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# Element Specific Chapters

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- *Arsenic* <211>
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## Stim Article in PF 42(4)

### STIMULI TO THE REVISION PROCESS

Stimuli articles do not necessarily reflect the policies  
of the USPC or the USP Council of Experts

## Future of Element-Specific Chapters in the *USP-NF*

USP's Chemical Analysis Expert Committee and Kahkashan Zaidi<sup>a</sup>

### ABSTRACT

The Chemical Analysis Expert Committee (CAEC) is evaluating the idea of removing element-specific chapters and limit tests in monographs from the *USP-NF*. The CAEC is considering the effect of this proposal, as well as the effect of retaining these chapters and limit tests. The CAEC strongly encourages comments and discussions regarding this proposal.

1. Limit tests and references to element specific chapters are included in about **1000 monographs**?

Table 1. Number of Monographs with References to Element-Specific Chapters by Type

	Excipients	Drug Substances/ Drug Products	Dietary Supplements	Food	Biologics
Number of monographs	150	272	256	166	12

# USP monographs with limits for specific elements that differ from the limits in <232>

ARSENIC	2 ppm	ALUMINUM DICHLOROHYDREX PROPYLENE GLYCOL	01-Chemical Medicines	
<b>ARSENIC</b>	<b>NMT 1 ug/g</b>	<b>FRUCTOSE</b>	<b>01-Chemical Medicines</b>	
ARSENIC	NMT 10 ppm	GENTIAN VIOLET	01-Chemical Medicines	
ARSENIC	NMT 10 ppm	AMMONIUM MOLYBDATE	01-Chemical Medicines	
<b>ARSENIC</b>	<b>NMT 16 ppm</b>	<b>DIBASIC SODIUM PHOSPHATE</b>	<b>01-Chemical Medicines</b>	
ARSENIC	NMT 8 ppm	MONOBASIC SODIUM PHOSPHATE	01-Chemical Medicines	
ARSENIC	4 ppm	SUCRALFATE	01-Chemical Medicines	
ARSENIC	NMT 4 ppm	SUBLIMED SULFUR	01-Chemical Medicines	
ARSENIC	3 ppm	TANNIC ACID	01-Chemical Medicines	
ARSENIC	2 µg/g	ZILEUTON	01-Chemical Medicines	
ARSENIC	NMT 3 ppm	ZINC ACETATE	01-Chemical Medicines	
ARSENIC	1.5 ppm	ZINC STEARATE	01-Chemical Medicines	
<b>ARSENIC</b>	<b>14 ppm</b>	<b>ZINC SULFATE</b>	<b>01-Chemical Medicines</b>	
ARSENIC	the limit is 10 µg per g.	BISMUTH CITRATE	01-Chemical Medicines	
LEAD	NMT 10 ppm	CALCIUM ACETATE	01-Chemical Medicines	
LEAD	NMT 10 ppm	CALCIUM CITRATE	01-Chemical Medicines	
LEAD	10 ppm	CHLOROPHYLLIN COPPER COMPLEX SODIUM	01-Chemical Medicines	
<b>LEAD</b>	<b>NMT 30 ppm</b>	<b>BASIC FUCHSIN</b>	<b>01-Chemical Medicines</b>	
<b>LEAD</b>	<b>NMT 30 ppm</b>	<b>GENTIAN VIOLET</b>	<b>01-Chemical Medicines</b>	
LEAD	NMT 10 ppm	GLUCONOLACTONE	01-Chemical Medicines	
LEAD	10 ppm	HYDROXYAMPHETAMINE HYDROBROMIDE	01-Chemical Medicines	
LEAD	NMT 5 ppm	MAGNESIUM PHOSPHATE	01-Chemical Medicines	
<b>LEAD</b>	<b>NMT 20 ppm</b>	<b>ANTIMONY SODIUM TARTRATE</b>	<b>01-Chemical Medicines</b>	
LEAD	NMT 10 ppm	POTASSIUM NITRATE	01-Chemical Medicines	
LEAD	10 ppm	ZINC STEARATE	01-Chemical Medicines	
<b>LEAD</b>	<b>20 ppm</b>	<b>ZINC SULFATE</b>	<b>01-Chemical Medicines</b>	
LEAD	10 µg per g	BISMUTH CITRATE	01-Chemical Medicines	
LEAD	10 ppm	BISMUTH SUBSALICYLATE	01-Chemical Medicines	
LEAD	10 ppm	BISMUTH SUBSALICYLATE MAGMA	01-Chemical Medicines	
MERCURY	3 ppm	HEXYLRESORCINOL	01-Chemical Medicines	
<b>PALLADIUM</b>	<b>NMT 10 ppm</b>	<b>GALANTAMINE HYDROBROMIDE</b>	<b>01-Chemical Medicines</b>	
<b>PALLADIUM</b>	<b>NMT 5 ug/g</b>	<b>PRAMIPEXOLE DIHYDROCHLORIDE</b>	<b>01-Chemical Medicines</b>	
<b>PALLADIUM</b>	<b>20 ppm</b>	<b>RAMIPRIL</b>	<b>01-Chemical Medicines</b>	
<b>PALLADIUM</b>	<b>10 ppm</b>	<b>ROPINIROLE HYDROCHLORIDE</b>	<b>01-Chemical Medicines</b>	
<b>PALLADIUM</b>	<b>NMT 10 ppm</b>	<b>VALACYCLOVIR HYDROCHLORIDE</b>	<b>01-Chemical Medicines</b>	
SELENIUM	NMT 30 ppm	MAFENIDE ACETATE	01-Chemical Medicines	
SELENIUM	NMT 30 ug/g	MAGNESIUM SULFATE	01-Chemical Medicines	
SILVER	10 µg per g	BISMUTH CITRATE	01-Chemical Medicines	
SILVER	10 ppm	BISMUTH SUBSALICYLATE	01-Chemical Medicines	
SILVER	10 ppm	BISMUTH SUBSALICYLATE MAGMA	01-Chemical Medicines	
ZINC	0.05%	GENTIAN VIOLET	01-Chemical Medicines	

# Excipient Monographs with Specific Limits

ALUMINUM	2.0%	TALC	04-Excipients
ALUMINIUM	0.2 ppm	SODIUM CHLORIDE	04-Excipients
ANTIMONY	NMT 2 µg/g	TITANIUM DIOXIDE	04-Excipients
ARSENIC	3 µg/g	MONOBASIC POTASSIUM PHOSPHATE	04-Excipients
ARSENIC	3 ppm	PROPYLENE GLYCOL ALGINATE	04-Excipients
ARSENIC	NMT 1.5 ppm	POTASSIUM ALGINATE	04-Excipients
CADMIUM	NMT 0.2 ppm	CHITOSAN	04-Excipients
CADMIUM	NMT 1 ppm	FERROSO-FERRIC OXIDE	04-Excipients
CADMIUM	3 ppm	MAGNESIUM STEARATE	04-Excipients
CALCIUM	0.9%	TALC	04-Excipients
LEAD	NMT 0.5 µg/g	CORN SYRUP SOLIDS	04-Excipients
LEAD	NMT 0.5 ppm	CHITOSAN	04-Excipients
LEAD	NMT 0.5 mg/kg	INOSITOL	04-Excipients
LEAD	25 µg/g	HYDROPHOBIC COLLOIDAL SILICA	04-Excipients
LEAD	NMT 10 ppm	FERROSO-FERRIC OXIDE	04-Excipients
LEAD	NMT 5 ppm	GALACTAN	04-Excipients
LEAD	NMT 10 µg/g	GUAR GUM	04-Excipients
LEAD	NMT 10 ppm	HYDROXYPROPYL CELLULOSE	04-Excipients
LEAD	NMT 15 µg/g	MAGNESIUM ALUMINUM SILICATE	04-Excipients
LEAD	10 ppm	MAGNESIUM STEARATE	04-Excipients
LEAD	NMT 10 ppm	MONOSODIUM GLUTAMATE	04-Excipients
LEAD	NMT 10 ppm	PROPYLENE GLYCOL ALGINATE	04-Excipients
LEAD	NMT 0.5 µg/g	GALACTOSE	04-Excipients
LEAD	NMT 10 µg/g	PURIFIED SILICEOUS EARTH	04-Excipients
LEAD	NMT 10 ppm	SODIUM ALGINATE	04-Excipients
LEAD	40 µg/g	BENTONITE	04-Excipients
LEAD	15 µg/g	PURIFIED BENTONITE	04-Excipients
MERCURY	NMT 0.2 ppm	CHITOSAN	04-Excipients
MERCURY	NMT 1 ppm	FERROSO-FERRIC OXIDE	04-Excipients
MERCURY	NMT 3 µg/g	FERRIC OXIDE	04-Excipients
MERCURY	NMT 1 µg/g	TITANIUM DIOXIDE	04-Excipients
NICKEL	NMT 200 ppm	FERROSO-FERRIC OXIDE	04-Excipients
NICKEL	NMT 1 µg/g	GLYCERYL DISTEARATE	04-Excipients
NICKEL	5 ppm	MAGNESIUM STEARATE	04-Excipients
NICKEL	NMT 1 µg/g	MALTITOL	04-Excipients
PHOSPHOROUS	700 µg/g	ALPHA-LACTALBUMIN	04-Excipients
SELENIUM	NMT 10 ppm	SODIUM SULFITE	04-Excipients
SELENIUM	30 µg/g	MONOTHIOGLYCEROL	04-Excipients
TIN	NMT 0.1 µg/g	MEDIUM-CHAIN TRIGLYCERIDES	04-Excipients

## Questions:

- a. Are these element specific limit tests in monographs necessary?
- b. Are there known **quality- or safety-related** reasons to keep specific elemental impurity limit(s) in the monographs (drug substances, excipients and Drug Products)?

**USP needs stakeholder's  
Feedback**



**It will not be an Easy Task**

**BUT IF IT CAN BE DONE THEN,**

- a. Removing references and (special) limits from drug product monographs would:
  - a. Align those monographs with (232), providing industry with only one set of elements and limits, as well as one analytical procedure.
  - a. Will **simplify compliance** and establishment of consistent, safety-based elemental impurity limits with the focus on the drug product rather than component-specific limits.
- b. With (233) in place, analytical procedures specific to individual elements are no longer necessary





# Questions ?



# Questions



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# Thank You