HMA
Heads of Medicines Agencies

HOMEOPATHIC MEDICINAL PRODUCT WORKING GROUP

(HMPWG)

2ND LIST OF FIRST SAFE DILUTIONS (FSD)

DISCUSSION IN THE SUBGROUP FSD	4th October 2016
DISCUSSION IN THE HMPWG	November / December 2016
ADOPTION BY THE HMPWG for public consultation	5th January 2017
TRANSMISSION TO HMA for release for consultation	15 February 2017
DEADLINE FOR COMMENTS	16 May 2017
DISCUSSION IN THE SUBGROUP FSD	To be scheduled
DISCUSSION IN HMPWG	26-27 June 2017

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**
Ambra grisea Ph. Franç.	Ph. Eur. 1.1.11 (Ph. Franç.): MT = 1/20	content of starting material	PDE	2µg ambrein/kg/day → 6 µg ambrein/day (neonate)	Taha SA, Raza M, Gader AG, Hafeez MA. A study of ambrein treatment for the evaluation of change in plasma biochemical parameters in rat. Jpn J Pharmacol. 1995 Mar; 67(3): 205-9	10 g MT = 500 mg raw material → 10 g D5 = 5 µg raw material	**D5**	No validated assay and no upper limit of ambrein; worst case assumption is applicable (basis amount of raw material). Derivation of PDE ambrein: LOAEL rat 10 mg/kg/day divided by UF (F1-F5 = 5 x10 x 10 x 1 x 10) → 2 µg ambrein/kg/day x 3 kg bw neonate = 6 µg ambrein/day
Ambra grisea HAB	preparation of MT = D1: 10 parts comminuted substance + 100 parts ethanol	content of starting material	PDE	2µg ambrein/kg/day → 6 µg ambrein/day (neonate)	Taha SA, Raza M, Gader AG, Hafeez MA. A study of ambrein treatment for the evaluation of change in plasma biochemical parameters in rat. Jpn J Pharmacol. 1995 Mar; 67(3): 205-9	10 g MT = D1: 1000 mg raw material → 10 g D7 = 1 µg raw material	**D7**	No validated assay and no upper limit of ambrein; worst case assumption is applicable (basis amount of raw material) Derivation of PDE ambrein: LOAEL rat 10 mg/kg/day divided by UF (F1-F5 = 5 x10 x 10 x 1 x 10) → 2 µg ambrein/kg/day x 3 kg bw neonate = 6 µg ambrein/day
Antimonite Sb_2S_3 HAB See Antimonium crudum (Ph. Franç.) and Stibium sulfuratum nigrum (HAB)	Ph. Eur. 4.1.1 (HAB 6)	Sb_2S_3: 9.0-10.5 % in D1 Mr 339.7 Relative content Sb in stock = 71.69 %	PDE	24 µg Sb/kg/day → 72 µg Sb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1050 mg Sb_2S_3 = 752.75 mg Sb → 10g D6 = 7.53 µg Sb	**D6**	Derivation of PDE antimony: NOAEL 6000 µg Sb/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) = 24 µg Sb/kg/d x 3 kg bw neonate = 72 µg Sb/d

1	2	3	4	5	6	7	8	9
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Antimonium crudum **Sb_2S_3** Ph. Franç. See Antimonite (HAB) and Stibium sulfuratum nigrum. (HAB)	Ph. Eur. 4.1.2 (Ph. Franç.)	Sb_2S_3: 98.0-102.0 % in stock Mr 339.7 Relative content Sb in stock = 71.69 %	PDE	24 µg Sb/kg/day → 72 µg Sb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1020 mg Sb_2S_3 = 731.24 mg Sb → 10g D6 = 7.31 µg Sb	**D6**	Derivation of PDE antimony: NOAEL 6000 µg Sb/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) = 24 µg Sb/kg/d x 3 kg bw neonate = 72 µg Sb/d
Argentite **Ag_2S** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Ag_2S: 9.0-10.5 % in D1 Mr 247.8 Relative content Ag in stock = 87.06 %	PDE	3.3 µg Ag/kg/day → 9.9 µg Ag/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1050 mg Ag_2S = 914.13 mg Ag → 10 g D6 = 9.14 µg Ag	**D6**	Derivation of PDE silver: PDE is consistent with the RfD (reference dose) of 5 µg Ag/kg/day (US EPA, 2003); LOAEL 20 mg Ag/kg divided by UF (F1-F5 = 12 x 10 x 5 x 1 x 10 = 6000) → 0.0033 mg Ag/kg/d x 3 kg bw neonate → 0.0099 mg Ag/d = 9.9 µg Ag/d
Argentum colloidale **Ag** HAB	specific preparation: 1 part stock is solubilized in 99 parts H_2O → 1 part of this solution + 9 parts H_2O = D3	Ag: 0.067-0.078 % in D3	PDE	3.3 µg Ag/kg/day → 9.9 µg Ag/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D3 = 7.8 mg Ag → 10 g D6 = 7.8 µg Ag	**D6**	Derivation of PDE silver: PDE is consistent with the RfD (reference dose) of 5 µg Ag/kg/day (US EPA, 2003); LOAEL 20 mg Ag/kg divided by UF (F1-F5 = 12 x 10 x 5 x 1 x 10 = 6000) → 0.0033 mg Ag/kg/d x 3 kg bw neonate → 0.0099 mg Ag/d = 9.9 µg Ag/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**
Argentum metallicum Ag HAB	Ph. Eur. 4.1.1 (HAB 6)	Ag: 9.4-10.6 % in D1	PDE	3.3 µg Ag/kg/day → 9.9 µg Ag/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg Ag → 10 g D7 = 1.06 µg Ag	**D7**	Derivation of PDE silver: PDE is consistent with the RfD (reference dose) of 5 µg Ag/kg/day (US EPA, 2003); LOAEL 20 mg Ag/kg divided by UF (F1-F5 = 12 x 10 x 5 x 1 x 10 = 6000) → 0.0033 mg Ag/kg/d x 3 kg bw neonate → 0.0099 mg Ag/d = 9.9 µg Ag/d
Argentum metallicum Ag Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	Ag: 99.0-100.5 % in stock	PDE	3.3 µg Ag/kg/day → 9.9 µg Ag/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1005 mg Ag → 10 g D7 = 1.005 µg Ag	**D7**	Derivation of PDE silver: PDE is consistent with the RfD (reference dose) of 5 µg Ag/kg/day (US EPA, 2003); LOAEL 20 mg Ag/kg divided by UF (F1-F5 = 12 x 10 x 5 x 1 x 10 = 6000) → 0.0033 mg Ag/kg/d x 3 kg bw neonate → 0.0099 mg Ag/d = 9.9 µg Ag/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**
Argentum nitricum **$AgNO_3$** HAB	Ph. Eur. 3.1.1 (HAB 5a)	$AgNO_3$: 9.4-10.6 % in D1 Mr 169.9 Relative content Ag in stock = 63.49 % Relative content NO_3 in stock = 36.51 %	PDE	3.3 µg Ag/kg/day → 9.9 µg Ag/day (neonate) ADI for nitrate: 3.7 mg/kg bw, expressed as nitrate ion → 11.1 mg/day (neonate)	Ag: ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013) Nitrate: WHO FOOD ADDITIVES SERIES: 50 NITRATE	10 g D1 = 1060 mg $AgNO_3$ = 672.99 mg Ag and 387 mg nitrate → 10 g D6 = 6.73 µg Ag and 3.87 µg nitrate	**D6**	Derivation of PDE silver: PDE is consistent with the RfD (reference dose) of 5 µg Ag/kg/day (US EPA, 2003); LOAEL 20 mg Ag/kg divided by UF (F1-F5 = 12 x 10 x 5 x 1 x 10 = 6000) → 0.0033 mg Ag/kg/d x 3 kg bw neonate → 0.0099 mg Ag/d = 9.9 µg Ag/d
Argentum nitricum **$AgNO_3$** Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	$AgNO_3$: 99.0-100.5 % in stock Mr 169.9 Relative content Ag in stock = 63.49 % Relative content NO_3 in stock = 36.51 %	PDE	3.3 µg Ag/kg/day → 9.9 µg Ag/day (neonate) ADI for nitrate: 3.7 mg/kg bw, expressed as nitrate ion → 11.1 mg/day (neonate)	Ag: ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013) Nitrate: WHO FOOD ADDITIVES SERIES: 50 NITRATE	10 g D1 = 1005 mg $AgNO_3$ = 638.1 mg Ag and 366.9 mg nitrate → 10 g D6 = 6.38 µg Ag and 3.67 µg nitrate	**D6**	Derivation of PDE silver: PDE is consistent with the RfD (reference dose) of 5 µg Ag/kg/day (US EPA, 2003); LOAEL 20 mg Ag/kg divided by UF (F1-F5 = 12 x 10 x 5 x 1 x 10 = 6000) → 0.0033 mg Ag/kg/d x 3 kg bw neonate → 0.0099 mg Ag/d = 9.9 µg Ag/d **Conclusive remark:** **The PDE of silver is more conservative and thus the relevant one for FSD assessment.**

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Stock*/raw/starting material**	**Method of Preparation**	**Toxic component concentration**	**Basis for FSD**	**Acceptable amount**	**Reference**	**Calculation method**	**FSD**	**Remarks**
Auri solutio colloidalis Au HAB	75 parts Sodium hydrogen carbonate (Ph. Eur.) + solution of 2 parts Natrium tetrachloroauratum (HAB) + 1800 parts purified water. Addition of 100 parts of acacia solution R and 35 parts of anhydrous formic acid R.	Au: 0.095-0.105 % in D3	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 D3 = 10.5 mg Au → 10 g D7 = 1.05 µg Au	**D7**	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
Aurum chloratum $H[AuCl_4] \cdot 3\ H_2O$ HAB	Ph. Eur. 3.1.1 (HAB 5a) Ph. Eur. 4.1.2 (Ph. Franç.)	Au: 4.7-5.1 % in D1	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 D1 = 510 mg Au → 10 g D6 = 5.1 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
Aurum metallicum Au HAB	Ph. Eur. 4.1.1 (HAB 6)	Au: 9.5-10.5 % in D1	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 D1 = 1050 mg Au → 10 g D7 = 1.05 µg Au	**D7**	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

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Aurum metallicum **Au** Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	Au: 98.0-101.0 in stock	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 D1 = 1010 mg Au → 10 g D7 = 1.01 µg Au	**D7**	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
Barium carbonicum **$BaCO_3$** HAB See Baryta carbonica (Ph. Franç.)	Ph. Eur. 4.1.1 (HAB 6)	$BaCO_3$: 9.3-10.6 % in D1 Mr 197.3 Relative content Ba in stock = 69.6 %	PDE	1460 µg Ba/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg $BaCO_3$ = 737.76 mg Ba → 10 g D4 = 737.8 µg Ba	**D4**	Derivation of PDE barium: NOAEL = 14.6 mg Ba/d : UF (F1-F5 = 1 x 10 x 1 x 1 x 1) = 1.46 mg Ba/d = 1460 µg Ba/d **Applicable to newborns, hence NO further weight adjustment to PDE ICH Q3D necessary.**
Barium chloratum **$BaCl_2 \cdot 2H_2O$** HAB/Ph. Eur.	Ph. Eur. 3.1.1 (HAB 5a) Ph. Eur. 4.1.2 (Ph. Franç.)	$BaCl_2 \cdot 2H_2O$: 9.4-10.6 % in D1 Mr 244.3 Relative content Ba in stock = 56.21 %	PDE	1460 µg Ba/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg $BaCl_2 \cdot 2H_2O$ = 595.83 mg Ba → 10 g D4 = 595.8 µg Ba	**D4**	Derivation of PDE barium: NOAEL = 14.6 mg Ba/d : UF (F1-F5 = 1 x 10 x 1 x 1 x 1) = 1.46 mg Ba/d = 1460 µg Ba/d **Applicable to newborns, hence NO further weight adjustment to PDE ICH Q3D necessary.**
Baryta carbonica **$BaCO_3$** Ph. Franç. See Barium carbonicum (HAB)	Ph. Eur. 4.1.2 (Ph. Franç.)	$BaCO_3$: 98.0-101.0 % in stock Mr 197.3 Relative content Ba in stock = 69.6 %	PDE	1460 µg Ba/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1010 mg $BaCO_3$ = 702.96 mg Ba → 10 g D4 = 702.96 µg Ba	**D4**	Derivation of PDE barium: NOAEL = 14.6 mg Ba/d : UF (F1-F5 = 1 x 10 x 1 x 1 x 1) = 1.46 mg Ba/d = 1460 µg Ba/d **Applicable to newborns, hence NO further weight adjustment to PDE ICH Q3D necessary.**

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Bellis perennis HAB	Ph. Eur. 1.1.3 (HAB 2a): D1 = 2 MT + 8 ethanol	N/A	MRL	no need for MRL	Committee for Veterinary Medicinal Products - Bellis perennis - Summary Report (EMEA/MRL/663/99-FINAL; http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500010965.pdf)	·/·	**MT**	
Bellis perennis Ph. Franç.	Ph. Eur. 1.1.10 (Ph. Franç.)	N/A	MRL	no need for MRL	Committee for Veterinary Medicinal Products - Bellis perennis - Summary Report (EMEA/MRL/663/99-FINAL; http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2009/11/WC500010965.pdf)	·/·	**MT**	
Blatta orientalis HAB	Monograph specific preparation for the MT = D1. Ph. Eur. 1.1.9 (HAB 4b) from D2 onwards	Chitin	ADI	no limit	USEPA/Office of Pesticide Programs; Biopesticide Active Ingredient Factsheet- Chitin; Poly-N-acetyl-D-glucosamine (128991). Issued 3/01. Available from, as of March 15, 2004: http://www.epa.gov/pesticides/biopesticides/ingredients/index.htm **PEER REVIEWED**	·/·	**MT**	

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Cadmium sulfuricum **$CdSO_4 \cdot {}^{8}/_{3}\, H_2O$** HAB/Ph. Eur.	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$CdSO_4 \cdot {}^{8}/_{3}\, H_2O$: 9.4-10.7 % in D1 Mr 256.5 Relative content Cd in stock = 43.83 %	PDE	0.1 µg Cd/kg/day → 0.3 µg Cd/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1070 mg $CdSO_4 \cdot {}^{8}/_{3}H_2O$ = 468.98 mg Cd → 10 g D8 = 0.0469 µg Cd	**D8**	Derivation of PDE cadmium: MRL = 0.1 µg Cd/kg x 3 kg bw neonate → 0.3 µg Cd/d (no UF) Preparations applied as a spray shall be assessed on the basis of the inhalation PDE for cadmium (=1,7 µg/day).
Calcium stibiato-sulfuratum HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Mixture of Sb_2S_3, S and Calcium carbonicum Hahnemanni ($CaCO_3$) D1: 0.85-1.2 % Sb, 1.7-2.4 % S	PDE	24 µg Sb/kg/day → 72 µg Sb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 120 mg Sb → 10 g D5 = 12 µg Sb	**D5**	Derivation of PDE antimony: NOAEL 6000 µg Sb/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) = 24 µg Sb/kg/d x 3 kg bw neonate = 72 µg Sb/d
Chalcosine **Cu_2S** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Cu_2S: 8.1-10.0 % in D1 Mr 159.2 Relative content Cu in stock = 79.84 %	PDE	68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1000 mg Cu_2S = 798.4 mg Cu → 10 g D5 = 79.84 µg Cu	**D5**	Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/d

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Chininum arsenicosum **$C_{20}H_{24}N_2O_2$ + As_2O_3** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$C_{20}H_{24}N_2O_2$: 8.5-9.7 % in D1 As_2O_3: 0.86-0.99 % in D1 Mr 197.8 (As_2O_3) Relative content As in As_2O_3= 75.76 %	PDE As LHRD quinine	0.3 µg As/kg/day → 0.9 µg As/day (neonate) 0.81 mg quinine/day (neonate)	Arsenic: ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013) Quinine: http://www.merckmanuals.com	10 g D1 = 99 mg As_2O_3 = 75 mg As and 970 mg quinine → 10 g D6 = 0.75 µg As and 9.7 µg quinine	**D6**	Derivation of PDE arsenic: MRL = 0.0003 mg As/kg/d x 3 kg bw neonate → 0.9 µg As/d (no UF) Derivation of LHRD Quinine: LHRD is based on the lowest daily dose of quinine for children in treatment of uncomplicated chloroquine-resistant P. falciparum malaria = 9 mg quinine/kg every 8 hours corresponding to 81 mg quinine/day for 3 kg neonate **Conclusive remark:** **The PDE of arsenic is more conservative and thus the relevant one for FSD assessment.**
Cobaltum metallicum **Co** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Co: 9.4-10.6 % in D1	PDE	1 µg Co/kg/day → 3 µg Co/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg Co → 10 g D7 = 1.06 µg Co	**D7**	Derivation of PDE cobalt: NOAEL = 1 mg/d: UF (F1-F5 = 1 x 10 x 2 x 1 x 1) = 50 µg Co/d ÷ 50 kg = 1 µg Co/kg/d x 3 kg bw neonate → 3 µg Co/d
Cuprite **Cu_2O** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Cu_2O: 8.1-10.5 % in D1 Mr 143.1 Relative content Cu in stock = 88.82 %	PDE	68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1050 mg Cu_2O = 932.61 mg Cu → 10 g D5 = 93.26 µg Cu	**D5**	Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/d

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Cuprum aceticum **$Cu(C_2H_3O_2)_2 \cdot H_2O$** HAB/Ph. Eur.	Ph. Eur. 3.1.1 (HAB 5a) Ph. Eur. 4.1.2 (Ph. Franç.)	$Cu(C_2H_3O_2)_2 \cdot H_2O$: 0.94 - 1.06 % in D2 Mr = 199.7 Relative content Cu in stock = 31.83 %	PDE	68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg $C_4H_6CuO_4 \cdot H_2O$ = 337.29 mg Cu → 10 g D5 = 33.73 µg Cu	**D5**	Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/d
Cuprum arsenicosum HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Precipitated copper subarsenite: 2.5-3.4 % As in D1, 3.4-4.3 % Cu in D1	PDE	0.3 µg As/kg/day → 0.9 µg As/day (neonate) 68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 340 mg As and 430 mg Cu → 10 g D7 = 0.34 µg As and 0.43 µg Cu	**D7**	Derivation of PDE arsenic: MRL = 0.0003 mg As/kg/d x 3 kg bw neonate → 0.9 µg As/d (no UF). Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/d **Conclusive remark: The PDE of arsenic is more conservative and thus the relevant one for FSD assessment.**
Cuprum metallicum **Cu** HAB/Ph. Eur.	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Cu: 9.5-10.5 % in D1	PDE	68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1050 mg Cu → 10 g D5 = 105.0 µg Cu	**D5**	Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/d
Cuprum oxydatum nigrum **CuO** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	CuO: 9.1-10.6 % in D1 Mr 79.55 Relative content Cu in stock = 79.88 %	PDE	68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg CuO = 846.73 mg Cu → 10 g D5 = 84.67 µg Cu	**D5**	Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/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**
Cuprum sulfuricum $CuSO_4 \cdot 5H_2O$ HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$CuSO_4 \cdot 5H_2O$: 9.4-10.6 % in D1 Mr 249.7 Relative content Cu in stock = 25.45 %	PDE	68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg $CuSO_4 \cdot 5H_2O$ = 269.77 mg Cu → 10 g D5 = 26.98 µg Cu	**D5**	Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/d
Dioptase $Cu_6(Si_6O_{18}) \cdot 6 H_2O$ HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$Cu_6(Si_6O_{18}) \cdot 6 H_2O$: 8.6-10.5 % in D1 Mr 946 Relative content Cu in stock = 40.3 %	PDE	68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1050 mg $Cu_6(Si_6O_{18}) \cdot 6 H_2O$ = 423.15 mg Cu → 10 g D5 = 42.32 µg Cu	**D5**	Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/d
Dyscrasite Ag_3Sb HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Ag_3Sb: 6.7-8.1 % Ag, 2.2-2.8 % Sb in D1	PDE	3.3 µg Ag/kg/day → 9.9 µg Ag/day (neonate) 24 µg Sb/kg/day → 72 µg Sb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 810 mg Ag and 280 mg Sb → 10 g D6 = 8.1 µg Ag and 2.8 µg Sb	**D6**	Derivation of PDE silver: PDE is consistent with the RfD (reference dose) of 5 µg Ag/kg/day (US EPA, 2003); LOAEL 20 mg Ag/kg divided by UF (F1-F5 = 12 x 10 x 5 x 1 x 10 = 6000) → 0.0033 mg Ag/kg/d x 3 kg bw neonate → 0.0099 mg Ag/d = 9.9 µg Ag/d Derivation of PDE antimony: NOAEL 6000 µg Sb/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) = 24 µg Sb/kg/d x 3 kg bw neonate = 72 µg Sb/d **Conclusive remark:** **The PDE of silver 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**
Lithium carbonicum Li_2CO_3 HAB See Lithium carbonicum (Ph. Franç.)	Ph. Eur. 4.1.1 (HAB 6)	Li_2CO_3: 9.4-10.6 % in D1 Mr 73.9 Relative content Li in stock = 18.79 %	PDE	11.2 µg Li/kg/day → 33.6 µg Li/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg Li_2CO_3 = 199.17 mg Li → 10 g D5 = 19.92 µg Li	**D5**	Derivation of PDE lithium: POD = lowest human single oral dose of 300 mg Li-carbonate equiv. to 56 mg Li, representing one-third of the recommended daily adult dose (authorized medicinal product); LHRD/100-approach 56 mg/100 = 560 µg Li/day (50 kg) = 11.2 mg Li/kg/day = 33.6 µg Li/day (neonate) (UF = F1-F5 = 1 x 10 x 1 x 1 x 10; F5 = 10 due to LOAEL hum)
Lithium carbonicum Li_2CO_3 Ph. Franç.	Ph. Eur. 4.1.2 (Ph. Franç.)	Li_2CO_3: 98.5-100.5 % in stock Mr 73.9 Relative content Li in stock = 18.79 %	PDE	11.2 µg Li/kg/day → 33.6 µg Li/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1005 mg Li_2CO_3 = 188.84 mg Li → 10 g D5 = 18.88 µg Li	**D5**	Derivation of PDE lithium: POD = lowest human single oral dose of 300 mg Li-carbonate equiv. to 56 mg Li, representing one-third of the recommended daily adult dose (authorized medicinal product); LHRD/100-approach 56 mg/100 = 560 µg Li/day (50 kg) = 11.2 mg Li/kg/day = 33.6 µg Li/day (neonate) (UF = F1-F5 = 1 x 10 x 1 x 1 x 10; F5 = 10 due to LOAEL hum)

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**
Lithium citricum $C_6H_5Li_3O_7$ HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$C_6H_5Li_3O_7$: 6.8-8.1 % in D1 Mr 282.0 Relative content Li in stock = 7.38 %	PDE	11.2 µg Li/kg/day → 33.6 µg Li/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 810 mg $C_6H_5Li_3O_7$ = 59.78 mg Li → 10 g D5 = 5.98 µg Li	**D5**	Derivation of PDE lithium: POD = human single oral dose of 300 mg Li-carbonate equiv. to 56 mg Li, representing one-third of the recommended daily adult dose (authorized medicinal product); LHRD/100-approach 56 mg/100 = 560 µg Li/day (50 kg) = 11.2 mg Li/kg/day = 33.6 µg Li/day (neonate) (UF = F1-F5 = 1 x 10 x 1 x 1 x 10; F5 = 10 due to LOAEL hum)
Malachite $Cu(OH)_2 \cdot CuCO_3$ HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$Cu(OH)_2 \cdot CuCO_3$: 9.0-10.5 % in D1 Mr 221.1 Relative content Cu in stock = 57.48 %	PDE	68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1050 mg $Cu(OH)_2 \cdot CuCO_3$ = 603.54 mg Cu → 10 g D5 = 60.35 µg Cu	**D5**	Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/d
Minium Pb_3O_4 HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Pb_3O_4: 9.3-10.5 % in D1 Mr 686 Relative content Pb in stock = 90.61 %	PDE	5 µg Pb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1050 mg Pb_3O_4 = 951.41 mg Pb → 10 g D7 = 0.95 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) **Applicable to newborns, hence NO further weight adjustment to PDE ICH Q3D necessary.**

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**
Natrium tetrachloroauratum Na[$AuCl_4$] · 2 H_2O HAB/Ph. Eur.	Ph. Eur. 3.1.1 (HAB 5a) Ph. Eur. 4.1.2 (Ph. Franç.)	Na[$AuCl_4$] · 2 H_2O: 9.5-10.5 % in D1 Mr 397.8 Relative content Au in stock = 49.52 %	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 D1 = 1050 mg Na[$AuCl_4$] · 2 H_2O = 519.96 mg Au → 10 g D6 = 5.19 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
Olivenite $Cu_2(OH)AsO_4$ HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$Cu_2(OH)AsO_4$: 8.1-10.5 % in D1 Mr 283.0 Relative content 26.47 % As and 44.91 % Cu in stock	PDE	0.3 µg As/kg/day → 0.9 µg As/day (neonate) 68 µg Cu/kg/day → 204 µg Cu/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1050 mg $Cu_2(OH)AsO_4$ = 277.94 mg As and 471.55 mg Cu → 10 g D7 = 0.278 µg As and 0.472 µg Cu	**D7**	Derivation of PDE arsenic: MRL = 0.0003 mg/kg/d x 3 kg bw neonate → 0.9 µg As/d (no UF). Derivation of PDE copper: NOEL 17 mg Cu/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.068 mg Cu/kg/d x 3 kg bw neonate → 0.204 mg Cu/d = 204 µg Cu/d **Conclusive remark:** **The PDE of arsenic is more conservative and thus the relevant one for FSD assessment.**
Platinum metallicum **Pt** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Pt: 0.93-1.06 % in D2	PDE	2.16 µg Pt/kg/day → 6.48 µg Pt/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D2 = 106 mg Pt → 10 g D7 = 1.06 µg Pt	**D7**	Derivation of PDE Platinum: $BMDL_{10}$ 1.08 mg Pt/kg/day divided by UF (F1-F5 = 5 x 10 x 10 x 1 x 1) → 0.00216 mg Pt/kg/d x 3 kg bw neonate → 0.00648 mg Pt/d = 6.48 µg Pt/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**
Plumbum aceticum $C_4H_6O_4Pb \cdot 3H_2O$ HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$C_4H_6O_4Pb \cdot 3H_2O$: 9.4-10.8 % in D1 Mr 379.3 Relative content Pb in stock = 54.63 %	PDE	5 µg Pb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1080 mg $C_4H_6O_4Pb \cdot 3H_2O$ = 590 mg Pb → 10 g D7 = 0.59 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) **Applicable to newborns, hence NO further weight adjustment to PDE ICH Q3D necessary.**
Pyromorphite HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Pb: 6.8-8.4 % in D1	PDE	5 µg Pb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 840 mg Pb → 10 g D7 = 0.84 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) **Applicable to newborns, hence NO further weight adjustment to PDE ICH Q3D necessary.**
Scorodite $Fe^{3+}[AsO_4] \cdot 2H_2O$ HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	As: 2.9-3.7 % in D1	PDE	0.3 µg As/kg/day → 0.9 µg As/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 370 mg As → 10 g D7 = 0.37 µg As	**D7**	Derivation of PDE arsenic: MRL = 0.0003 mg As/kg/d x 3 kg bw neonate → 0.9 µg As/d (no UF)
Selenium Se HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Se: 9.3-10.6 % in D1	PDE	3.4 µg Se/kg/day → 10.2 µg Se/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg Se → 10 g D7 = 1.06 µg Se	**D7**	Derivation of PDE selenium: NOAEL 1.7 mg Se/kg/d divided by UF (F1-F5 = 5 x 10 x 1 x 10 x 1) → 0.0034 mg Se/kg/d x 3 kg bw neonate → 0.0102 mg Se/d = 10.2 µg Se/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**
Stannum metallicum **Sn** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Sn: 9.4-10.6 % in D1	PDE	128 µg Sn/kg/day → 384 µg Sn/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg Sn → 10 g D5 = 106 µg Sn	**D5**	Derivation of PDE tin: NOAEL 32 mg Sn/kg divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.128 mg Sn/kg/d x 3 kg bw neonate → 0.384 mg Sn/d = 384 µg Sn/d
Stibium arsenicosum **Sb_2O_5** **As_2O_3** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Mixture of Sb_2O_5 (Mr 323.5) and As_2O_3 (Mr 197.8): 4.7-5.4 % As_2O_3 and 4.7-5.4 % Sb_2O_5 in D1 Relative content 75.76 % As in As_2O_3 and 75.28 % Sb in Sb_2O_5	PDE	0.3 µg As/kg/day → 0.9 µg As/day (neonate) 24 µg Sb/kg/day → 72 µg Sb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 540 mg As_2O_3 = 409.1 mg As 540 mg Sb_2O_5 = 406.5 mg Sb → 10 g D7 = 0.409 µg As and 0.406 µg Sb	**D7**	Derivation of PDE arsenic: MRL = 0.0003 mg As/kg/d x 3 kg bw neonate → 0.9 µg As/d (no UF). Derivation of PDE antimony: NOAEL 6000 µg Sb/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) = 24 µg Sb/kg/d x 3 kg bw neonate = 72 µg Sb/d **Conclusive remark:** **The PDE of arsenic is more conservative and thus the relevant one for FSD assessment.**
Stibium metallicum **Sb** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Sb: 9.4-10.6 % in D1	PDE	24 µg Sb/kg/day → 72 µg Sb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg Sb → 10 g D6 = 10.6 µg Sb	**D6**	Derivation of PDE antimony: NOAEL 6000 µg Sb/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) = 24 µg Sb/kg/d x 3 kg bw neonate = 72 µg Sb/d
Stibium sulfuratum aurantiacum HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Mixture of Sb_2S_5 and S: 5.2-6.8 % Sb in D1	PDE	24 µg Sb/kg/day → 72 µg Sb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 680 mg Sb → 10 g D5 = 68 µg Sb	**D5**	Derivation of PDE antimony: NOAEL 6000 µg Sb/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) = 24 µg Sb/kg/d x 3 kg bw neonate = 72 µg Sb/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**
Stibium sulfuratum nigrum **Sb_2S_3** HAB See Antimonite (HAB) and Antimonium crudum. (Ph. Franç.)	Ph. Eur. 4.1.1 (HAB 6)	Sb_2S_3: 9.3-10.6 % in D1 Mr 339.7 Relative content Sb in stock = 71.69 %	PDE	24 µg Sb/kg/day → 72 µg Sb/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg Sb_2S_3 = 759.91 mg Sb → 10 g D6 = 7.59 µg Sb	**D6**	Derivation of PDE antimony: NOAEL 6000 µg Sb/kg/d divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) = 24 µg Sb/kg/d x 3 kg bw neonate = 72 µg Sb/d
Thallium aceticum oxydulatum **$C_2H_3O_2Tl$** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	$C_2H_3O_2Tl$: 9.3-10.6 % in D1 Mr 263.4 Relative content Tl in stock = 77.59 %	PDE	0.16 µg Tl/kg/day → 0.48 µg Tl/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg $C_2H_3O_2Tl$ = 822.45 mg Tl → 10 g D8 = 0.082 µg Tl	**D8**	Derivation of PDE thallium: LOAEL 0.04 mg Tl/kg divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.00016 mg Tl/kg/d x 3 kg bw neonate → 0.00048 mg Tl/d = 0.48 µg Tl/d
Thallium sulfuricum **Tl_2SO_4** HAB	Ph. Eur. 4.1.1 (HAB 6) Ph. Eur. 4.1.2 (Ph. Franç.)	Tl_2SO_4: 9.3-10.6 % in D1 Mr 504.8 Relative content Tl in stock = 80.98 %	PDE	0.16 µg Tl/kg/day → 0.48 µg Tl/day (neonate)	ICH guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)	10 g D1 = 1060 mg Tl_2SO_4 = 858.39 mg Tl → 10 g D8 = 0.086 µg Tl	**D8**	Derivation of PDE thallium: LOAEL 0.04 mg Tl/kg divided by UF (F1-F5 = 5 x 10 x 5 x 1 x 1) → 0.00016 mg Tl/kg/d x 3 kg bw neonate → 0.00048 mg Tl/d = 0.48 µg Tl/d

*As defined in the Ph. Eur.

**For information related to the identity, refer to "Guidance on module 3 of the homeopathic medicinal product dossier"