 mg potassium/day (neonate)	Reference Dose for Oral Exposure (RfD), Nitrate CASRN 14797-55-8 United States Environmental Protection Agency Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D2 = 107 mg KNO_3 = 65.62 mg NO_3 = 41.38 mg K → 10 g D4 = 1.07 mg KNO_3 = 0.6562 mg NO_3 = 0.4138 mg K	**D4**	

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Kalium nitricum **KNO_3** Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	KNO_3: 99.0-101.0 % in stock Mr 101.1 K: relative content = 38.67 % NO_3: relative content = 61.33 %	NO_3: RfD K: mean intakes per day adequate for the majority of infants of the first half-year of life	1.6 mg nitrate/kg/day → 4.8 mg nitrate/day (neonate) 400 mg potassium/day (neonate)	Reference Dose for Oral Exposure (RfD), Nitrate CASRN 14797-55-8 (United States Environmental Protection Agency) Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1010 mg KNO_3 = 619.43 mg NO_3 = 390.57 mg K → 10 g D4 = 1.01 mg KNO_3 = 0.62 mg NO_3 = 0.39 mg K	**D4**	
Kalium phosphoricum **K_2HPO_4** Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	K_2HPO_4: 98.0-101.0 in stock Mr 174.2 K: relative content = 44.89 % PO_4: relative content = 54.54 %	mean intakes per day adequate for the majority of infants of the first half-year of life	100 mg phosphate/day (neonate) 400 mg potassium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1010 mg K_2HPO_4 = 550.9 mg PO_4 = 453.39 mg K → 10 g D2 = 101 mg K_2HPO_4 = 55.09 mg PO_4 = 45.34 mg K	**D2**	
Kalium phosphoricum **KH_2PO_4** HAB	Ph. Eur. 3.1.1 (HAB 5a) for solution Ph. Eur. 4.1.1 (HAB 6) for trituration	KH_2PO_4: 0.93-1.06 % in D2 Mr 136.1 K: relative content = 28.73% PO_4: relative content = 69.8%	mean intakes per day adequate for the majority of infants of the first half-year of life	100 mg phosphate/day (neonate) 400 mg potassium/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D2 = 106 mg KH_2PO_4 = 73.99 mg PO_4 = 30.45 mg K	**D2**	

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Kalium sulfuricum **K_2SO_4** HAB	Ph. Eur. 3.1.1 (HAB 5a) for solution Ph. Eur. 4.1.1 (HAB 6) for trituration	K_2SO_4: 9.4-10.6 % in D1 Mr 174.3 K: relative content = 44.86 % SO_4: relative content = 55.14 %	SO_4: 100 mg sulphate ion/kg/day = uncritical K: mean intakes per day adequate for the majority of infants of the first half-year of life	100 mg sulphate ion/kg/day → 300 mg sulphate ion/day (neonate) 400 mg potassium/day (neonate)	Scientific Opinion on the use of potassium sulphate and sodium sulphate as sources of respectively potassium and sodium added for nutritional purposes to food supplements, EFSA Journal 2010;8(12):1940 Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1060 mg K_2SO_4 = 584.48 mg sulphate = 475.52 mg K → 10 g D2 = 106 mg K_2SO_4 = 58.448 mg sulphate = 47.552 mg K	**D2**	

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Kalium sulfuricum **K_2SO_4** Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	K_2SO_4: 98.5-101.0 % in stock Mr 174.3 K: relative content = 44.86 % SO_4: relative content = 55.14 %	SO_4: 100 mg sulphate ion/kg/day = uncritical K: mean intakes per day adequate for the majority of infants of the first half-year of life	100 mg sulphate ion/kg/day → 300 mg sulphate ion/day (neonate) 400 mg potassium/day (neonate)	Scientific Opinion on the use of potassium sulphate and sodium sulphate as sources of respectively potassium and sodium added for nutritional purposes to food supplements, EFSA Journal 2010;8(12):1940 Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1010 mg K_2SO_4 = 556.9 mg SO_4 = 453.1 mg K → 10 g D2 = 101 mg K_2SO_4 = 55.69 mg SO_4 = 45.31 mg K	**D2**	
Magnesium phosphoricum **$MgHPO_4 \cdot 3H_2O$** HAB/Ph. Eur.	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$MgHPO_4 \cdot 3\ H_2O$: 9.3-10.8 % in D1 Mr 174,3 Mg: relative content = 13,9% $P0_4$: relative content = 54,5%	mean intakes per day adequate for the majority of infants of the first half-year of life	25 mg magnesium/day (neonate) 100 mg phosphate/day (neonate)	Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union, EFSA Journal 2013;11(10):3408	10 g D1 = 1080 mg $MgHPO_4 \cdot 3\ H_2O$ = 150.12 mg Mg = 588.6 mg $P0_4$ → 10 g D2 = 108 mg $MgHPO_4 \cdot 3\ H_2O$ = 15.012 mg Mg = 58.86 mg $P0_4$	**D2**	
Petroleum rectificatum HAB/Ph. Eur.	Ph. Eur. 1.1.10 (Ph. Franç.)	Aromatic hydrocarbons	TTC	0.15 µg petroleum/day (neonate)	HMPWG - Points to consider on non-clinical safety of homeopathic medicinal products of botanical, mineral and chemical origin (2007)	10 g MT = 1000 mg raw material → 10 g D7 = 0.1 µg raw	**D7**	TTC is chosen for assessment due to the genotoxic and carcinogenic potential of aromatic

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Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
					Questions and Answers on First Safe Dilutions (2015)	material		hydrocarbons. In consequence of missing information on the content of aromatic hydrocarbons in the raw material, the calculation is based on the whole starting material.
Petroleum rectificatum HAB/Ph. Eur.	Ph. Eur. 3.1.1 (HAB 5a)	Aromatic hydrocarbons	TTC	0.15 µg petroleum/day (neonate)	HMPWG - Points to consider on non-clinical safety of homeopathic medicinal products of botanical, mineral and chemical origin (2007) Questions and Answers on First Safe Dilutions (2015)	10 g D2 = 100 mg raw material → 10 g D8 = 0.1 µg raw material	**D8**	TTC is chosen for assessment due to the genotoxic and carcinogenic potential of aromatic hydrocarbons. In consequence of missing information on the content of aromatic hydrocarbons in the raw material, the calculation is based on the whole starting material.
Rauwolfia serpentina HAB	Ph. Eur. 1.1.8 (HAB 4a)	Reserpine: 0.10-0.30 % in MT	LHRD	0.0001 mg reserpine/kg/day → 0.0003 mg reserpine/day (neonate)	http://www.merckmanuals.com	10 g MT = 30 mg reserpine → 10 g D6 = 0.3 µg reserpine	**D6**	Pediatric dosing: Hypertension: 0.01 to 0.02 mg/kg/24 hours divided every 12 hours; maximum dose: 0.25 mg/day (not recommended in children) LHRD = 0,01 mg/kg/d

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Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
								LHRD/100 = 0,0001 mg/kg/d
Rauwolfia serpentina, ethanolic decoctum HAB	HAB 19f	Reserpine: 0.10-0.30 % in MT	LHRD	0.0001 mg reserpine/kg/day → 0.0003 mg reserpine/day (neonate)	http://www.merckmanuals.com	10 g MT = 30 mg reserpine → 10 g D6 = 0.3 µg reserpine	**D6**	Pediatric dosing: Hypertension: 0.01 to 0.02 mg/kg/24 hours divided every 12 hours; maximum dose: 0.25 mg/day (not recommended in children) LHRD = 0,01 mg/kg/d LHRD/100 = 0,0001 mg/kg/d
Reserpinum **$C_{33}H_{40}N_2O_9$** Ph. Eur.	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Reserpine: 98.0-102.0 %	LHRD	0.0001 mg reserpine/kg/day → 0.0003 mg reserpine/day (neonate)	http://www.merckmanuals.com	10 g D1 = 1020 mg Reserpine → 10 g D8 = 0.102 µg	**D8**	Pediatric dosing: Hypertension: 0.01 to 0.02 mg/kg/24 hours divided every 12 hours; maximum dose: 0.25 mg/day (not recommended in children) LHRD = 0,01 mg/kg/d LHRD/100 = 0,0001 mg/kg/d

1	2	3	4	5	6	7	8	9
Stock/raw/starting material	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Symphytum officinale HAB	Ph. Eur. 1.1.5 (HAB 3a): D1 = 3 MT + 7 ethanol	whole plant material	TDI	0.007 µg PA/kg/day → 0.021 µg PA/day (neonate)	Public statement on contamination of herbal medicinal products/traditional herbal medicinal products with pyrrolizidine alkaloids EMA/HMPC/328782/2016 Scientific Opinion on Pyrrolizidine alkaloids in food and feed, EFSA Journal 2011;9(11):2406	10 g MT = 5555.56 mg fresh plant material → 10 g D9 = 0.0167 µg fresh plant material	**D9**	As there are no validated data regarding the content of pyrrolizidine alkaloids in the starting material, the calculation is based on the content of whole plant. However, an assessment on the basis of pyrrolizidine alkaloids is possible if their content is determined by a validated method.
Symphytum officinale Ph. Franç.	Ph. Eur. 1.1.10 (Ph. Franç.)	whole plant material	TDI	0.007 µg PA/kg/day → 0.021 µg PA/day (neonate)	Public statement on contamination of herbal medicinal products/traditional herbal medicinal products with pyrrolizidine alkaloids EMA/HMPC/328782/2016 Scientific Opinion on Pyrrolizidine alkaloids in food and feed, EFSA Journal 2011;9(11):2406	10 g MT = 1000 mg fresh plant material → 10 g D8 = 0.01 µg fresh plant material	**D8**	As there are no validated data regarding the content of pyrrolizidine alkaloids in the starting material, the calculation is based on the content of whole plant. However, an assessment on the basis of pyrrolizidine alkaloids is possible if their content is determined by a validated method.