



Comments on draft document

Table 1: Origin of comments

2nd List of First Safe Dilution (FSD) as released for public consultation until 16th of May 2017

Organisation or individual	Contact details (e-mail address, telephone number, name of contact person)
ECHAMP ECHAMP E.E.I.G. – European Coalition on Homeopathic and Anthroposophic Medicinal Products	Rue Washington 38-40 B-1050 Brussels Tel: +32 2 649 94 40 amandine.oset@echamp.eu

Interested parties are invited to send
comments together with a copy of the cited references.

This will facilitate the assessment of comments, suggestions and corresponding justifications.

When the reference consists of a book chapter, the copy must include
the page of the book showing the year of publication.

Comments without copies of the supporting literature will not be considered.

Comments should be sent electronically and in Word format (not pdf).

Comments and the identity of the sender will be made public
unless a justified objection is received at the time of the submission.

Please submit comments on each document separately.

Table 2: Comments

GENERAL COMMENTS ON DRAFT DOCUMENT

Interested party	Comment and Rationale	Outcome
<i>ECHAMP</i>	<p>In the Q3D-Guideline (Guideline for Elemental Impurities!) the following is stated in the Introduction: “Since elemental impurities do not provide any therapeutic benefit to the patient, element impurity should be controlled within acceptable limits in the drug product. (...) The PDEs established in this guideline are considered to be protective of public health for all patient populations.”</p> <p>We do not agree with the body weight adjustment in the PDE calculation in cases where the ICH Q3D-Guideline is used as reference. It is shown below in several examples, that if the Q3D-values are taken without weight adjustment, these values are confirmed by calculating the respective FSD on the base of drinking water and food regulations. Moreover, these are the intended calculation principles for FSDs.</p> <p>See also specific comments.</p> <p>The FSD calculation proposed is based on the worst case scenario that one whole unit (10 ml or 10 g) is taken daily during life-time exposure with a lifelong bodyweight of 3 kg (which corresponds to the bodyweight of neonates). This is highly unrealistic.</p>	
<i>ECHAMP</i>	Please publish the assessment reports of First Safe Dilutions	
<i>ECHAMP</i>	<p>According to the decision tree of the HMPWG PtC on non-clinical safety of homeopathic medicinal products of botanical, mineral and chemical origin (in the following called PtC), substances allowed as food or constituents of food have to be assessed according to Regulation 178/2002/EC modified by 1642/2003/EC and all related directives and Food supplements 2002/46/EC. This also includes drinking water regulations. The correct approach for the evaluation of the pure metals would therefore be to use the limit values from the food sector.</p> <p>We suggest to use the same kind of calculation for substances regulated by the drinking water regulations as done in the case of Barium salts.</p> <p>See also Specific Comments.</p>	

Interested party	Comment and Rationale	Outcome
<i>ECHAMP</i>	Please note, that calculations performed are always considering the worst case of (pharmacopoeial) analytical requirements.	

SPECIFIC COMMENTS ON TEXT

Section number and heading	Interested party	Comment and Rationale	Outcome
Antimonite Sb ₂ S ₃ HAB	ECHAMP	No weight adjustment necessary PDE = 1200 µg Sb/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 753 µg Sb > FSD = D4	
Antimonite Sb ₂ S ₃ HAB	ECHAMP	<p>According to the PtC decision tree substances allowed as food or constituents of food have to be assessed according to the limit values from the food sector.</p> <p>According to the publication "Antimony in Drinking-water" by the WHO (<i>WHO 2003</i>), the TDI value (tolerable daily intake) is considered to be 360 µg antimony as potassium antimony (III) oxide tartrate for a person with a body weight of 60 kg (calculated from a study on subacute toxicity). Assuming that approximately 60 µg antimony (range 10-70 µg) are ingested with the diet, this leaves a remaining 300 µg that could be taken in in other ways.</p> <p>Assuming an absorption rate of 10 % for antimony trisulphide in comparison with antimony potassium tartrate, this leads to a TDA for antimonite of 4.18 mg. This assumption is based on the factor of about 10 between the oral LD₅₀ values on rats and on the fact that an absorption rate of 15 % was reported for antimony potassium tartrate and 1.5 % for antimony trisulphide. This is in accordance with the data reported by the <i>WHO (2003)</i>. The <i>WHO (2003)</i> mentioned that although quantitative information on the absorption of antimony is not available for all forms, 10 % for antimony potassium tartrate and 1 % for all other forms of antimony have been recommended as reference values for gastrointestinal absorption in humans.</p> <p>Summarising the data, the total daily amount (TDA) which could be administered and which could be assessed as being safe, is assumed to be 3,000 µg antimony (used as antimonite), corresponding to 4,180 µg antimonite (with 71.7 % antimony in antimonite):</p>	

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		<p>FSD = D4</p> <p>10 g of the D4 trituration contains 1,000 µg antimonite and is therefore safe.</p>	
Antimonium crudum Sb ₂ S ₃ Ph.Franç.	<i>ECHAMP</i>	<p>No weight adjustment necessary</p> <p>PDE = 1200 µg Sb/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>10 g D4 = 731 µg Sb > FSD = D4</p>	
Argentite Ag ₂ S HAB	<i>ECHAMP</i>	<p>No weight adjustment necessary</p> <p>PDE = 167 Ag/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>10 g D5 = 91.4 µg Ag > FSD = D5</p>	
Argentum colloidal Ag HAB	<i>ECHAMP</i>	<p>No weight adjustment necessary</p> <p>PDE = 167 µg Ag/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>10 g D5 = 78 µg Ag > FSD = D5</p>	
Argentum colloidal Ag HAB	<i>ECHAMP</i>	<p>According to the PtC decision tree substances which are constituents of food have to be assessed according the limit values from the food sector. Colloidal silver and silver ions are used for disinfection of drinking water.</p> <p>In drinking water 0.1 mg Ag/l is allowed (WHO 2006), this results in 0.2 mg/day (2 litre drinking water).</p> <p>This is consistent with the BfR-value of 0.08 mg/l (intake of 2 litre drinking water per day) and the value of 0.08 mg/l of the German Additive Regulation (Zusatzstoff-Zulassungsverordnung (Anlage 6a (zu § 6a); Zusatzstoffe, die für Trinkwasser zugelassen sind)</p> <p>(https://www.gesetze-im-internet.de/zzulv_1998/anlage_6a.html)</p> <p>(http://www.bfr.bund.de/cm/343/bfr_raet_von_nanosilber_in_lebensmittel_n_und_produkten_des_taeeglichen_bedarfs_ab.pdf)</p>	

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		<p>The amount of 2 litre drinking water applies to all age groups; this is also in line with the calculation of PDE/ FSD for Barium (see Q3D Guideline: Summary of PDE for Barium)</p> <p>10 g D5 = 78 µg Ag; FSD = D5</p>	
Argentum metallicum Ag HAB	ECHAMP	<p>No weight adjustment necessary</p> <p>PDE = 167 µg Ag/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>10 g D5 = 106 µg Ag > FSD = D5</p>	
Argentum metallicum Ag HAB	ECHAMP	<p>According to the PtC decision tree substances allowed as food or constituents of food have to be assessed according to the limit values from the food sector.</p> <p>In drinking water are 0.1 mg Ag/l allowed (WHO 2006), this are 0.2 mg/day (2 litre drinking water).</p> <p>10 g D5 = 106 µg Ag > FSD = D5</p>	
Argentum metallicum Ag HAB/ Ph. Franc.	ECHAMP	<p>According to the PtC decision tree substances which are constituents of food have to be assessed according to the limit values from the food sector. Elemental silver is used in the food sector for coloring of food (E174); e.g. decoration of sweets, pralines and liquors; quantum satis</p> <p>See German Zusatzstoff-Zulassungsverordnung: https://www.gesetze-im-internet.de/bundesrecht/zzulv_1998/gesamt.pdf</p> <p>or</p> <p>Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02008R1333-20140414&from=DE</p> <p>and</p> <p>Commission Regulation (EU) No 1129/2011 of 11 November 2011 amending Regulation (EC) No 1333/2008 of the European Parliament</p>	

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		<p>and of the Council of 16 December 2008 on food additives http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02008R1333-20140414&from=DE</p> <p>There is no ADI for elemental silver (E174) due to the fact that elemental silver is insoluble and only toxic after intake in the gram-range. See Hagers Handbuch 1995 Folgeband 1; S. 80</p> <p>Silber E 175 Dieses Pigment wird in Form des reinen Metalls in sehr geringen Mengen verwendet. Silber kann vom Darm resorbiert und in Geweben abgelagert werden. Vergiftungen treten erst nach Verzehr von Grammengen auf. Die Zulassung ist auf Oberflächen- und dekorative Färbung beschränkt. Die Toxikologie der Silbersalze ist für die Bewertung dieser Farbstoffanwendung nicht relevant. Wegen der Unlöslichkeit bestehen weder toxikologische noch gesundheitliche Bedenken^{9, 29, 45} (→ Bd. 7, 293).</p> <p>(Remark: "E 175" is a mistake in the cited literature source. Silver is E 174!)</p> <p>The resorption of elemental silver is not comparable with the resorption of Ag⁺, therefore an ADI for elemental Ag, calculated on base of oral intake of silver nitrate is not applicable.</p> <p>Due to the fact there is no ADI for elemental silver in food, the WHO value for drinking water can be used: See: http://www.who.int/water_sanitation_health/dwq/chemicals/silver.pdf</p>	

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		<p>On the basis of present epidemiological and pharmacokinetic knowledge, a total lifetime oral intake of about 10 g of silver can be considered as the human NOAEL. As the contribution of drinking-water to this NOAEL will normally be negligible, the establishment of a health-based guideline value is not deemed necessary. On the other hand, special situations may exist where silver salts are used to maintain the bacteriological quality of drinking-water. Higher levels of silver, up to 0.1 mg/litre (a concentration that gives a total dose over 70 years of half the human NOAEL of 10 g), could then be tolerated without risk to health.</p> <p>In drinking water 0.1 mg Ag/l is allowed (WHO 2006), this results in 0.2 mg/day (2 litre drinking water).</p> <p>This is consistent with the BfR-value of 0.08 mg/l and the assumed intake of 2 l water per day as well as the value of 0.08 mg/l of the German Zusatzstoff-Zulassungsverordnung.</p> <p>https://www.gesetze-im-internet.de/zzulv_1998/anlage_6a.html</p> <p>http://www.bfr.bund.de/cm/343/bfr_raet_von_nanosilber_in_lebensmittel_n_und_produkten_des_taeeglichen_bedarfs_ab.pdf</p> <p>10 g D5 = 106 µg Ag(HAB); FSD = D5 10 g D5 = 100,5 µg Ag(Ph. Franc.); FSD = D5</p>	
Argentum metallicum Ag Ph.Franc.	<i>ECHAMP</i>	No weight adjustment necessary PDE = 167 µg Ag/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D5 = 100.5 µg Ag > FSD = D5	
Argentum nitricum AgNO ₃ HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 167 µg Ag/day (for all patient populations according to ICH guideline Q3D on elemental impurities) ADI for nitrate = 3.7 mg/kg b.w., expressed as nitrate ion (according to WHO Food Additives Series: 50 nitrate) 10 g D5 = 67.3 µg Ag and 38.7 µg nitrate > FSD = D5	
Argentum nitricum AgNO ₃ HAB	<i>ECHAMP</i>	According to the PtC decision tree substances which are constituents of food have to be assessed according the limit values from the food sector. Silver ions (including silver nitrate) are used for disinfection of	

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		<p>drinking water.</p> <p>In drinking water 0.1 mg Ag/l is allowed (WHO 2006), this results in 0.2 mg/day (2 litre drinking water).</p> <p>This is consistent with the BfR-value of 0.08 mg/l (intake of 2 litre drinking water per day) and the value of 0.08 mg/l of the German Additive Regulation (Zusatzstoff-Zulassungsverordnung (Anlage 6a (zu § 6a); Zusatzstoffe, die für Trinkwasser zugelassen sind)</p> <p>https://www.gesetze-im-internet.de/zzulv_1998/anlage_6a.html</p> <p>http://www.bfr.bund.de/cm/343/bfr_raet_von_nanosilber_in_lebensmitteln_und_produkten_des_taeeglichen_bedarfs_ab.pdf</p> <p>The amount of 2 litre drinking water applies to all age groups; this is also in line with the calculation of PDE/ FSD for Barium (see Q3D Guideline: Summary of PDE for Barium)</p> <p>10 g D5 = 67,3 µg Ag; FSD = D5</p>	
Argentum nitricum AgNO ₃ Ph.Franc.	<i>ECHAMP</i>	<p>No weight adjustment necessary</p> <p>PDE = 167 µg Ag/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>ADI for nitrate = 3.7 mg nitrate/kg b.w., expressed as nitrate ion (according to WHO Food Additives Series: 50 nitrate)</p> <p>10 g D5 = 63.8 µg Ag and 36.7 µg nitrate > FSD = D5</p>	
Auri solutio colloidalis Au HAB	<i>ECHAMP</i>	<p>No weight adjustment necessary</p> <p>PDE = 134 µg Au/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>10 g D5 = 51 µg Au > FSD = D5</p>	
Aurum chloratum H[AuCl ₄] · 3 H ₂ O HAB	<i>ECHAMP</i>	<p>No weight adjustment necessary</p> <p>PDE = 134 µg Au/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>10 g D5 = 51 µg Au > FSD = D5</p>	

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Aurum metallicum Au HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 134 µg Au/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D5 = 105 µg Au > FSD = D5	
Aurum metallicum Au HAB/ Ph. Franc.	<i>ECHAMP</i>	<p>Elementary gold is used in the food sector for coloring of food (E175); e.g. decoration of sweets, pralines and liquors; quantum satis Addition regarding “quantum satis”:</p> <p>See German Zusatzstoff-Zulassungsverordnung: https://www.gesetze-im-internet.de/bundesrecht/zzulv_1998/gesamt.pdf</p> <p>or</p> <p>Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02008R1333-20140414&from=DE</p> <p>and</p> <p>Commission Regulation (EU) No 1129/2011 of 11 November 2011 amending Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02008R1333-20140414&from=DE</p> <p>According to manufacturers the addition of about 0.05g (50 mg) of gold (E 175; 22-23 Karat) per bottle of liquid (liqueur, sparkling wine) is recommended to get a good result.</p> <p>Hagers Handbuch 1995 Folgeband 1; S. 80 The toxicology of gold salts is not relevant for the assessment of elemental gold. Because of the insolubility there are neither toxicological nor health concerns concerning elementary gold.</p>	

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		<p>Gold E 175 Nur das reine Metall wird in sehr geringen Mengen verwendet. Die Zulassung ist auf Oberflächen- und dekorative Färbung beschränkt. Die Toxikologie der Goldsalze ist für die Bewertung dieser Anwendung nicht relevant. Wegen der Unlöslichkeit bestehen weder toxikologische noch gesundheitliche Bedenken^{9, 29} (→ Bd. 3, 333; 7, 331).</p> <p>“Elemental gold is poorly absorbed and consequently is not considered as biologically active” (ICH guideline Q3D on elemental impurities) Therefore a PDE for Au³⁺, calculated on base of parenteral (intraperitoneal) application is not applicable for the calculation of FSD for the oral intake of elemental gold.</p> <p>This is contrary the principles of the factors considered in the safety assessment for establishing the PDE:</p> <ul style="list-style-type: none"> - The likely oxidation state of the element in the drug product - Route of administration <p>(Guideline for Elemental impurities; 3.1. Principles of the Safety Assessment of Elemental Impurities for Oral, Parenteral and Inhalation Routes of Administration; Page 2)</p> <p>Due to the fact, that elemental gold is insoluble, poorly absorbed and used in food, Article 14 of 2001/83 EC subparagraph 1 should be used for calculation of FSD:</p>	

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		<p>- there is a sufficient degree of dilution to guarantee the safety of the medicinal product; in particular, the medicinal product may not contain either more than one part per 10 000 of the mother tincture or more than 1/100th of the smallest dose used in allopathy with regard to active substances whose presence in an allopathic medicinal product results in the obligation to submit a doctor's prescription.</p> <p>FSD = D4; 10 g D4 contain 1,05 mg Au (HAB) or 1,01 mg (Ph. Franc.)</p>	
Aurum metallicum Au Ph.Franc.	<i>ECHAMP</i>	No weight adjustment necessary PDE = 134 µg Au/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D5 = 101 µg Au > FSD = D5	
Cadmium sulfuricum CdSO ₄ * 8/3 H ₂ O Ph.Eur. / HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 5 µg Cd/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D6 = 4.69 µg Cd > FSD = D6	
Calcium stibiato-sulfuratum HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 1200 µg Sb/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D3 = 1200 µg Sb/day > FSD = D3	
Chalcosine Cu ₂ S HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 798.4 µg Cu > FSD = D4	
Chininum	<i>ECHAMP</i>	No weight adjustment necessary	

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arsenicum C ₂₀ H ₂₄ N ₂ O ₂ + As ₂ O ₃ HAB		PDE = 15 µg As/day (for all patient populations according to ICH guideline Q3D on elemental impurities) LHRD quinine = 81 mg quinine/day (neonate) 10 g D5 = 7.5 µg As and 97 µg quinine > FSD = D5	
Cobaltum metallicum Co HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 50 µg Co/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D6 = 10.6 µg Co > FSD = D6	
Cuprite Cu ₂ O HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 932.6 µg Cu > FSD = D4	
Cuprum aceticum Cu[C ₂ H ₃ O ₂] ₂ · H ₂ O Ph.Eur. / HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D3 = 3373 µg Cu > FSD = D3	
Cuprum aceticum Cu[C ₂ H ₃ O ₂] ₂ · H ₂ O Ph.Eur. / HAB	<i>ECHAMP</i>	According to the PtC decision tree substances allowed as food or constituents of food have to be assessed according to the limit values from the food sector. In drinking water are 2 mg Cu/l allowed (98/83/EC; TWVO 2001; WHO 2006), this are 4 mg/day (2 litre drinking water). 10 g D3 = 3.4 mg Cu > FSD = D3	
Cuprum arsenicosum HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities) PDE = 15 µg As/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D6 = 4.3 µg Cu and 3.4 µg As > FSD = D6	
Cuprum	<i>ECHAMP</i>	No weight adjustment necessary	

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metallicum Cu Ph.Eur. / HAB		PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 1050 µg Cu > FSD = D4	
Cuprum metallicum Ph.Eur/ HAB	<i>ECHAMP</i>	According to the PtC decision tree substances allowed as food or constituents of food have to be assessed according to the limit values from the food sector. In drinking water 2 mg Cu/l are allowed (98/83/EC; TWVO 2001; WHO 2006), this are 4 mg/day (2 litre drinking water). 10 g D4 = 1,05 mg Cu; FSD =D4	
Cuprum oxydatum nigrum CuO HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 846.7 µg Cu > FSD = D4	
Cuprum oxydatum nigrum CuO HAB	<i>ECHAMP</i>	According to the PtC decision tree substances allowed as food or constituents of food have to be assessed according to the limit values from the food sector. In drinking water 2 mg Cu/l are allowed (98/83/EC; TWVO 2001; WHO 2006), this are 4 mg/day (2 litre drinking water). 10 g D4 = 846.7 µg Cu; FSD = D4	
Cuprum sulfuricum CuSO ₄ · 5 H ₂ O HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D3 = 2698 µg Cu > FSD = D3	
Cuprum sulfuricum CuSO ₄ · 5 H ₂ O HAB	<i>ECHAMP</i>	According to the PtC decision tree substances allowed as food or constituents of food have to be assessed according to the limit values from the food sector. In drinking water are 2 mg Cu/l allowed (98/83/EC; TWVO 2001; WHO 2006), this are 4 mg/day (2 litre drinking water). 10 g D3 = 2.7 mg Cu > FSD = D3	

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Diopside Cu ₆ (Si ₆ O ₁₈) * 6 H ₂ O HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 423.2 µg Cu > FSD = D4	
Dyscrasite Ag ₃ Sb HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 167 µg Ag/day (for all patient populations according to ICH guideline Q3D on elemental impurities) PDE = 1200 µg Sb/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D5 = 81 µg Ag and 28 µg Sb > FSD = D5	
Lithium carbonicum Li ₂ CO ₃ HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 560 µg Li/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 199.2 µg Li > FSD = D4	
Lithium carbonicum Li ₂ CO ₃ Ph.Franc.	<i>ECHAMP</i>	No weight adjustment necessary PDE = 560 µg Li/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 188.8 µg Li > FSD = D4	
Lithium citricum C ₆ H ₅ Li ₃ O ₇ HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 560 µg Li/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 59.8 µg Li > FSD = D4	
Malchite Cu(OH) ₂ * CuCO ₃ HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 603.5 µg Cu > FSD D4	
Sodium tetrachloroaurate Na[AuCl ₄] * 2 H ₂ O Ph.Eur./HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 134 µg Au/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D5 = 51.9 µg Au > FSD = D5	
Olivenite	<i>ECHAMP</i>	No weight adjustment necessary	

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Cu ₂ (OH)AsO ₄ HAB		<p>PDE = 3400 µg Cu/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>PDE = 15 µg As/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>10 g D6 = 4.72 µg Cu and 2.78 µg As > FSD = D6</p>	
Olivenite Cu ₂ (OH)AsO ₄ HAB	<i>ECHAMP</i>	<p>According to the PtC decision tree substances allowed as food or constituents of food have to be assessed according to the limit values from the food sector.</p> <p>In drinking water are 10 µg As/l allowed (98/83/EC; WHO 2006), this are 20 µg/day (2 litre drinking water).</p> <p>10 g D6 = 2.78 µg As > FSD = D6</p>	
Platinum metallicum Pt HAB	<i>ECHAMP</i>	<p>No weight adjustment necessary</p> <p>PDE = 108 µg Pt/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>10 g D5 = 106.0 µg Pt > FSD = D5</p>	
Scorodite Fe ³⁺ [AsO ₄] · 2 H ₂ O HAB	<i>ECHAMP</i>	<p>No weight adjustment necessary</p> <p>PDE = 15 µg As/day (for all patient populations according to ICH guideline Q3D on elemental impurities)</p> <p>10 g D6 = 3.7 µg As > FSD = D6</p>	
Scorodite Fe ³⁺ [AsO ₄] · 2 H ₂ O HAB	<i>ECHAMP</i>	<p>According to the PtC decision tree substances allowed as food or constituents of food have to be assessed according to the limit values from the food sector.</p> <p>In drinking water are 10 µg As/l allowed (98/83/EC; WHO 2006), this are 20 µg/day (2 litre drinking water).</p> <p>10 g D6 = 3.7 µg As > FSD = D6</p>	
Selenium Se HAB	<i>ECHAMP</i>	<p>In the literature there are several data to evaluate the safety, which can lead to different values that are considered safe. In the case of selenium, this results in different FSDs. Following the approach 1) (used in the</p>	

Section number and heading	Interested party	Comment and Rationale	Outcome
		<p>Draft of the 2nd list of FSD), the PDE from the Q3D is the basis for the FSD. In approach 2) the drinking water regulation is the basis for the calculation and a different value results.</p> <p>1) No weight adjustment necessary PDE = 170 µg Se/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D5 = 106 µg Se > FSD = D5</p>	
Selenium Se HAB	<i>ECHAMP</i>	<p>2) According to the decision tree of the HMPWG PtC, substances allowed as food or constituents of food have to be assessed according to Regulation 178/2002/EC modified by 1642/2003/EC and all related directives and Food supplements 2002/46/EC. This also includes drinking water regulations.</p> <p>The allowed Selen value in drinking water is 10 µg/l, this results in 20 µg /day (2 litre drinking water). http://www.who.int/water_sanitation_health/dwq/chemicals/selenium.pdf</p> <p>10 g D6 = 10,6 µg Selen; FSD=D6</p>	
Stannum metallicum Sn HAB	<i>ECHAMP</i>	<p>No weight adjustment necessary PDE = 6400 µg Sn/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 1060 µg Sn > FSD = D4</p>	
Stibium arsenicosum Sb HAB	<i>ECHAMP</i>	<p>According to the PtC decision tree substances allowed as food or constituents of food have to be assessed according to the limit values from the food sector.</p> <p>In drinking water are 10 µg As/l allowed (98/83/EC page 18; WHO 2006 page 306-309), this are 20 µg/day for adults (2 litre drinking water a day), D6 (4.1 µg As/10 g) is safe. FSD = D6</p>	

Section number and heading	Interested party	Comment and Rationale	Outcome
Stibium metallicum Sb HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 1200 µg Sb/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 1060 µg Sb > FSD = D4	
Stibium sulfuratum aurantiacum HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 1200 µg Sb/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D4 = 759 µg Sb > FSD = D4	
Thallium aceticum oxydulatum C ₂ H ₃ O ₂ Tl HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 8 µg Tl/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D7 = 0.82 µg Tl > FSD = D7	
Thallium sulfuricum Tl ₂ SO ₄ HAB	<i>ECHAMP</i>	No weight adjustment necessary PDE = 8 µg Tl/day (for all patient populations according to ICH guideline Q3D on elemental impurities) 10 g D7 = 0.82 µg Tl > FSD = D7	