Swedish Match

Quality and Environmental Management System

Document Title
Quantitative Analysis of (b) (4) in Tobacco, Tobacco Products, Fiber-based Matrices, and Tobacco Derived Products with (b) (4)

Valid From
30/11/2017

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Part of Process
Contract Analysis APS

Approved By
(b) (6)

Document Type
Method Description

Document Publisher
(b) (6)

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Purpose

To quantitatively determine the concentrations of beryllium (Be), chromium (Cr), nickel (Ni), arsenic (As), selenium (Se), cadmium (Cd), mercury (Hg), lead (Pb), ^{235}Uranium (U-235), and ^{238}Uranium (U-238). Measurements are carried out on tobacco, tobacco products, fibre-based matrices, and tobacco derived products ((b) (4), also known as purified products), by ICP-MS (Inductively Coupled Plasma Mass Spectrometry).

Applies to

APS

General information

Principle of the method

The metals are released from the sample matrix through microwave digestion using water, nitric acid with a concentration of 67-69%, and hydrogen peroxide 30%. A clear solution is then obtained that is injected and analysed using an ICP-MS. The calculations are made using the MassHunter software associated with the instrument.

ICP-MS is a mass spectrometry analysis that ionises samples with inductively coupled plasma.
The plasma is generated from argon gas and reaches temperatures of up to around 10000 °C.
The samples are fed into the plasma in the form of an aerosol of fine liquid droplets.
The ions are separated on the basis of their mass-to-charge (m/z) ratio, in a mass spectrometer. By adopting this method the different elements in a sample (and their natural isotopes) can be separated and their concentrations can be determined.
A collision cell with helium gas makes it possible to reduce the influence of the most important polyatomic interferences in ICP-MS.
(b) (4)

Through the APS method, Be, Ni, Se, U-235 and U-238 are analysed, in addition to As, Cd, Cr, Hg and Pb. For other differences see Appendix 1.
The capacity is about (b) (4) single samples/week.

Note: All reference documents and additional information stated “available upon request” are in Swedish. They are available upon request but need to be translated into English first.

Method scope, measurement range and measurement uncertainty

Scope

The method is used for the quantitative analysis of (b) (4) and (b) (4) in tobacco, tobacco products, fiber-based matrices, and tobacco derived products. The method is also used for the quantification of the above elements in e-cigarette liquid (not included in the accreditation).

Measurement range

Element	Calibration range (ppb – weight)	Measurement range for sampling, dilution to 50 ml (ppm by weight) as is	Measurement range for sampling, dilution to 50 ml (Bq/kg) as is
(b) (4)			

Measurement uncertainty

The combined relative measurement uncertainty for each element is specified with a coverage factor of 2 for all matrices.
The increased measurement uncertainty is an estimate that applies across the entire measuring range.
Data has been used in the calculations from precision within the laboratory, linearity, uncertainty in the calibration curve, bias estimated from accuracy, the weighing of samples, standard impurity and to measuring the volume of sample tubes.
The largest contributors to measurement uncertainty applicable to all analytes, comes from precision within the laboratory, as well as bias from accuracy, followed by uncertainty in the standard curve.

Combined relative measurement uncertainty.

	Measurement uncertainty for triplicate samples (%)	Measurement uncertainty for duplicate samples (%)	Measurement uncertainty for single samples (%)
Measurement uncertainty Be:	44	45	46
Measurement uncertainty Cr:	30	31	34
Measurement uncertainty Ni:	35	35	37
Measurement uncertainty As:	26*	28*	32*
Measurement uncertainty Se:	44*	45*	48*
Measurement uncertainty Cd:	13	14	17
Measurement uncertainty Hg:	24	28	37
Measurement uncertainty Pb:	25	26	29
Measurement uncertainty U-235	37	39	42
Measurement uncertainty U-238	39	41	48

* As and Se are difficult elements to ionize and require helium collision gas and a high energy helium collision, respectively. (b) (4) (a yield of between 120-150%) which is why the measurement uncertainty of this product is as high as 76% for As and 85% for Se (duplicate samples). The sugar content of the product is also very high, at 25-30% (mostly disaccharides), and the sample that the measurement uncertainty is based on is just below the established detection limit. No inaccurately low results will be reported for these elements. (b) (4)

Literature references

- Agilent 7700 Series ICP-MS, MassHunter Workstation User Guide
- Agilent 7700 Series ICP-MS, Hardware Maintenance Manual
- Agilent 7700 Series ICP-MS, ASX-500 Series Autosampler

(b) (4)

Internal reference documents (available upon request)

(b) (4)

Risk assessment and safety instructions

Risk assessment

Summarized risk assessment

All laboratory work must be conducted wearing safety equipment such as lab coats, protective goggles and protective gloves. Nitrous gases are formed following the digestion of samples in a microwave oven. Open the tubes carefully in a fume cabinet. HNO_3 and HCl are always added to water (the (b) (4)).
Due to the specific organ toxicity of methanol, putting it at a risk level of 3, risky analytical procedures involving this substance should be performed in a fume cabinet. Respiratory protection is, however, not required unless the formation of aerosols or vapour is great enough to warrant this type of protection.

Residue solutions containing Hg are collected separately for later disposal.
Other residue is collected separately for later disposal.

Hazard and precautionary statements

(b) (4)

H280 – Contains gas under pressure. May explode if heated.

P410 + P403 – Protect from sunlight. Store in a well-ventilated place.

(b) (4)

Not subject to labelling

(b) (4)

H272 – May intensify fire. Oxidizing.
H314 – Causes severe skin burns and eye damage (Category 1A).

P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P301 + P330 + P331 – IF SWALLOWED: Rinse your mouth. Do NOT induce vomiting.
P303 + P361 + P353 – IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower.
P304 + P340 – IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P309 + P310 – IF exposed or if you feel unwell: Contact the (b) (4) or a doctor immediately.

(b) (4)

H302 – Harmful if swallowed.
H318 – Causes serious eye irritation.
H332 – Harmful if inhaled.

P261 – Avoid breathing dust/fume/gas/mist/vapours/spray.
P264 – Wash hands thoroughly after handling.
P270 – Do not eat, drink or smoke when using this product.
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P304 + P340 – IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

P312 – Contact the (b) (4) /doctor immediately/…
P330 – Rinse mouth.

(b) (4)

H314 – Causes severe skin burns and eye damage (Category 1A).
H331 – Toxic if inhaled.

P261 – Avoid breathing dust/fume/gas/mist/vapours/spray.
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P301 + P330 + P331 – IF SWALLOWED: Rinse your mouth. Do NOT induce vomiting.
P303 + P361 + P353 – IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower.
P304 + P340 – IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P309 + P310 – IF exposed or if you feel unwell: Contact the (b) (4) or a doctor immediately.

(b) (4)

H314 – Causes severe skin burns and eye damage (Category 1B).
H318 – Causes serious eye irritation.
H371 – May cause damage to organs.
H400 – Very toxic to aquatic life.
H411 – Toxic to aquatic life with long lasting effects.

P260 – Do not breathe dust/fume/gas/mist/vapours/spray.
P264 – Wash hands thoroughly after handling.
P273 – Avoid release to the environment.
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P301 + P330 + P331 + P310 – IF INGESTED: Rinse your mouth. Do NOT induce vomiting. Contact the (b) (4) or a doctor immediately.

P303 + P361 + P353 + P310 – IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower: Contact the (b) (4) or a doctor immediately.
P304 + P340 + P310 – IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing: Contact the (b) (4) (b) (4) or a doctor immediately.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P309 + P310 – IF exposed or if you feel unwell: Contact the (b) (4) or a doctor immediately.

(b) (4)

H314 – Causes severe skin burns and eye damage (category 1B).
H318 – Causes serious eye irritation.
H371 – May cause damage to organs.

P260 – Do not breathe dust/fume/gas/mist/vapours/spray.
P264 – Wash hands thoroughly after handling.
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P301 + P330 + P331 + P310 – IF INGESTED: Rinse your mouth. Do NOT induce vomiting. Contact the SWEDISH POISONS INFORMATION CENTRE or a doctor immediately.
P303 + P361 + P353 + P310 – IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower: Contact the (b) (4) or a doctor immediately.
P304 + P340 + P310 – IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing: Contact the (b) (4) or a doctor immediately.

P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P309 + P310 – IF exposed or if you feel unwell: Contact the (b) (4) or a doctor immediately.

(b) (4)

H314 – Causes severe skin burns and eye damage (category 1B).
H318 – Causes serious eye irritation.
H371 – May cause damage to organs.

P260 – Do not breathe dust/fume/gas/mist/vapours/spray.
P264 – Wash hands thoroughly after handling.
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P301 + P330 + P331 + P310 – IF INGESTED: Rinse your mouth. Do NOT induce vomiting. Contact the (b) (4) or a doctor immediately.
P303 + P361 + P353 + P310 – IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower: Contact the (b) (4) (b) (4) or a doctor immediately.
P304 + P340 + P310 – IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing. Contact the (b) (4) or a doctor immediately.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P309 + P310 – IF exposed or if you feel unwell: Contact the (b) (4) (b) (4) or a doctor immediately.

(b) (4)

H314 – Causes severe skin burns and eye damage (category 1B).
H371 – May cause damage to organs.

P260 – Do not breathe dust/fume/gas/mist/vapours/spray.
P264 – Wash hands thoroughly after handling.
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P301 + P330 + P331 + P310 – IF INGESTED: Rinse your mouth. Do NOT induce vomiting. Contact the (b) (4) or a doctor immediately.
P303 + P361 + P353 + P310 – IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower: Contact the (b) (4) or a doctor immediately.
P304 + P340 + P310 – IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing: Contact the (b) (4) (b) (4) or a doctor immediately.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

P309 + P310 – IF exposed or if you feel unwell: Contact the (b) (4) or a doctor immediately.

(b) (4)

H314 – Causes severe skin burns and eye damage (category 1B).

P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P301 + P330 + P331 – IF SWALLOWED: Rinse your mouth. Do NOT induce vomiting.
P303 + P361 + P353 – IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower.
P304 + P340 – IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P309 + P310 – IF exposed or if you feel unwell: Contact the (b) (4) or a doctor immediately.

(b) (4)

H225 – Highly flammable liquid and vapour.
H301 + H311 + H331 – Toxic if swallowed, if on skin and if inhaled.
H370 – Causes damage to organs.

P210 – Keep away from heat/sparks/open flames/hot surfaces. – No smoking.
P243 – Take precautionary measures against static discharge.
P280 – Wear protective gloves/protective clothing/eye protection/face protection.
P302 + P352 – IF ON SKIN: Wash with plenty of soap and water.
P304 + P340 – IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
P309 + P311 – IF exposed or if you feel unwell: Contact the (b) (4) or a doctor.

(b) (4)

(b) (4)

(b) (4)

Equipment

Apparatus and laboratory utensils

- Microwave digester: (b) (4)
- (b) (4)
- (b) (4) is used to control the auto sampler, the ICP and the detector, as well as for the collection of raw data and Quantification.

Instrument parameters

(b) (4)

Data Analysis Method/Analyte:

Tune Mode	Mass	Name	Analyte / ISTD
(b) (4)			

Acq Method, Acq Parameters:

Peak pattern: 3 points
Replicates: 3
Sweeps / replicate: 50

Stabilazation	No Gas	He	HEHe
Time (sec)	0	10	10

(b) (4)

Data Analysis Method/Full Quant (calibration table):

(b) (4)

Mars 6 Xpress

Method for the digestion of samples:

(b) (4)

Method for cleaning the Teflon tubes:

(b) (4)

Description of Mars 6, Control Style "One Touch":

The temperature and pressure control system in Mars 6 uses a feedback-controlled algorithm, which means that a process variable (temperature or pressure) and an error (the difference between the actual temperature/pressure and the setpoint temperature/pressure), controls the process.
The controller attempts to minimise the error and adjust the process through the use of a manipulated variable (microwave effect).
Mars 6 uses a modified PID algorithm, to process the actual temperature
(reads one per second in fibreoptics or 100 times per second with IR) with set point temperature.
Based on specific mathematical operations, the system calculates an optimal power setting to achieve a setpoint temperature within a desired time (ramp time).

Other equipment

Teflon tube TFM 55 ml from (b) (4)
Teflon inner lid TFM from (b) (4)
Teflon screw cap TFM from (b) (4)
Sample tubes; Polypropylene Sample Cup, (b) (4)
Falcon tube Polypropylene from (b) (4)
Capping station from (b) (4)

Chemicals, reagents and solvents

All solutions are stored at room temperature.

Certificate for standard solutions, internal standards and tuning solutions are to be stored in the binder labelled
(b) (4) All metals contained in the solutions are listed on the certificates.

- Argon
- Water
- Nitric acid
- Hydrogen peroxide
- Hydrochloric acid
- Methanol
- ICP-MS Standard mix
- ICP-MS Hg standard
- ICP-MS Uranium standard
- ICP-MS Internal standard mix
- ICP-MS Tuning Solution
- Citranox acid detergent
- Microgrit WCA 15
  (Aluminum Oxide-Alumina powder)

(b) (4)

Washing solution

Check samples and reference materials

As check samples for metal analysis, a tobacco flour is analysed at every analytical run, (b) (4) The sample is an (b) (4) that is stored (b) (4)

The check sample jar in use is stored at room temperature.

Preparation of standards

General information

The risk of contamination is high when analysing metals. In order to achieve successful analyses with a high level of accuracy and good quality, it is necessary to keep cleanliness in mind throughout the process. Every part of the process is of importance to the end result.
Glassware must never be used.
All storage, dilution and other handling must be performed using plastic products.
All forms of pipetting and the use of dispensettes must be preceded by washing the instruments at least twice before use.

During all preparations of standards and dilution of acids, each tube used must first be filled with about 25 ml H_2O, prior to the addition of acid, or alternatively standard (b) (4) .

Traceability of standard

All standard certificates are stored in order of date in a designated binder and tab, signed and dated, at the opening of a new bottle/batch.

The standard comparison is performed upon preparation of a new stock standard (shelf life of three months).
When preparing new stock standards, standard comparisons should be performed on (b) (4) (b) (4) , (b) (4) and, for (b) (4) .
Stock standards are named for traceability in the following way: (b) (4) .
For example: (b) (4)
Calibration is carried out on the working standards diluted from the newly prepared stock standard.
(b) (4) , from the standard mix Hg-standard

(b) (4).
These are analysed as samples immediately after the standard curves.
The number of counts are compared and documented under each tab in the document according to the following instructions.

Verification of standard
Criteria for approved standard comparison are 90-110% (number of counts)

Preparations

Remember the (b) (4)

All solutions are stored at room temperature.

Diluent/Blank:

Internal standard:

(b) (4)

(b) (4)

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Working standards:

(b) (4)

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Preparation of other solutions

Rinsing solution for the autosampler ASX-500
(b) (4) with water in a bottle, specifically designed for the (b) (4)
Shelf life: 6 months
Hazard symbol: *Corrosive* (b) (4)

Rinsing solution for the Rinse Port (the autosampler)
(b) (4) with water in a plastic container (b) (4)
Shelf life: 6 months
Hazard symbol: *Harmful* (b) (4)

Citranox solution 2%, for the cleaning of cones

(b) (4)

Hazard symbol: *Harmful* (b) (4)

Microgrit WCA 15 mixture, for the cleaning of cones

Take about (b) (4) .

Hazard symbol: *Not subject to labelling.*

Sample handling

Sample storage and preparation

Tobacco flour and tobacco products stored in accordance with (b) (4)

Sample amount

Sample amount: The minimum quantity for performing an analysis and reanalysis with three replicates is (b) (4) .

Analysis

Calibration and verification of apparatus

Startup

(b) (4) should be performed before analysis.

The detailed instructions for this can be found in the document (b) (4)

Sample stability

The shelf life of prepared samples is (b) (4) when stored at room temperature.

Analytical procedure

General information

Keep in mind the major risk of contamination!

In order to achieve successful analyses with a high level of accuracy and good quality, it is necessary to keep cleanliness in mind throughout the process. Every part of the process is of importance to the end result.

Gloves and a laboratory coat must always be worn both to protect yourself from the acids, and to reduce the risk of contamination of the samples from clothes, hands, and jewellery.

New clean gloves should be worn when sealing the Teflon tubes with an inner lid and screw cap in preparation for microwave digestion. Take particular care to ensure that the small inner lid does not become contaminated by unclean gloves!

At a normal sample flow, one blank sample and two check samples are prepared per (b) (4) (b) (4) . The concentration of elements in the finished sample solution is very stable, ensuring a (b) (4) for a prepared sample. The two check samples are analysed first and last in each round of analysis and are documented in (b) (4).
The first and last check sample in the sample list are analysed after the samples in the QC batch are imported into the (b) (4)

Sample preparation

Whole and half pouches are used at the weigh out to achieve the desired weight.

- Blank sample: An empty Teflon tube is placed in position 1 in the sample wheel. To be noted in the LIMS with a weight of 1 g.
- Check samples are weighed out in (b) (4) The check samples are noted in (b) (4) with a weight of 1g!
  NOTE – the correctly factored check sample weight (b) (4) is noted separately in the
  (b) (4) list, to be written into the sample list in (b) (4) later.
  The samples are then weighed, in desired order, according to the following bullet point.
- The sample weight of (b) (4) , dry samples (b) (4) is recorded in (b) (4): Weigh out a (b) (4)

(b) (4) sample in a Teflon tube.
Tobacco, moist samples ((b) (4) Weigh out a (b) (4) sample in a Teflon tube.
Tobacco, moist samples ((b) (4) Weigh out a (b) (4) sample in a Teflon tube.
Tobacco derived products (b) (4): Under normal circumstances a full uncut pouch should be weighed out (the usual weight of these are (b) (4) Alternatively a (b) (4) sample can be weighed out, in a Teflon tube.
For e-cigarettes (not included in the accreditation), see specific instructions.

- Add 5 ml of water.
- Then add (b) (4). Hazard symbol: *Corrosive* (b) (4)
- Leave uncovered, in a fume cabinet for 1-3 hours
- Then add (b) (4). Hazard symbol: *Harmful* (b) (4) *Corrosive* (b) (4)
- Seal the Teflon tubes and place in the rotor. If all (b) (4) are not used, then ensure that the tubes are positioned so that equilibrium is achieved.
  In cases of uncertainty, see schedule from (b) (4) that can be found on the wall of the metal lab, or alternatively, contact the person responsible for method.
  Note: The minimum number of tubes for digestion is eight.
- Place the rotor in the microwave oven. Close the door and run the method (b) (4) located under the icon "(b) (4)". Press "start"
- Label the Falcon tubes with a serial number according to your own documentation in the (b) (4) list (each samples position in the rotor – at (b) (4)
  Label the sample stand with the number of the (b) (4).
- The samples must cool down to a maximum temperature of (b) (4) before the lid may be opened!
  The samples are then stable for at least three days. It is therefore acceptable to leave the samples in the microwave oven overnight, or alternatively from Friday to Monday before the next step is taken!
- Open the lid carefully – there is a risk of acid splashing!
  NOTE – Must be done in a fume cabinet!
- Pour the first sample into a pre-labelled (b) (4). Rinse the Teflon tube with about (b) (4), and decant the tube into the same Falcon tube that the sample was moved into. Now add (b) (4). Hazard symbol: *Corrosive* (b) (4) *Toxic* (b) (4)
- Fill up with H_2O to a final volume of (b) (4). This is repeated for each of the Teflon tubes.
  Hazard symbol: *Corrosive* (b) (4) *and Harmful* (b) (4)

Washing

- The Teflon tubes must be washed in acid between each digestion round as follows.
- Add 9 ml of water to each Teflon tube
- Add (b) (4)
- Seal each Teflon tube with a Teflon cap.
- Place each sealed Teflon tube inside the rotor.
- Place the rotor in the microwave oven and start the program (b) (4) which is located under the icon (b) (4)
- Following the end of the program, the rotor is taken out of the microwave oven and placed in a fume cabinet.
- Open the Teflon tubes very carefully one by one.
- Pour the contents of the tubes into acid residue.
- Each Teflon tube is rinsed by filling it up with water that is then poured down the sink. Repeat this rinsing once.
- Also rinse the caps with water.
- The Teflon tube and cap should then self-dry.
- The Teflon lids should be stored dust free in a specific box in the metal lab and the Teflon tubes should be covered with clean paper towels to prevent dust from entering them.

Calibration and analysis

Begin by initiating a startup and generating a tuning report.

Hazard symbol: (b) (4)
A standard curve for each element is generated in every analysis round.
The instrument performs a triple measurement on each standard and sample, and then displays the mean value, which is used.
There is a template for method parameters and for "sample list", in (b) (4) (b) (4).
It is opened and saved in a specific folder for each month, named Årmåndag sign.
Current method parameters are described in the paragraph: (b) (4)".
The detailed instructions for this can be found in the document *"Instruction for the Determination of* (b) (4)

Special instructions

Microwave oven

A rotor must always be filled with tubes to ensure equilibrium.
If all positions on the rotor are not used, the samples must be placed opposite to each other – as in a centrifuge. The minimum number of tubes that applies to both rotors is eight. See "(b) (4) *User Guidelines.*

For digestion, check that the pressure and temperature increases are similar in each tube in the rotor.
If leaks occur in any of the tubes, the temperature rise will be reduced.
In the event of major leaks, the sample will not be digested sufficiently and if any sample residue is left in the tube the sample needs to be re-digested.

Following digestion of tobacco flour, small grains of sand can sometimes remain at the bottom of the tube. This requires no action.
Black pouches produce a mildly discoloured solution, requiring no action.

E-cigarettes (not included in the accreditation)

Analysis of e-cigarette liquids is performed as follows:
Weigh using a plastic Pasteur pipette, in (b) (4) g e-cigarette liquid, directly into a 50 ml Falcon tube.
Record the exact weight to (b) (4) (g) in (b) (4) under Cadmium.
Add (b) (4) to the Falcon tube.
Hazard symbol: (b) (4)).
Dilute to (b) (4) ml, with water.
Analyse as per usual on the (b) (4) with a dilution factor of 50 in the (b) (4).

Maintenance and troubleshooting

Further instructions can be found in the document "Instruction for the *Determination of* (b) (4) and the (b) (4) User Manuals, as well as in the Maintenance Video.

Documentation

(b) (4)

The weighed-out weight, the scales used, (b) (4), different calculations and (b) (4) is all documented in (b) (4)

(b) (4)

The stock standard that was used for calibrating and for analysed batches, is documented in the relevant sample list. The analyst should be documented with a unique batch name and the (b) (4), for example: YYMMDD-XX. (b) (4)

Raw data binder

A printout of import file is saved in raw data.
The names of incoming QC batches, dates and signatures must be recorded in the printed import file with raw data.

Log book

The list in the first page of the log book details the information to be entered.

- Name of the results file has been imported into (b) (4)
- The QC-batch name
- (b) (4)
- New or upgraded software
- Other events and problem solving relevant to the final results

Instrument binder

Preventive maintenance as well as PM-service is documented in the instrument binder.

Data

Collection and storage of data

The collection of data and calculation of results are performed using the MassHunter software.
Name the file according to "YearMonthDay_signature". For example: (b) (4)
All raw data and used method including all method parameters are saved in MassHunter once every individual run.

A safety backup is created in accordance with the instructions in (b) (4) quality manual.

Calculations

Calculations are performed in the (b) (4) software.
The method includes a calibration table with linear calibration curves.
For (b) (4) the calibration table has seven levels. For (b) (4) and (b) (4) there are five levels, and the concentrations are stated in ppm (equals µg/g in the samples).
To correct potential unevenness in the sample flow, as well as unevenness in sensitivity throughout an analysis series, an internal standard is added in a continuous flow directly into the spray chamber.

The concentration of the calibration solutions is set againts the counts of the analyte and the calculation is performed using the straight-line function.

The software corrects the obtained quatified data by a (b) (4) ml). The results are listed in ppm in (b) (4), calculated based on the default weight, set to 1 g.
Correction of the sample weight, which is between (b) (4) g and (b) (4) g, depending on the matrix used, is performed during the import to (b) (4) Then the actual dilution factor has an (b) (4) (b) (4)

Quality assurance

Control chart

Check samples

Check samples are analysed and documented in accordance with (b) (4) (b) (4)
Check samples are prepared for each QC batch. Both the preparation runs of the check samples are analysed before and after each sample sequence.
The results are imported to the control chart in use, as Replicate 1 and Replicate 2 and are listed in ppm, as they are.
The mean value is calculated in an X chart, and the difference between Replicate 1 and Replicate 2 is calculated in an R chart.

Especially for Chromium, Nickel and Lead:

Cr, Ni and Pb are three elements that are particularly sensitive to contaminants in the sample solution or in the test tubes used for the analysis.
If one of the two check samples is approved for all eight elements and the other check sample is approved for (b) (4), but the concentration of one or two of the elements (b) (4) is too high, this indicates that the samples have been weighed out and digested
correctly, but that the sample has been contaminated during the handling of one of the elements more sensitive to contamination.
In these instances, it is acceptable to only use one of the check samples for the control chart in LIMS. The recorded samples will, in most cases, be analysed with at least duplicate samples.
(b) (4)
.
These cases are (b) (4)

When single samples are analysed, the results have to be carefully checked against a trend curve or alternatively be a part of a long series of similar samples, for example, from the same group of packaged samples.
This applies to all elements, but especially the contamination-sensitive (b) (4)

Digested blank

A digested blank sample is prepared for each QC batch. The blank sample is automatically generated by (b) (4) at the creation of the QC batch and obtains a unique sample number (b) (4)
The digested blank sample is analysed as the first sample (double injection) in every QC batch.
The results are imported into a QC Chart in LIMS.

Certified reference material

Be, Cr, Ni, As, Se, Cd, Hg and Pb:
A certified tobacco sample is analysed once a year.
Reference material: (b) (4)

U-235 and U-238:
(b) (4) are analysed once a year, as well as every time the batch of Uranium standard 10 ppm is replaced with a new batch.

Digested blank

A digested blank (double injection) is analysed for every QC batch and is imported into the (b) (4). The mean value is reported in an X-chart. All limit values are set to (b) (4) of the element's established LOQ.
The logging of markers for blanks occurs in a (b) (4) – since these elements are most susceptible to contamination.
If limit values are exceeded, this may be due to contamination of the sample during sample digestion, during transfer of the samples to test tubes for analysis, or because the utensils used have not been washed properly.

Measures in case of deviations from the limit values:

- The person responsible for method assesses whether a review of procedures for the handling of samples is required.
- Any changes to procedures should be documented in both the (b) (4) and the method description.
- If samples are approved in spite of limit values having been exceeded, this approval must be carried out in consultation with the person responsible for method. The evaluation with accompanying comment must also be documented in the (b) (4).

<u>Standard curve criteria</u>

For each Quantification the linearity and accuracy of the standard curve is verified in MassHunter. The correlation coefficient should be (b) (4)
If the standard curve does not meet established requirements, one or several measures, detailed in INS "*Determination of* (b) (4), will initially be taken. See paragraphs "Troubleshooting with measures" and "Unapproved calibration curve." *Measures*.

The counts of the calibration blanks should be below the following number for each element:

(b) (4)

Analyses may be approved, even if the calibration blanks exceeds the set points, providing that the check samples and standard curves are approved. However, measures should be taken, before the next analysis timepoint, to lower the counts for the calibration blanks. These measures can, for example, include replacing/cleaning the cones, and preparing a new calibration blank.

Duplicate and triplicate samples

When analysing with duplicate samples, the difference between the samples should not be greater than (b) (4) of what was measured when determining repeatability.

Element or Isotope	Permissible difference between triplicate samples	Permissible difference between duplicate samples.	Permissible difference between duplicate samples Low results	Permissible difference between duplicate samples Very low results
(b) (4)				

If the response in a sample is higher than the highest standard

High samples are diluted from the existing digested sample solution, with an automatic pipette in a (b) (4), to a concentration that is within the counts of the standard curve. Keep in mind the risk of contamination and wash the pipette tip with the sample solution two times before dilution.
Dilute with '(b) (4) to ensure that uniform acid concentration is obtained. Only reanalyse the high analyte in the dilution.

Reporting of analysis results

The results are transferred from (b) (4). The values are imported into (b) (4) in ppm (ppm by weight) with the default weight set to (b) (4) g. In LIMS, the values are adjusted to account for sample amount and moisture content.
Concentrations < LOQ are specified as < (current LOQ), e.g.: (b) (4) (b) (4) are reported to the client in ppm (weight), in a dry sample, with two significant figures.
(b) (4) are recalculated from ppm (weight) to (b) (4) using the following conversion factors included into LIMS:
U-235 in ppm (weight) is multiplied by (b) (4)
U-238 in ppm (weight) is multiplied by (b) (4) are reported to the client in (b) (4), without revision, with two significant figures.

Revision history

23/01/2014 New document.

26/02/2014 The correct date of the new document under the heading history.
Colours added to the table under the heading; Sample Comparisons.

05/05/2015 Corrections to deviation indications (b) (4) from (b) (4)s (b) (4), when applying for accreditation (b) (4).
(b) (4): -E-cigarette liquid has been removed from the accreditation application.
-The basis for the calculation of measurement uncertainty has been clarified in the validation report.
-Limits to "Carry over" have been added to the validation report.
-A comparison of (b) (4) has been added under "Accuracy" in the validation report.
(b) (4): Comparison with the FDA-method added as Appendix 1.
(b) (4) Limits for digested blanks added to the method.

19/08/2016 Extension of the method by two elements: U-235 and U-238.
Additional validation reviewed and approved in (b) (4)
Paths have been updated.
Results from new sample comparisons have been added to the validation report.
The standard point of (b) (4) ppm (mixed working standard) has been deleted from the standard curves. The measurement range for Be, As and Se has been changed. For other elements the measurement range remains unchanged.

21/11/2017 A new matrix has been added for tobacco derived products (b) (4). An additional validation was performed (Repeatability, accuracy, extraction yield and specificity).

Swedish Match

Quality and Environmental Management System

Document Title
Quantitative Analysis of (b) (4) in Tobacco, Tobacco Products, Fiber-based Matrices, and Tobacco Derived Products with (b) (4)

Valid From
30/11/2017

Page
32(49)

Part of Process
Contract Analysis APS

Approved By
(b) (6)

Document Type
Method Description

Document Publisher
(b) (6)

2017-05

The following updates have been made to the MTB, based on the new guide:
- Units of concentration have been changed to units of weight.
- The measurement uncertainty for (b) (4), and Uranium has been modified, and an acceptable difference for triplicate samples, regarding all the elements, has been added.
- Documentation has been detailed. (b) (4)
- Instructions for responding to a sample that is outside the measurement range have been added.
- (b) (4) have been updated

Person responsible

Director APS

Validation

Validation report

The validation examined ten samples in total, distributed in five different matrices.
The validated samples are (b) (4)

In addition, four different types of (b) (4), cigar tobacco, and two certified ground samples; (b) (4) and (b) (4) have been examined to gain information from samples with concentrations above LOQ for each element.
The following table summarises the type of validation conducted for each sample.
The linearity is estimated based on the analysis of standard solutions.
LOD and LOQ were calculated based on ten digested blanks that were digested and analysed by different people at five different timepoints.
Calculations and all the data used in the calculations are available upon request.

(b) (4)

The validation followed a validation plan and the scope is marked with "X" in the table below. In 2016 an additional validation for (b) (4) and (b) (4) was conducted. Extensions made to these are marked with a Y in the table below. In the sample (b) (4). there were only measurable levels of (b) (4)

(b) (4)

Selectivity/Specificity

(b) (4) as possible have been selected.
A (b) (4) enables the separation of the most important polyatomic interferences in (b) (4)

Carry Over

Carry Over was assessed by (b) (4) standard followed by a blank injection.
Carry Over is reported below, as a percentage of the lowest standard and highest standard, respectively, for each element. The results are averaged based on three different analytical rounds.
Approved Carry Over is the number of counts corresponding to (b) (4).
The results are approved.

	Carry Over in % of the highest standard	Carry Over in % of the lowest standard
(b) (4)		

Repeatability

In order to assess the repeatability of each element, (b) (4) with a total of ten different matrices, with varying concentration levels for each element.

The pooled RSD data for each element is displayed below.

(b) (4)

(b) (4)

For the assessment of acceptable difference between duplicate samples, regularly occurring "normal concentrations" for each element, in the most common matrices, have also been taken into consideration. In addition, the (b) (4) (contamination-sensitive elements). (b) (4) Table, see heading "Quality assurance"

Precision within the laboratory

Precision within the laboratory was determined by analysing (b) (4), with varying concentrations of each element.

(b) (4)

The pooled RSD data for each element is displayed below:

(b) (4)

(b) (4)

Sample comparison

1. (b) (4)

To assess the reproducibility of Be, Cr, Ni, As, Se, Cd, Hg and Pb the samples from Coresta's proficiency test from 2012 have been analysed retrospectively using frozen samples.
(b) (4) participated in the proficiency test with analyses performed on an older instrument, (b) (4) (b) (4)

Comparison have been made against the mean value from the proficiency test and against the new results from (b) (4) (from new composite samples). The samples selected are '(b) (4) and the (b) (4) check sample (b) (4) (b) (4)
In addition to these comparisons, three certified reference products from LGC standards have been analysed (b) (4)
Assessments in relation to the certified values, and the mean value produced by (b) (4) (b) (4), as well as a comparison with (b) (4) have all been performed.

(b) (4) Hence comparisons against proficiency test have only been performed for these elements.
There are no results from any proficiency test for (b) (4) For these elements, comparisons have only been made against (b) (4) and certified reference samples.
As regards the certified reference products, some of the elements contained in reference samples have certified values and other elements in these samples have "information values".

The comparison in relation to mean values from (b) (4) indicates sufficient reproducibility and demonstrates results that are similar to all of the means in the proficiency test.
The results are summarised in the following table:

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Part of Process
Contract Analysis APS

Approved By
(b) (6)

Document Type
Method Description

Document Publisher
(b) (6)

Values in **bold Green** are APS values obtained (b) (4)

(b) (4)

Brief summary of results for each element:

- (b) (4): No proficiency test has been conducted with respect to (b) (4), only comparisons with (b) (4) results. All analysis results are consistent with the results from (b) (4). However, all but one result are deemed to be below established LOQ. There are certified results from (b) (4) " that are in agreement with the (b) (4) results and are satisfactory in comparison with the certified values.
- (b) (4) Good agreement with the mean value from the proficiency test. Low result in comparison with the certified values. High values in comparison with the (b) (4) results, whith lower values than (b) (4) for the certified samples, and a large spread between the two different rounds of analysis performed.

- (b) (4). Low results in comparison with the certified values. High values in comparison with the Eurofins results. There is, however, a very large spread between the two different rounds of analysis performed by (b) (4)
- (b) (4) the certified values and the results from (b) (4)
- (b) (4) the certified values and the results from (b) (4)
- (b) (4) the certified values and the results from (b) (4).
- (b) (4) All analytical results are consistent with the results from (b) (4) However, all but one result is deemed to be below established LOQ. All certified reference samples have concentrations above LOQ and are very consistent with the certified results.
- (b) (4) the certified values and the results from (b) (4).

2. Sample comparison (b) (4)

In March of 2015 a sample comparison was conducted by the (b) (4)

The sample comparison involved investigating and comparing the concentrations of Arsenic, Beryllium, Cadmium, Chromium, Cobalt, Nickel, Lead, and Selenium in three certified reference materials and in one CORESTA reference product (b) (4) (b) (4) exhibited a Z-score "Good" or "Satisfactory" for (b) (4) in all investigated samples.

3. Supervised by Swedac; Microwave digestion and analysis of certified reference materials, 2016

(b) (4) along with a witnessed analysis of a certified reference sample, brought by the supervising party. (b) (4) (b) (4) Rye grass – rye flour).
Results (b) (4) are very consistent with the certified values and are presented below.

Analysis of certified reference material (b) (4) (European reference materials)
The analysis was done under audit by the Swedish accreditation body (b) (4)

(b) (4)

4. (b) (4)

In July of 2016 (b) (4) participated in a Proficiency Test organised by LGC-standards.
In the sample comparison, (b) (4) and the concentrations of Arsenic, Selenium, Cadmium, Mercury and Lead were examined.
(b) (4) for all elements when the (b) (4) measurement uncertainty is taken into account.

Accuracy (trueness)

Pouch snus, tobacco flour, chewing tobacco and tobacco derived products (b) (4) have been (b) (4) and (b) (4) that was administered in (b) (4). (This is done in order to minimise the risk of contamination for (b) (4) by decreasing the number of times pipetting occurs per digestion tube).
For each element, the original concentration, and (b) (4), are used for assessing and calculating accuracy. Which concentrations are used is determined by the original concentration of each respective element in the samples.
(b) (4) and six unspiked replicates have been quantified.

The mean level of accuracy regarding elements, based on three different concentrations, is shown in the following table.
The accuracy is sufficient for all elements in the tested matrices, except for (b) (4) (b) (4) (resulting in larger uncertainty of measurement). No inaccurately low results will be reported for these elements.

(b) (4)

(b) (4) level, with (b) (4). The accuracy of (b) (4) is very good – between (b) (4). For Hg the accuracy is (b) (4). (b) (4) are measured at slightly higher levels than they should be at, most likely due to the high concentration of organic material in samples (no digestion takes place), which are not fully compensated for by adding (b) (4) to the internal standard. The accuracy of (b) (4) and the accuracy of (b) (4)
No inaccurately low results will be reported for these elements.

Comparison of the check sample (b) (4) has been performed by comparing it with the established mean in (b) (4) obtained using the previous test method used in the laboratory. This method (accredited) used the Graphite Furnace Atomic Absorption Spectroscopy (b) (4) technique. No comparisons for (b) (4) could be done, since these elements never were analyzed on the (b) (4) instrument. The results are presented in the following table:

(b) (4)

The check sample results fall within the established limits of the check sample, both for GF-AAS and for ICP-MS

(b) (4) Additional validation 2016

To assess reproducibility when analysing (b) (4), an SRM (Standard Reference Material) from NIST (National Institute of Standards and Technology) has been analysed with three replicates. The results are very consistent with the certified values, and are presented below. The certified values were obtained using Silicon surface-barrier alpha-particle spectrometer.

NIST, Standard Reference Material® 4359 (Dried Seaweed)				
Certified values according to certificate				
	Median ± (k=2) [mBq•g-1] (Bq/kg)	**95/95 Tolarence Limit (d)' [mBq•g-1] (Bq/kg)**	**Repl.**	**CAS Results 2016-04-26 (Bq/kg)**
(b) (4)				

Bias from accuracy data

The estimated error in the method in relation to the true value in % (bias) is calculated as the square root of the sum of the yield-100 from "accuracy", and the uncertainty in the addition of the amount of analyte. Bias from "accuracy" is used for calculating measurement uncertainty.

Bias from (b) (4) is not included in the calculation. The bias would have been lower with (b) (4) included. (b) (4) is therefore subject to estimated bias.

Results are presented in the following table:

Bias from accuracy for each element is presented in terms of percentage

(b) (4)

(b) (4)

Extraction yield (Recovery)

In order to calculate the extraction yield, (b) (4) and tobacco derived products (b) (4) were all spiked with (b) (4) in one concentration, at one timepoint, and with six replicates.
The sample solution was spiked and was analysed both before and after reprocessing. Neutral samples (unspiked) from the product were also analysed in order to deduct the original concentration when calculating the yields.
Presented in the table below are the mean values for pouch snus, tobacco flour and chewing tobacco. The mean value for (b) (4) is presented separately since the extraction yield of the tobacco matrices would not be representative of tobacco and tobacco products if (b) (4) was included in the mean.

(b) (4)

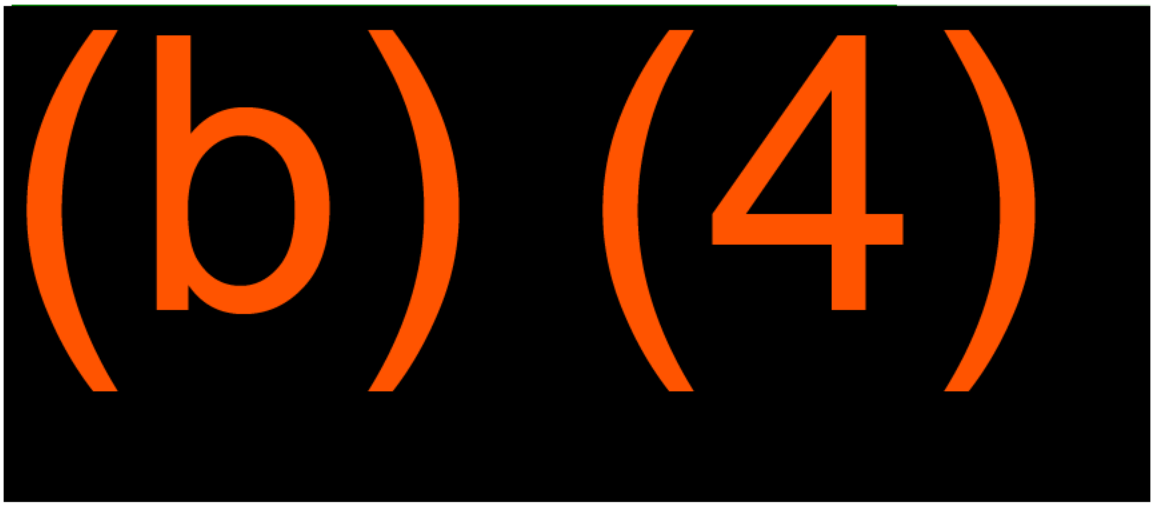
Limit of detection (LOD) and Limit of Quantification (LOQ)

Limits of detection and limits of Quantification for (b) (4) and U-238 have been determined by investigating the blank levels obtained and the variability of the blank signal. (b) (4) and analysis timepoints. The digested blanks was digested according to the method, (b) (4), whereupon the concentration in the solution was measured.

Calculation of LOD:
(b) (4)

Calculation of LOQ:
(b) (4)

(b) (4)



Linearity

The linearity was examined by analysing six calibration solutions in three series with concentrations of (b) (4) for (b) (4) and (b) (4) for (b) (4). For Hg, four calibration solutions, with the concentration of 0.05 – 1 ppb, have been analysed. For (b) (4) four calibration solutions with concentrations of (b) (4) have been analysed.
The relationships are linear and linearity is calculated on an unweighed standard curve.

(b) (4)

Robustness

The robustness of the method regarding (b) (4), has been assessed with the help of data from the (b) (4). For the different days of analysis, the (b) (4)

Established mean values (ppm) and standard deviations for the first 50-60 rounds of analysis (the number varies for different elements) and for Uranium, 25 results:

(b) (4)

(b) (4)
(2009). The effects of varying amounts of added acid and water during digestion were then examined. These amounts ranged from 2 ml HNO_3 + 1 ml H_2O_2 + 8 ml water, to 8 ml HNO_3 + 3 ml H_2O_2.
No significant differences in concentrations could be observed.

In addition, a comparison between digestion in CAS' previous microwave (b) (4) and the current microwave (b) (4) has been conducted. No significant difference could be observed.

The concentrations of acids and water appropriate for digestion in "Mars 6" were determined to be:
(b) (4) following digestion, in order to stabilise potential concentrations of Hg.

Stability

The stability of the standard solutions detailed in the method description, has proven to be sufficient.
(b) (4) kept at room temperature.

The criteria for approved standard comparison is (b) (4)

Prepared samples are stable for at least three months according to the criteria (b) (4) compared to newly prepared samples.

Measurement range

High samples outside the measurement range is (b) (4), until a concentration that is within the counts of the standard curve is achieved.
(b) (4) to ensure that uniform acid concentration is obtained.

(b) (4)

(b) (4)

Measurement uncertainty

The combined relative measurement uncertainty for each element is specified with a (b) (4) (b) (4).
The increased measurement uncertainty is an estimate that applies across the entire measuring range.
Data used in the calculations are derived from (b) (4)

Combined relative measurement uncertainty.

(b) (4)

* As and Se are difficult elements to ionise as they require "Helium collision gas" and a "High Energy Helium collision", respectively, in order for ionisation to occur. (b) (4) which is why the (b) (4) The sugar content of the product is

also very high, at (b) (4) and the sample that the measurement uncertainty is based on is (b) (4)

Comments

(b) (4)

Conclusion

2017-11: The fit-for-purpose method is designed to analyse the elements in tobacco, tobacco products, fibre-based matrices and tobacco derived products. (b) (4)

Appendices

Appendix 1

Comparison of differences between the FDA method and the APS method.

(b) (4)		

Swedish Match

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