



**Malvern
Panalytical**

EPSILON 4 PHARMACEUTICALS & COSMETICS



TRUST YOUR PRODUCT QUALITY

Analyze accurately and frequently

The Epsilon 4, an energy dispersive X-ray fluorescence (EDXRF) benchtop spectrometer, is a perfect alternative for the pharmaceutical industry where ICP and AAS are traditionally used. Equipped with the latest advances in excitation and detection technologies, Epsilon 4 analyzes trace elements with low detection limits over the whole elemental range.

Switch to XRF for the analysis of elemental impurities in pharmaceuticals and comply with the USP chapters 232, 233 & 735. Low infrastructural requirements enable analysis close to production facilities and shorten the feedback loop, therefore making fast corrective actions possible. Little sample preparation and low utility requirements significantly reduce the cost per analysis. Discover below the possibilities of XRF analysis for pharma and cosmetic applications.

Epsilon 4's value for the pharma & cosmetics industry

- Orthogonal analysis method for elemental impurities in pharmaceutical products
- Simple, fast and safe sample preparation
- Low sample volumes
- Low cost of ownership, low infrastructural requirements, small footprint
- Compatible with other analytical techniques like ICP and AAS
- Non-destructive analysis
- Minimum downtime and maintenance
- Elemental screening of unknown samples with Omnia



Audit trail software

To comply with mandatory regulations and procedures, Malvern Panalytical offers:

- Enhanced Data Security software that enables users to comply with FDA 21 CFR Part 11
- Installation and operational qualification packages (IQ and OQ)

FDA 21 CFR Part 11

Check for counterfeit drugs and cosmetics

Use positive material identification with PASS/FAIL analysis in the FingerPrint solution for a fast authenticity check

Pharma calibration standards

Three cellulose-based sets of standards have been developed to set up calibrations for the three categories:

- Toxic elements
- Catalyst residues
- PGM particles

Unknown material screening

Pre-screening of raw materials with Omnia standardless analysis

Catalysts and metals residues analysis

According to USP chapter <735> XRF is an alternative analytical technique to screen API and excipients for residues.

USP <232>, <233> and <735>

NON-DESTRUCTIVE ELEMENTAL ANALYSIS OF IMPURITIES

According to ICH Q3D and USP<232>

The introduction of USP<232> and ICH Q3D helps the pharmaceutical industry to re-evaluate the analysis of elemental impurities (heavy metals) in pharmaceuticals. USP chapter <735> and EP 2.2.37 enable the use of X-ray fluorescence spectrometry for this analysis.

Three sets of cellulose calibration standards containing Cd, Pb, As, Hg, Co, V, Ni, Tl, Pd, Ir, Rh, Ru, Se, Pt, Mo, Cu and Cr were used to set up calibrations for these elements. Only 100 mg of powder material was required, which was placed into a special disposable holder before analysis.

All 17 elements were analyzed within 1 hour. When fewer elements are required for analysis, the measurement time can be shorter. The limit of quantification levels (LoQ) were calculated by taking 10 times the standard deviation from 20 measurements on a blank standard. USP <232> and ICH Q3D guidelines stipulate a control threshold of 30% of the Permitted Daily Exposure (PDE), where additional controls may be required if the concentration exceeds the control threshold. For all elements, the LoQ values were smaller than the required threshold of 30% of the PDE, based on 1 g daily dose.

Elemental group	Element	LoQ (µg/g)	USP <232> & ICH Q3D 30% oral PDE* (µg/g)	Elemental group	Element	LoQ (µg/g)	USP <232> & ICH Q3D 30% oral PDE* (µg/g)
1	Cd	1.17	1.5	2B	Ir	0.17	30
1	Pb	0.53	1.5	2B	Rh	1.17	30
1	As	0.47	4.5	2B	Ru	0.37	30
1	Hg	0.33	9	2B	Se	0.20	45
2A	Co	0.17	15	2B	Pt	0.33	30
2A	V	0.30	30	3	Mo	0.47	900
2A	Ni	0.13	60	3	Cu	0.17	900
2B	Tl	0.33	2.4	3	Cr	0.23	3300
2B	Pd	2.23	30				

*Limits set by ICH Q3D are based on 1 g daily dose.



Malvern Panalytical offers three sets of cellulose-based standards, covering 17 elements mandated in USP <232> and ICH Q3D. The standards contain elemental concentrations ranging from 0 to 200 µg/g. The separate sets contain 5 different standards plus a validation sample.

THE POWER OF BENCHTOP XRF SYSTEMS

Combining the latest excitation and detection technology and smart design, the analytical performance of Epsilon 4 approaches that of more powerful and floor-standing spectrometers. Selective excitation and careful matching of the X-ray tube output to the capabilities of the detection system underlie the system's outstanding performance.



Epsilon 4 - Highly flexible analytical tools suitable for a wide range of applications:

- 10-watt version - used for elemental analysis (F - Am) in areas from R&D through to process control
- 15-watt version - used for higher sample throughput with improved and extended light-element capabilities (C - Am)
- 15-watt version - used for higher sample throughput in challenging environments (F - Am)

H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	L	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	A															
		L	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
		A	Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Z Possible to analyze with Epsilon 4
Z Not possible to analyze with Epsilon 4
Z Possible with Epsilon 4 and optional detector

Reduce helium consumption

The high performance of Epsilon 4 enables many applications to be operated in air atmosphere, without longer overhead time and costs involved for helium or maintenance of vacuum system. When measuring in air, low-energy X-ray photons characteristic of sodium, magnesium and aluminium, are sensitive to variations in air pressure and temperature. Built-in temperature and air pressure sensors compensate for these environmental variations, ensuring excellent results whatever the weather.

Calibrated for years

A low-drift X-ray tube and an automatic drift correction system give compliant results for years without the need for re-calibration. This results in a more efficient use of the system and less cost of calibration maintenance.

Online remote support

In the unlikely event of the Epsilon 4 needing specialist attention, an on-line diagnostic facility is available in the local service centers. Problems can be diagnosed, and in many instances corrected, directly on-line. This significantly reduces system downtime and cuts maintenance costs to a minimum.

Accurate results

Our unique high-performance, metal-ceramic X-ray tube, specifically designed and manufactured for Epsilon 4, ensures high quality and reliable results. Flexible voltage settings from 4.0 to 50 kV and a maximum current setting up to 3.0 mA can be used to define application-specific excitation conditions that optimize the performance across the periodic table.

Ultimate light-elemental performance

With the optional SDD^{Ultra} detector, Epsilon 4 enables ultra-light element analysis of even carbon, nitrogen and oxygen.

Quality results through mature software

Accurate and precise results are obtained through advanced spectrum processing and state-of-the-art correction and quantification algorithms.

Safety guaranteed

Epsilon 4 complies with the latest Machinery Directive, CSA, IEC, EMC, Vollschutz norms and standards for protection and radiation safety to guarantee a safe instrument for the operator.

Unattended operation

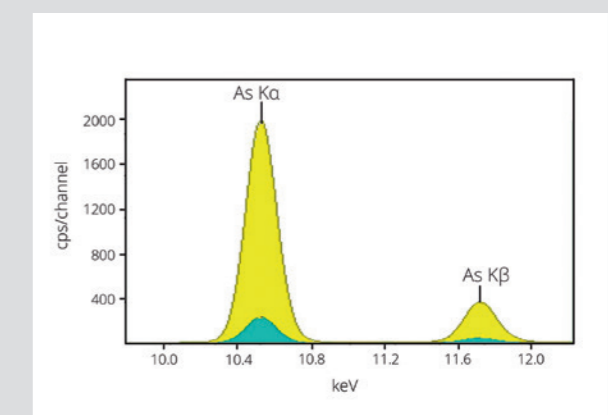
The unique combination of a 10-position removable sample changer with spinner enables the automatic processing of sample batches without the need for operator attention. Continuous rotation of the sample during measurement minimizes any errors caused by non-homogeneity or surface irregularities within individual samples and provides more accurate results. Automatic transfer of data to a central location gives you access to the latest results.

Fast and sensitive

Fast measurements are achieved by using the latest silicon drift detector technology that produces significantly higher intensities.

Unique detector electronics enable a linear count rate capacity to over **1,500,000 cps** (at 50% deadtime) and a count rate independent resolution typically better than 135 eV for better separation of analytical lines in the spectrum.

This allows the Epsilon 4 spectrometer to run at full power and therefore realizes a much higher sample throughput compared to traditional EDXRF benchtop instruments.



Ten times higher intensities for arsenic obtained with Epsilon 4, in comparison with its predecessor Epsilon3^{XLE}

FAST, REPRODUCIBLE ANALYTICAL METHOD

Compared to other analytical techniques XRF requires little or no sample preparation

XRF is an ideal means of determining the chemical composition of all kinds of material. Measurements in Epsilon 4 are carried out directly on the solid material (or liquid) with little to no sample preparation. There is no need for any dilution or digestion and therefore no disposal of chemical waste.

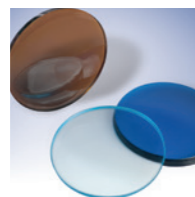
Epsilon 4 spectrometers can handle a large variety of sample types weighing from a few milligrams to larger bulk samples. Samples can be measured as:

- Solids
- Pressed powders
- Loose powders
- Liquids
- Fused beads
- Slurries
- Granules
- Filters
- Films and coatings

LIQUIDS



SOLIDS



AIR FILTERS



POWDERS



TAILORED SOLUTIONS THROUGH EXPERTISE

Experienced Malvern Panalytical staff work in close cooperation with you to provide not only training but also tailored analytical programs and procedures, balancing throughput and accuracy while minimizing setup and running costs.

Access to the right calibration samples is key in XRF. Malvern Panalytical helps in obtaining or creating the standards you need. We provide total solutions including standards for several key applications. We can also generate suites of in-house standards by certifying your materials through our ISO 17025 certified laboratory.

Sample preparation, although typically straightforward for XRF, is an important factor in the overall analytical precision and accuracy. Sample preparation needs to be quick, robust and reproducible, and the choice of sample preparation technique starts with your requirements and materials.

Combine XRF with the analytical solutions Malvern Panalytical offers, like near infrared spectroscopy, particle size analysis and X-ray diffraction. Our experts can advise you which approach suits best given your material types and analytical requirements.

Tap into our knowledge network through our global Expertise Centers to optimize your complete analytical process, including sample preparation methods and equipment.



Our aim is to make Epsilon 4 an essential part of your elemental analysis

The added value for you is what drives us:

- The largest support network in the industry
- Training programs customized to your needs
- Reference materials
 - *Certified reference materials (CRMs)*
 - *Synthetic reference materials tailored to your requirements*
- Analytical services
 - *Certify your samples through our ISO 17025 certified laboratory*
- Consultancy
 - *Norm compliance*
 - *Laboratory information management*
 - *Process automation*
 - *standard operating procedures*
 - *Interlaboratory standardization*





MEASURE IT IN YOUR OWN LANGUAGE

1. Load your sample
2. Select required method
3. Enter relevant sample information
4. Just click Measure
 - 測量
 - 測定
 - Mesurer
 - Messung
 - Mesure
 - Zmierzyć
 - Medida
 - Измерить
 - Médir

ENHANCE YOUR ANALYSIS THROUGH SOFTWARE OPTIONS

Five industry software options are available to further enhance the capabilities of Epsilon 4: Omnian, Stratos, Oil-Trace, Enhanced Data Security and FingerPrint.

These dedicated options add new functional dimensions to benchtop spectrometry and take the hard work out of regulatory compliance.

Elemental screening OMNIAN



Omnian software option is ideal when there is no conventional calibration established for materials that require analysis. When faced with non-routine samples or materials for which there are no certified reference materials, Omnian provides excellent insight into the elemental composition. Designed to provide fast and reliable quantification, Omnian's advanced fundamental parameters (FP) algorithm automatically deals with the analytical challenges posed by samples of widely differing types.



Enhanced data security AUDIT TRAIL SOFTWARE



The enhanced data security software option is designed for GMP and GLP environments, and supports FDA 21 CFR Part 11. The software includes every feature required to satisfy the strict environmental protocols, like multiple security levels, log in with user identification, reporting of date and time, results storing, extensive audit trails and LIMS integration.

Pass/Fail analysis FINGERPRINT



FingerPrint is a material type confirmation routine that uses a rapid statistical analysis of the spectrum for a simple PASS/FAIL answer. Spectra used for the FingerPrint routine can also be used for conventional compositional determination for a more complete diagnostic analysis.



WHY CHOOSE MALVERN PANALYTICAL?

We are global leaders in materials characterization, creating superior, customer-focused solutions and services which supply tangible economic impact through chemical, physical and structural analysis.

Our aim is to help you develop better quality products and get them to market faster. Our solutions support excellence in research, and help maximize productivity and process efficiency.

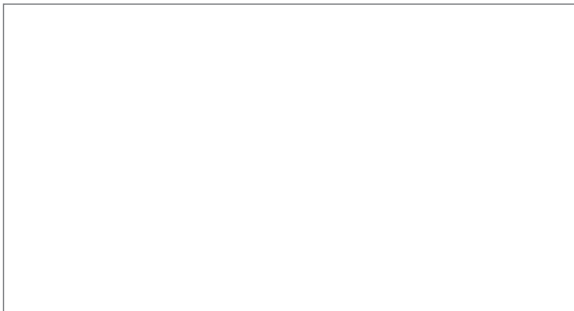
Malvern Panalytical is part of Spectris, the productivity-enhancing instruments and controls company.
www.spectris.com

SERVICE & SUPPORT

Malvern Panalytical provides the global training, service and support you need to continuously drive your analytical processes at the highest level. We help you increase the return on your investment with us, and ensure that as your laboratory and analytical needs grow, we are there to support you.

Our worldwide team of specialists adds value to your business processes by ensuring applications expertise, rapid response and maximum instrument uptime.

- Local and remote support
- Full and flexible range of support agreements
- Compliance and validation support
- Onsite or classroom-based training courses
- e-Learning training courses and web seminars
- Sample and application consultancy



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