

USP232/ICH Q3D STANDARDS

SCP SCIENCE

Providing Innovative Solutions to Analytical Chemists

REVISED ELEMENTAL IMPURITY LIMITS

Designed specifically for
USP232 / ICH Q3D Limits
and Guidelines

Available in 125 ml
and 500 ml bottles

Manufactured and tested
according to ISO Guide 34 and
ISO 17025 Accredited Quality
Management System



USP232 / ICH Q3D ELEMENTAL IMPURITIES

Limits and Guidelines:

In May 2016, United States Pharmacopeia published the following briefing to address the alignment of the Chapter 39 with International Conference on Harmonization's ICH Q3D.

(232) Elemental Impurities—Limits, USP 39 page 268.

USP's Elemental Impurities Expert Panel approved a recommendation to the General Chapters — Chemical Analysis Expert Committee that this chapter be revised to align with the ICH Q3D Step 4 document to the greatest extent possible. Therefore, this revision is being proposed to include additional elements and their specific limits in this chapter.

ICH Q3D will be effective for existing products

- New products effective June 01, 2016
- Existing products effective January 01, 2018

USP <232>, <233> will come into effect on January 1, 2018

- <231> Heavy Metals will be deleted
- <232> Elemental Impurities- Limits, and <233> Elemental Impurities- Procedures will reach official implementation date

This revision addresses and specifies the limits for the amounts of elemental impurities in drug products. The compliance with the limits specified in the table below is required for all drug products. The guideline by USP 232 and ICH Q3D separates the various elemental impurities into the four different classifications listed below:

CLASS I	Elements As, Cd, Hg and Pb are human toxicants across all administration routes. These require special consideration during risk assessment, due to their high toxicity and the potential for them to be present in finished dosage form through contributions of naturally derived materials.
CLASS II	Human toxicants to a greater or lesser extent based on route of administration. Class 2 elements are further divided in sub-classes 2A and 2B based on their relative likelihood of occurrence in the drug product. <ul style="list-style-type: none"> • Class 2A elements have relatively high probability of occurrence in the drug product. It includes Co, Ni and V. • Class 2B elements have a reduced probability of occurrence in the drug product related to their low abundance and low potential to be co-isolated with other material. This class include: Ag, Au, Ir, Os, Pd, Pt, Rh, Ru, Se and Tl.
CLASS III	Relatively low toxicity by oral route of administration, but require consideration in the risk assessment for other routes of administration. The elements in this class include: Ba, Cr, Cu, Li, Mo, Sb, and Sn.
OTHER ELEMENTS	Elemental impurities that have been evaluated, but for which a PDE has not been established due to their low inherent toxicity and/or regional regulations. Some of the elements considered include: Al, B, Ca, Fe, K, Mg, Mn, Na, W and Zn.

The classification scheme is intended to focus the risk assessment on those elements that are the most toxic, but also have a reasonable probability of inclusion in the drug product. The extent of exposure has been determined for each elemental impurity of interest for three routes of administration; oral, parenteral and inhalational. The risk assessment is obligatory if the listed elemental impurities are intentionally added in the production process, and is recommended if not intentionally added.

Table 1: Elements to be considered in the Risk Assessment

ELEMENTS	CLASS	I.A.*	IF NOT INTENTIONALLY ADDED		
			ORAL	PARENTERAL	INHALATION
Cd	1	yes	yes	yes	yes
Pb	1	yes	yes	yes	yes
As	1	yes	yes	yes	yes
Hg	1	yes	yes	yes	yes
Co	2A	yes	yes	yes	yes
V	2A	yes	yes	yes	yes
Ni	2A	yes	yes	yes	yes
Tl	2B	yes	no	no	no
Au	2B	yes	no	no	no
Pd	2B	yes	no	no	no
Ir	2B	yes	no	no	no
Os	2B	yes	no	no	no

ELEMENTS	CLASS	I.A.*	IF NOT INTENTIONALLY ADDED		
			ORAL	PARENTERAL	INHALATION
Rh	2B	yes	no	no	no
Ru	2B	yes	no	no	no
Se	2B	yes	no	no	no
Ag	2B	yes	no	no	no
Pt	2B	yes	no	no	no
Li	3	yes	no	yes	yes
Sb	3	yes	no	yes	yes
Ba	3	yes	no	no	yes
Mo	3	yes	no	no	yes
Cu	3	yes	no	yes	yes
Sn	3	yes	no	no	yes
Cr	3	yes	no	no	yes

* I.A. - If Intentionally Added (all routes)

Based on these regulations, SCP SCIENCE created a series of standards to cover the two categories 1) as intentionally added elemental impurities, 2) and non-intentionally added, by grouping elements based on the USP and Q3D classification as 1, 2A, 2B, and 3 and based on their compatibility. Note that several multi-element standards are concentrated by a factor of 10X in order to guarantee a minimum 12 month shelf-life.

SCP SCIENCE – USP232/ICH Q3D Standards:

ORAL:

140-131-10x

USP232/ICH Q3D Oral STD# 1 IA: Ag (150 ppm), As (15 ppm), Cd (5 ppm), Co (50 ppm), Hg (30 ppm), Ni (200 ppm), Pb (5 ppm), Se (150 ppm), Tl (8 ppm), V (100 ppm) in 10% HNO₃ - **Elements Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-101	USP232/ICH Q3D Oral STD# 1 IA	125 ml
140-131-105	USP232/ICH Q3D Oral STD# 1 IA	500 ml

140-131-11x

USP232/ICH Q3D Oral STD# 2 IA: Au (100 ppm), Ir (100 ppm), Os (100 ppm), Pd (100 ppm), Pt (100 ppm), Rh (100 ppm), Ru (100 ppm) in 10% HCl - **Elements Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-111	USP232/ICH Q3D Oral STD# 2 IA	125 ml
140-131-115	USP232/ICH Q3D Oral STD# 2 IA	500 ml

140-131-12x

USP232/ICH Q3D Oral STD# 3 IA: Ba (140 ppm), Cr (1100 ppm), Cu (300 ppm), Li (55 ppm), Mo (300 ppm), Sb (120 ppm), Sn (600 ppm) in 5% HNO₃ / 0.5% HF - **Elements Intentionally Added**

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-121	USP232/ICH Q3D Oral STD# 3 IA	125 ml
140-131-125	USP232/ICH Q3D Oral STD# 3 IA	500 ml

140-131-14x

USP232/ICH Q3D Oral STD# 4 NIA: As (15 ppm), Cd (5 ppm), Co (50 ppm), Hg (30 ppm), Ni (200 ppm), Pb (5 ppm), V (100 ppm) in 10% HNO₃ - **Elements Not Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-141	USP232/ICH Q3D Oral STD# 4 NIA	125 ml
140-131-145	USP232/ICH Q3D Oral STD# 4 NIA	500 ml

PARENTERAL:

140-131-20x

USP232/ICH Q3D Parenteral STD# 1 IA: Ag (10 ppm), As (15 ppm), Cd (2 ppm), Co (5 ppm), Hg (3 ppm), Ni (20 ppm), Pb (5 ppm), Se (80 ppm), Tl (8 ppm), V (10 ppm) in 10% HNO₃ - **Elements Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-201	USP232/ICH Q3D Parenteral STD# 1 IA	125 ml
140-131-205	USP232/ICH Q3D Parenteral STD# 1 IA	500 ml

PARENTERAL:**140-131-21x**

USP232/ICH Q3D Parenteral STD# 2 IA: Au (100 ppm), Ir (10 ppm), Os (10 ppm), Pd (10 ppm), Pt (10 ppm), Rh (10 ppm), Ru (10 ppm) in 10% HCl - **Elements Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-211	USP232/ICH Q3D Parenteral STD# 2 IA	125 ml
140-131-215	USP232/ICH Q3D Parenteral STD# 2 IA	500 ml

140-131-22x

USP232/ICH Q3D Parenteral STD# 3 IA: Ba (700 ppm), Cr (1100 ppm), Cu (300 ppm), Li (250 ppm), Mo (1500 ppm), Sb (90 ppm), Sn (600 ppm) in 5% HNO₃ / 0.5% HF - **Elements Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-221	USP232/ICH Q3D Parenteral STD# 3 IA	125 ml
140-131-225	USP232/ICH Q3D Parenteral STD# 3 IA	500 ml

140-131-24x

USP232/ICH Q3D Parenteral STD# 4 NIA: As (15 ppm), Cd (2 ppm), Co (5 ppm), Cu (300 ppm), Hg (3 ppm), Li (250 ppm), Ni (20 ppm), Pb (5 ppm), Sb (90 ppm), V (10 ppm) in 10% HNO₃ - **Elements Not Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-241	USP232/ICH Q3D Parenteral STD# 4 NIA	125 ml
140-131-245	USP232/ICH Q3D Parenteral STD# 4 NIA	500 ml

INHALATION:**140-131-30x**

USP232/ICH Q3D Inhalation STD# 1 IA: Ag (7 ppm), As (2 ppm), Ba (300 ppm), Cd (2 ppm), Co (3 ppm), Cr (3 ppm), Cu (30 ppm), Hg (1 ppm), Li (25 ppm), Mo (10 ppm), Ni (5 ppm), Pb (5 ppm), Sb (20 ppm), Se (130 ppm), Sn (60 ppm), Tl (8 ppm), V (1 ppm) in 10% HNO₃ / 0.1% HF - **Elements Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-301	USP232/ICH Q3D Inhalation STD# 1 IA	125 ml
140-131-305	USP232/ICH Q3D Inhalation STD# 1 IA	500 ml

140-131-31x

USP232/ICH Q3D Inhalation STD# 2 IA: Au (1 ppm), Ir (1 ppm), Os (1 ppm), Pd (1 ppm), Pt (1 ppm), Rh (1 ppm), Ru (1 ppm) in 5% HCl - **Elements Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-311	USP232/ICH Q3D Inhalation STD# 2 IA	125 ml
140-131-315	USP232/ICH Q3D Inhalation STD# 2 IA	500 ml

140-131-33x

USP232/ICH Q3D Inhalation STD# 3 NIA: As (2 ppm), Ba (300 ppm), Cd (2 ppm), Co (3 ppm), Cr (3 ppm), Cu (30 ppm), Hg (1 ppm), Li (25 ppm), Mo (10 ppm), Ni (5 ppm), Pb (5 ppm), Sb (20 ppm), Sn (60 ppm), V (1 ppm) in 10% HNO₃ / 0.1% HF - **Elements Not Intentionally Added** - 10X concentrate

CATALOG NUMBER	DESCRIPTION	FORMAT
140-131-331	USP232/ICH Q3D Inhalation STD# 3 NIA	125 ml
140-131-335	USP232/ICH Q3D Inhalation STD# 3 NIA	500 ml

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