Metals and trace metals determination in clinical samples

Fast, accurate and reliable procedures to determine metals and trace metals in clinical samples

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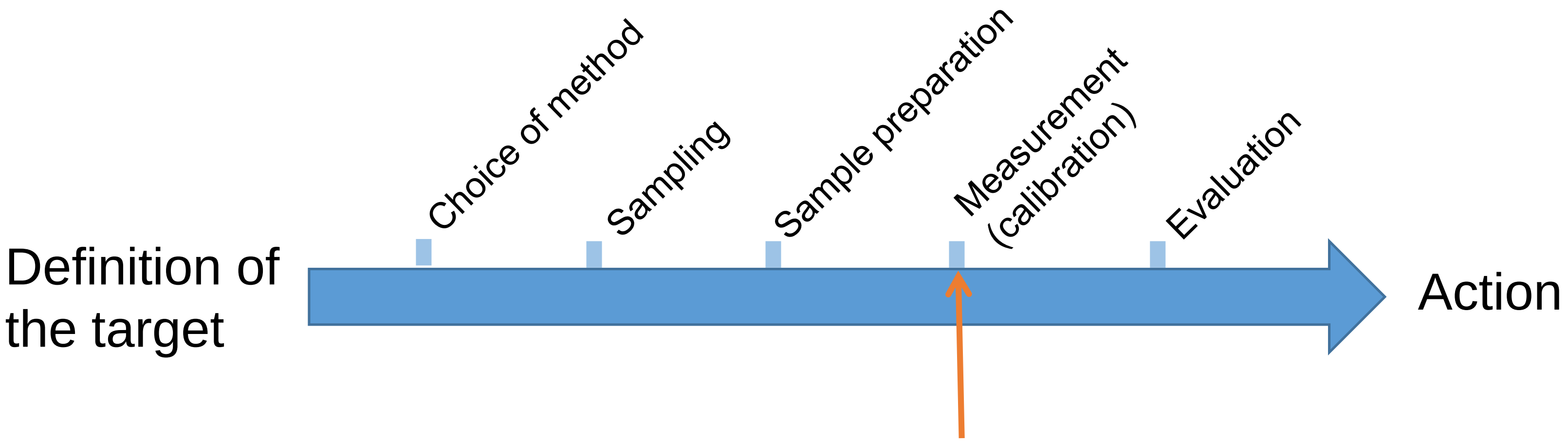
The analytical sequence



- CV AAS
- GF AAS
- ICP-OES
- ICP-MS
- ICP-MS-MS
- Etc…

The gradual decrease of detection limits

	Detection limit	Analogy	
1960	ppm	First gray hair	
1970	ppb	Needle in a Haystack	
1980	ppt	Contact lens on 100 miles beach	

“The four players in the Analytical Performance” Table 2 by Leo de Galan JAAS,27:1173,2012

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The Elemental Analysis today

“Instrumental analysis has continuously evolved in the last decades and determination of trace elements is becoming a routine task in analytical laboratories.

*Inductively coupled plasmas with argon gas are successfully applied for measurements of emission lines (**ICP OES**) and isotopes (**ICP-MS**) for most elements of periodic table.*

However, a laboratory must have full control of analytical blanks and sample preparation for obtaining accurate results.”

“Think Blank” book R.C. Richter - J.A. Nóbrega - C. Pirola

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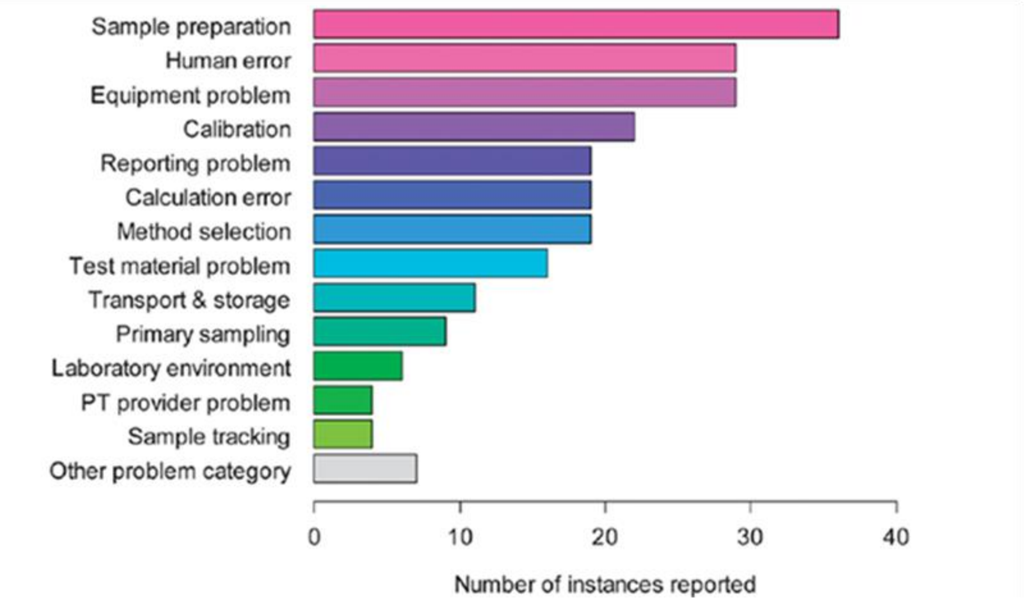
Trace metal analysis challenges

- Prevent contamination from materials used, cleaning methods, reagents and environment
- Interferences caused by complex matrices (complete digestion of organic matter)
- Avoid losses during the sample prep

Better blanks make it realistically feasible
to reach lower detection limits

What causes most errors in chemical analysis?

Analytical Methods, 5:2914–2915, 2013.



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Key parameters in a digestion

- Sample type/amount The choice of the right configuration strongly depends on your samples and your analysis technique
- Productivity Number of samples per day/ week
- Ease of use Handling time, easy to work with
- Flexibility Capability to be used with any number of vessels and different configurations
- Reliability Robustness, hardware construction

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Case study:

Clinical sample preparation for trace metals analysis

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Clinical sample preparation needs

- Low blanks
- Low reagents volume
- Low sample amount
- Lower contact surface
- Low dilution factor

Introducing the Vessel-Inside-Vessel

Microwave digestion techniques typically require a minimum volume of reagents of about 5/10mL to achieve accurate temperature monitoring of the reaction conditions. However sometimes it is important to maintain a very low dilution factor, particularly when working at concentrations near the method detection limit.

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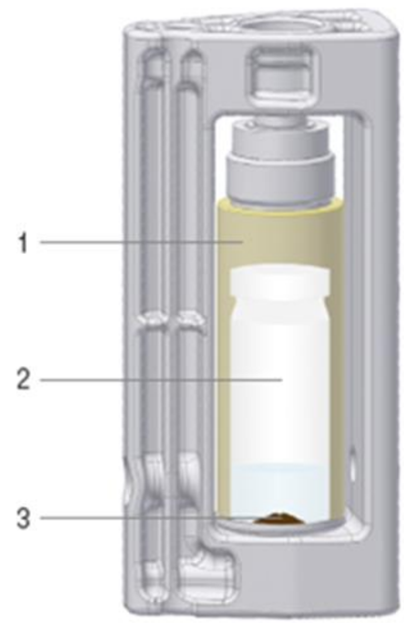
Vessel-Inside-Vessel

This has led Milestone to develop a “Vessel-Inside-Vessel” technology, using smaller secondary vessel (1) inside the primary microwave vessel (2). The secondary vessel contains the sample and digestion reagents (3), while the primary vessel contains the solution that absorb microwave.



Vessel-inside-vessel schematics

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Vessel-Inside-Vessel

This setup reduces the amount of acid required for digestion, lowering the dilution factor and increasing the detection limit. A variety of inserts are available from Milestone (quartz or TFM) and different sizes and shapes to accomplish all application requirements.

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The Ethos configuration

- Ethos Up

Advanced Microwave Digestion system

- Direct temperature control

- SK-15

High Pressure Rotor and micro-inserts

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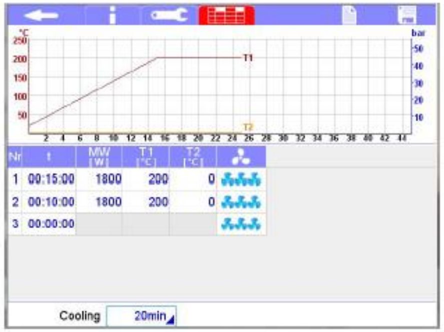
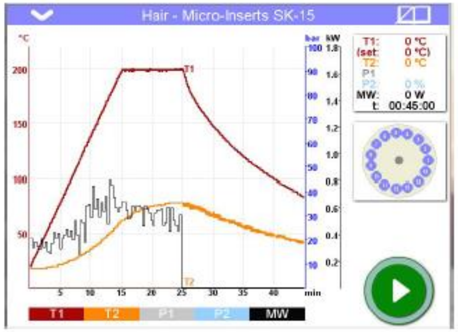
Digestion of Hair samples
(IAEA-085)
Sample spiked with 50ppb of As, Cd, Cr, Pb, Se, Ni, Mn

Sample Name	Sample weight	Reagents into the vials	Reagents into the SK15 vessel	Micro-sampling config.
Human hair IAEA - 085	100 mg	HNO_3 - 2 ml	H_2O dist. - 10 ml	TFM rack for 3 micro-inserts. Quartz vials

Sample	Method	Temperature profile
Human hair IAEA-085		

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Digestion of Hair samples

(IAEA-085)

Results obtained by ICP-OES and expressed in ppb

Replicate	As	Cd	Cr	Pb	Se	Ni	Mn
1	49.2	48.1	54.9	47.9	51.9	50.7	51.0
2	39.0	47.5	53.0	49.4	49.4	49.9	51.4
3	49.2	48.3	53.2	48.3	51.9	50.4	52.3
Average	**45.8 ± 5.9**	**48.0 ± 0.4**	**53.7 ±1.0**	**48.5 ± 0.8**	**51.1 ± 1.4**	**50.3 ± 0.4**	**51.6 ± 0.7**
% Recovery	**91.6**	**95.9**	**107.4**	**97.1**	**102.1**	**100.7**	**103.1**

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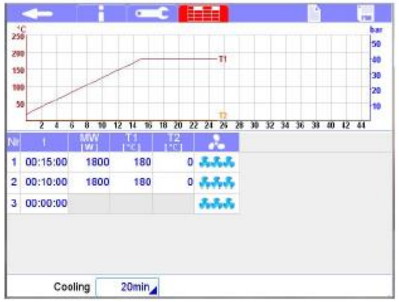
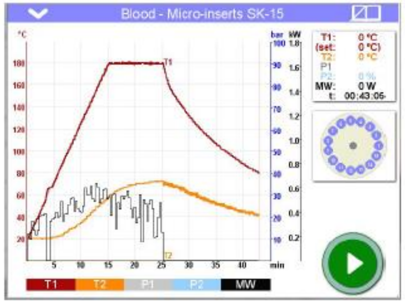
Digestion of Animal blood

Sample Name	Sample weight	Reagents into the vials	Reagents into the SK15 vessel	Micro-sampling config.
Animal Blood sample	100 mg	HNO_3 - 2 ml	H_2O dist. - 10 ml	TFM rack for 3 micro-inserts. Quartz vials.

Animal blood		

Digestion of Animal blood

Results obtained by ICP-OES and expressed in ppb

S1	54,79	39,56	14,38	31,61	11,00	148,5
S2	56,08	39,52	14,30	32,59	10,80	148,2
B4	< 2	< 2	< 2	< 2	< 2	< 10
Average	**55,4**	**39,5**	**14,3**	**32,1**	**10,9**	**148,4**
Std. Dev.	**0,9**	**0,0**	**0,1**	**0,7**	**0,1**	**0,2**

B = Blank; S = Sample

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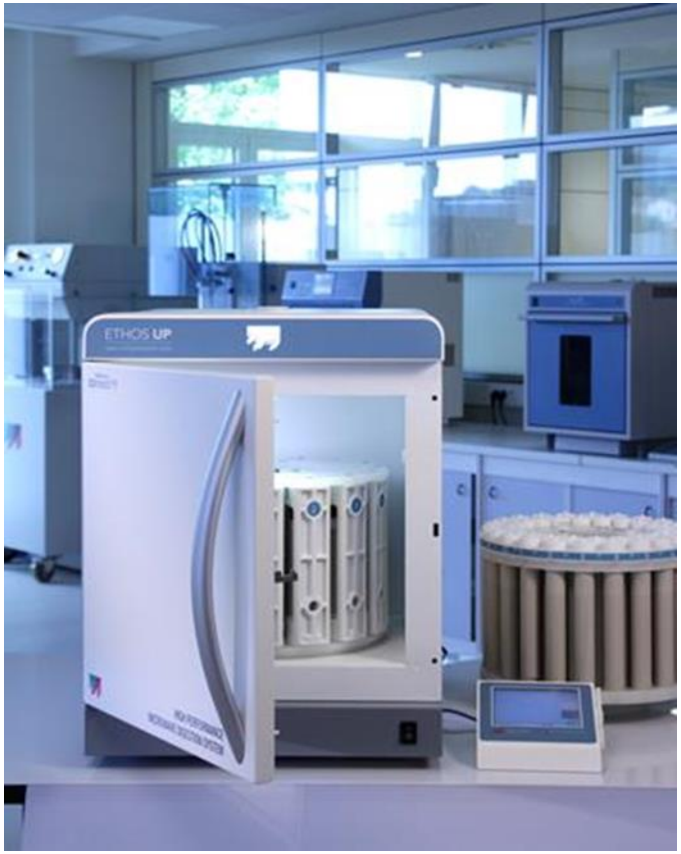
Milestone solutions for Clinical applications

Ethos UP



UltraWAVE

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Milestone Ethos UP

- High productivity
- Ease of use
- High safety
- Full control of the reaction conditions
- Connectivity

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Milestone SK-15 high pressure rotor

- 15 positions segmented
- Digestion of large sample size
- Fully closed vessels
- Vent-and-reseal technology
- 100 bar and 300°C

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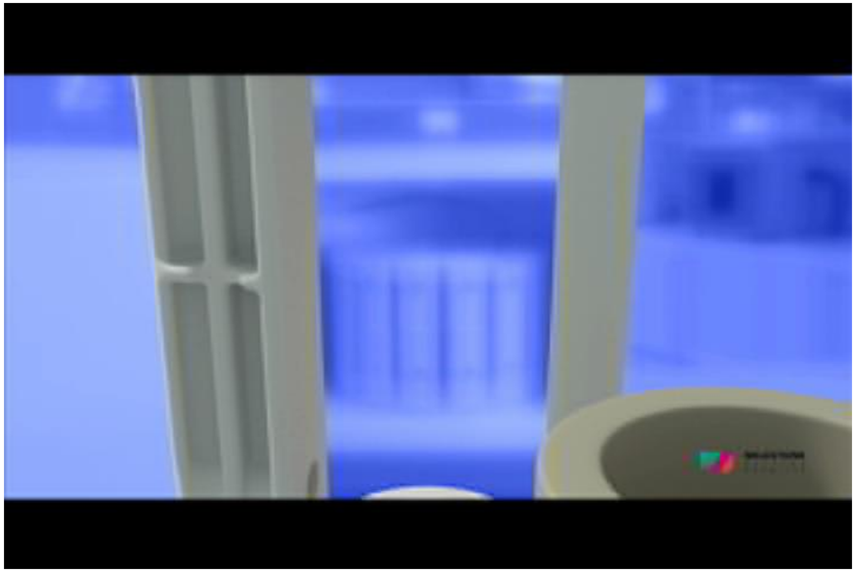
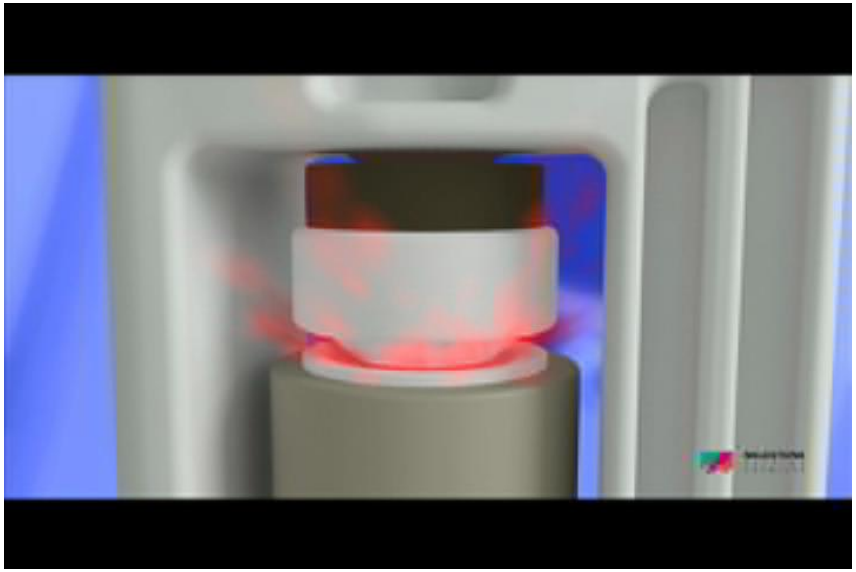
Milestone SK-15

SK-15 assembling



SK-15 vent-and-reseal technology



Milestone MAXI-44 high throughput rotor

- Up to 44 samples simultaneously
- Easy handling
- Full temperature control
- Digestion of a large wide of samples
- Self regulating mechanism

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Milestone MAXI-44

Built-in application notes

No method development required

Over 300 pre-installed digestion methods

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Milestone UltraWAVE

The Game Changer in Microwave Sample Preparation

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UltraWAVE Single Reaction Chamber (SRC)

- Easy handling
  - No assembly/disassembly of vessels
  - No cleaning- ability to use disposable vials
- Extreme Productivity
  - High sample throughput
  - One digestion program for everything
- Lower operating costs
  - Reduced labor and consumables costs
- Digest completely mixed sample matrices simultaneously
  - One run for all sample type
- Highest Temperature and Pressure Available
  - Max. pressure 199 bar, max temp. 300deg.C
  - Digest even the most difficult/stable samples

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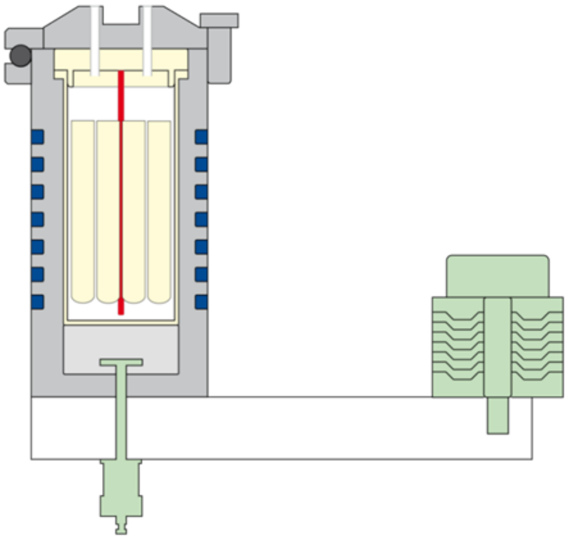
SRC Design - UltraWAVE

- 1L stainless steel reaction vessel With 900mL PTFE reactor
- Sample rack is lowered into the chamber and into a base load All samples digested together under same temperature and pressure. Direct T and P sensors continuously control the digestion parameters.
- Whole chamber is pressurized Nitrogen pressure avoid sample loss ; Vials are closed with loose fitting covers
- Fast water cooling A chiller quickly cool the reactor using a water chiller



For the first time, a microwave controls the temperature and pressure in every vessel regardless of sample type or acid chemistry being used!

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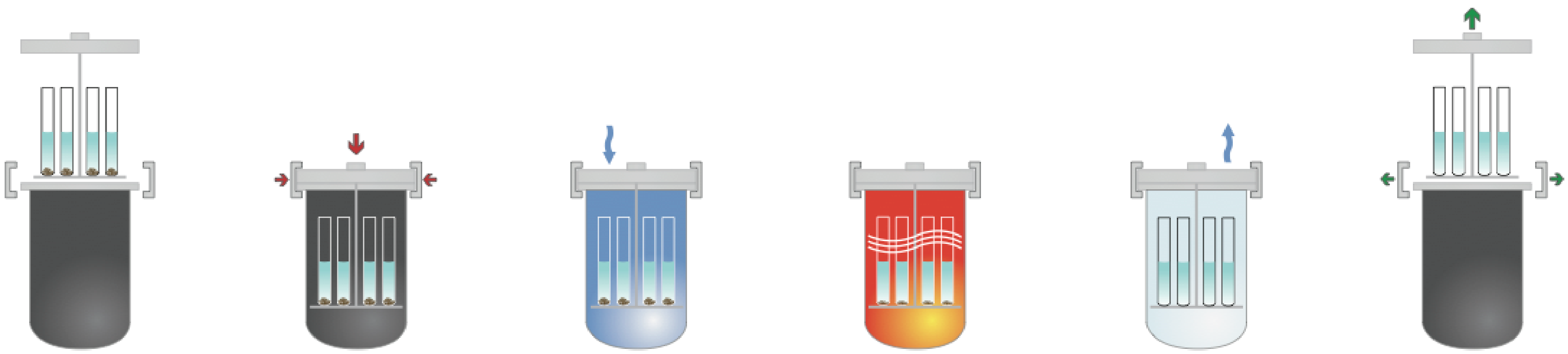
Digestion Sequence

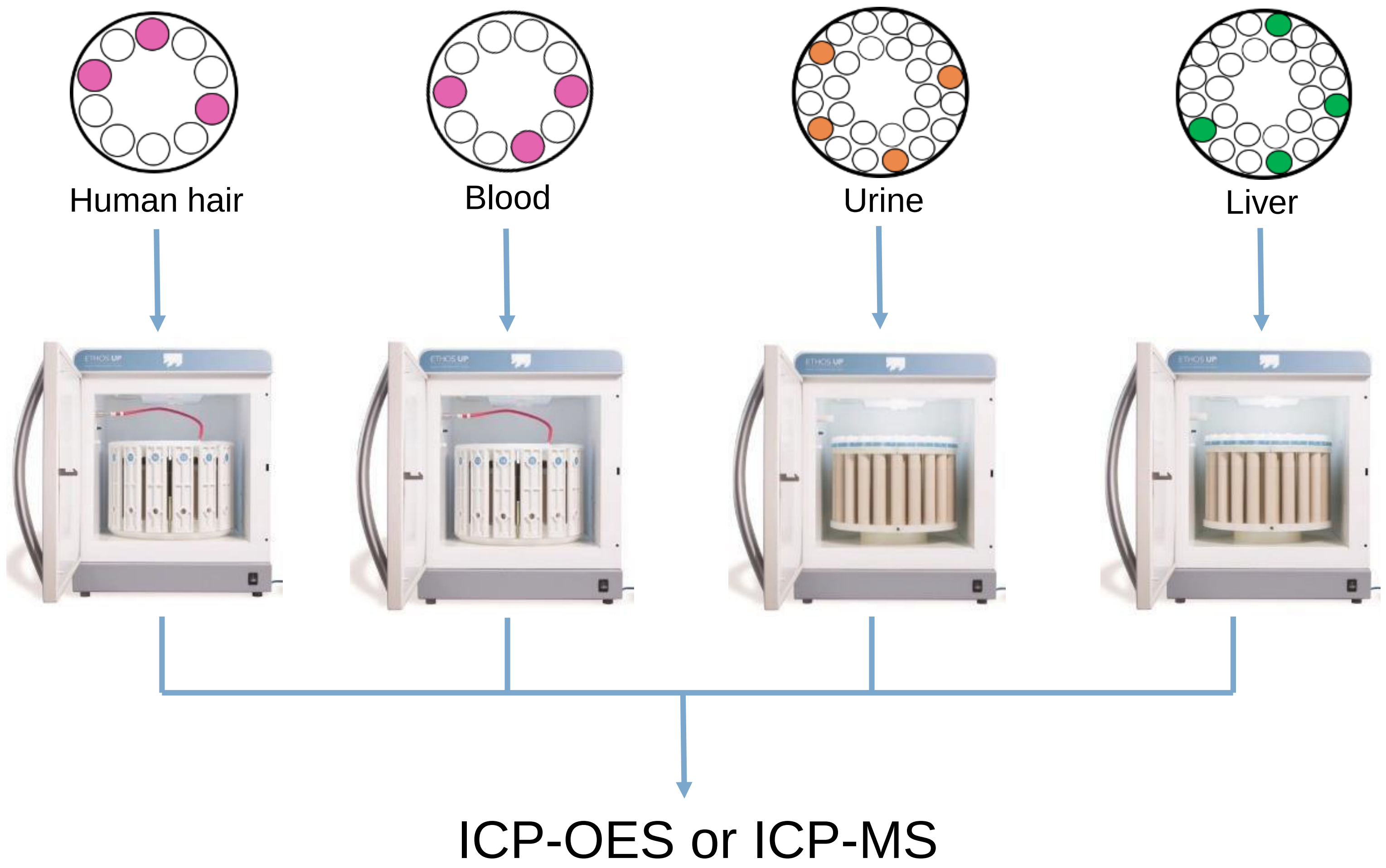


1. Sample rack is lowered automatically into microwave chamber
2. Chamber clamp is secured by the operator. Interlocks prevent operation without clamp in place
3. Chamber is pre-pressurized with inert gas to prevent sample boiling. Cross contamination is eliminated
4. Microwave energy is applied. All samples under same temperature and pressure conditions
5. Very fast cooling step due to water cooling of chamber. Chamber is vented and acid vapors extracted
6. Clamp is released and sample rack automatically rises from chamber

Sample Racks and Vials

- Wide choice of sample rack
- No need to close and open the vials thanks to the pressure loaded before the run
- Vials available in Quartz, TFM or ***disposable glass***

Conventional approach (Rotors)



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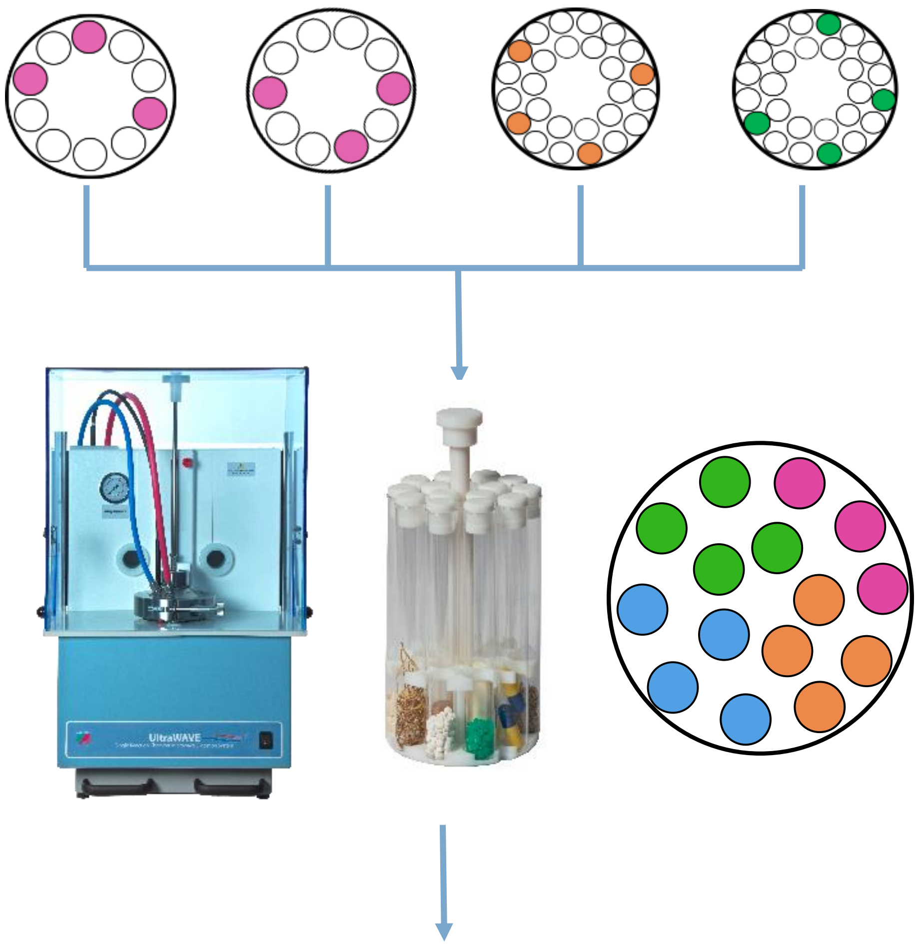
SRC Approach



ICP-OES or ICP-MS

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UltraWAVE Summary

- Ease handling
  - No need to close/ open the vials
- High performance
  - 300°C and 200 bar. Digestion of difficult sample and large sample amount
- High Throughput
  - Fast cooling, less handling
- Low running costs
  - Disposable glass vials, inexpensive vials

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Direct Mercury Analysis
Clinacal samples

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DMA-80
Direct Mercury Analysis

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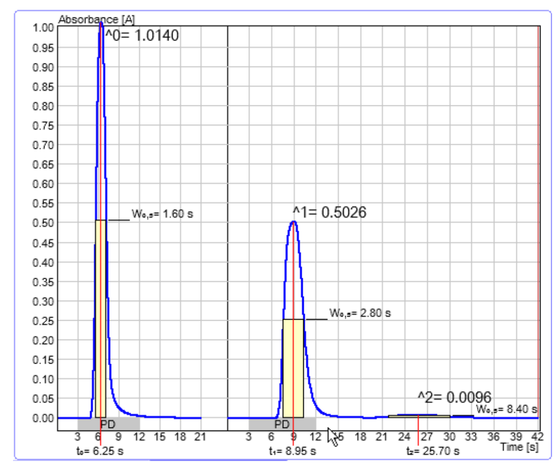
Advantages of Direct Mercury Analysis

- Ease of Use
- High Productivity
- Lowest cost of analysis
- Validated results (US EPA and ASTM methods) for solid and liquid matrices
- The sample is analyzed directly
- The combustion process fully release the mercury from the sample
- Fast analysis
- Connectivity



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DMA Principle of operation

1. Solid or liquid samples are weighed and introduced in the DMA-80
2. The sample is initially dried and then thermally decomposed in a oxygen or air flow
3. Combustion products are carried off and further decomposed in a hot catalyst bed
4. Mercury vapors are trapped on a gold amalgamator and subsequently desorbed for quantitation
5. The mercury content is determined using atomic absorption spectrophotometry at 254 nm

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DMA-80 Case study

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Mercury pollution in Guatemala

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

A combined ecological and epidemiologic investigation of metal exposures amongst Indigenous peoples near the Marlin Mine in Western Guatemala

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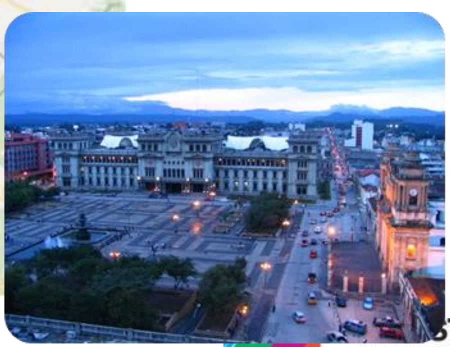
ABSTRACT

In August 2009 a combined epidemiological and ecological pilot study was conducted to investigate allegations of human rights abuses in the form of exposures to toxic metals experienced by mine workers and Indigenous Mam Mayan near the Marlin Mine in Guatemala. In the human study there were no differences in blood and urine metals when comparing five mine workers with eighteen non-mine workers, and there were no discernible relationships between metal exposures and self-reported health measures in any study group. On the other hand, individuals residing closest to the mine had significantly higher levels of certain metals (urinary mercury, copper, arsenic, and zinc) when compared to those living further away. The levels of blood aluminum, manganese, and cobalt were elevated in comparison to established normal ranges in many individuals; however, there was no apparent relationship to proximity to the mine or occupation, and thus are of unclear significance. In the ecological study, several metals (aluminum, manganese, and cobalt) were found significantly elevated in the river water and sediment sites directly below the mine when compared to sites elsewhere. When the human and ecological results are combined, they suggest that exposures to certain metals may be elevated in sites near the mine but it is not clear if the current magnitude of these elevations poses a significant threat to health. The authors conclude that more robust studies are needed while parallel efforts to minimize the ecological and human impacts of mining proceed. This is critical particularly as the impact of the exposures found could be greatly magnified by expected increases in mining activity over time, synergistic toxicity between metals, and susceptibility for the young and those with pre-existing disease.

Mercury contamination due to gold mines pollution



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Mercury in blood and urine of Guatemala population

Table 2
Reference (normal) range or threshold values for metals in relation to concentrations measured in the current study. Cited references are indicated in the table's footnote.

	Blood concentrations (μg/L)		Urine concentrations (μg/L)		Toxic effects when present in excess
	Median (range), current study	Reference range or threshold	Median (range), current study	Reference range or threshold	
Aluminum (Al)	52 (16.5–107.1)	0–6.2 (A)	2.71 (2.71–113.44)	16 (upper reference; T); 160 (Finnish action level; T)	Central nervous system, gastrointestinal, pulmonary (restrictive, obstructive) disease
Manganese (Mn)	13.2 (7.3–24.3)	4–15 A; 7–12 (T)	0.05 (0.04–4.34)	<1 (T)	Central nervous system, respiratory inflammation
Cobalt (Co)	0.4 (0.2–1.5)	0.5 (T)	0.24 (0.03–2.52)	<2 (T)	Respiratory system (asthma, lung cancer, fibrosing alveolitis)
Nickel (Ni)	1.80 (0.07–13.50)	Limited data (A)	0.07 (0.04–2.63)	0.5–4 L (T)	Carcinogen, contact allergen, respiratory toxicant
Copper (Cu)	828 (566–1347)	Not good indicator (A)	3.07 (0.15–19.01)	Not good indicator (A)	Pulmonary, gastrointestinal
Zinc (Zn)	6735 (4885–9050)	7000 (A)	83.8 (11.7–352.0)	Limited information (A)	Deficiency and toxicity result in varied health effects
Arsenic (As)	3.9 (3.2–8.5)	0–5 A; not good indicator (A)	0.06 (0.04–16.7)	<100 (A); <50 (T)	Multiple organ systems
Cadmium (Cd)	1.20 (0.74–2.40)	<1 (T); action level is 5.5 (Sweden; T)	0.11 (0.05–0.27)	<1 (T)	Pulmonary, renal, gastrointestinal, bone, hematological
Lead (Pb)	26.7 (3–44)	<100 (A)	0.23 (0.12–1.47)	0.69 (2001–2002 NHANES geometric mean)	Central nervous system
Mercury (Hg)	2.4 (0.6–13.0)	<20	0.11 (0.04–0.70)	<10 (T)	Central nervous system

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Mercury in blood and urine of Guatemala population

- A single calibration was used for different matrices
- Great accuracy even at low concentration
- Simplicity of operation
- Fast analysis
- High Flexibility

The DMA-80 sequence

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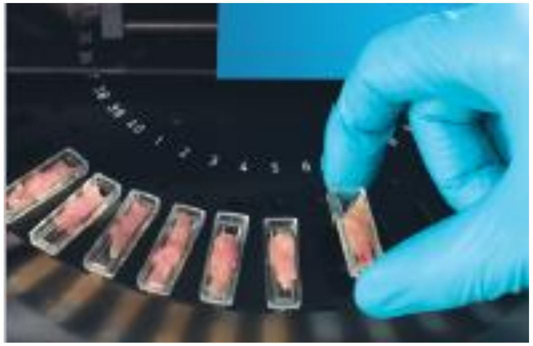
Three steps and start!

1

2



3

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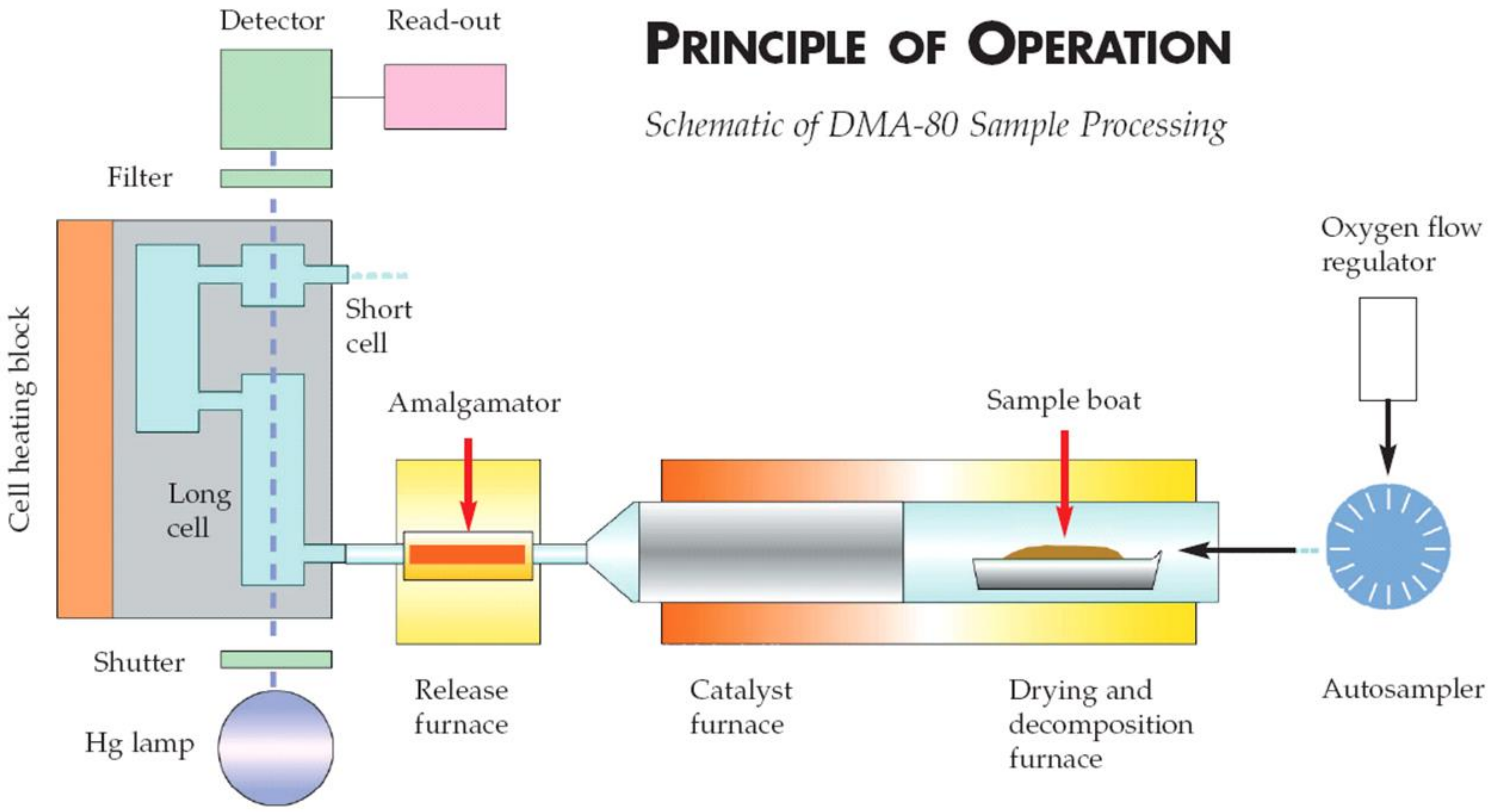
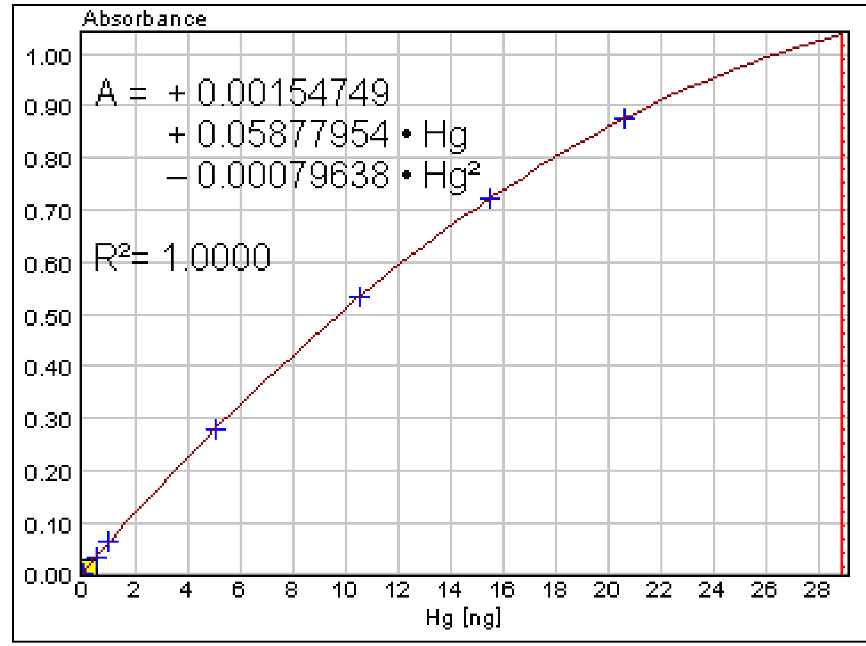
Principle of operation



ONE Calibration for all matrices

- Liquid standards to create a calibration curve
- Solid SRMs to verify the calibration curve
- Software automatically distributes calibration based on ng of mercury present in the samples
- Extremely long calibration life time.

Direct Analyzers



Square calibration

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ONE Calibration for all matrices

Certified material	Certified (µg/Kg)	DMA-80 (µg/Kg)
NIST 1568a Rice Flour	5,8 ± 0,5	5,9 ± 0,2
BCR-150 Skim Milk Powder	7,7 – 11,1	9,2 ± 0,2
NIST 1630a Coal	93,8 ± 3,7	93,4 ± 2,4
NIST 1633b Fly Ash	141 ± 19	149 ± 2
BCR-61 Aquatic Plant	210 – 250	221 ± 3
GSD-10 Stream Sediment	280 ± 40	270 ± 15
BCR-422 Cod Muscle	543 – 575	558 ± 8
IAEA-086 Human Hair	534 - 612	574 ± 12
NIST 2711 Soil	6250 ± 190	6240 ± 70
BCR-680 Polyethylene	24,3 – 26,3 mg/Kg	25,8 ± 0,5 mg/Kg

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DMA-80 Advantages

- **No sample preparation**
  - Direct Hg determination at trace level on solid, liquid and gas samples
  - No sample digestion step
  - No wet chemistry pre-treatment step
- **Easy of Use**
  - Weigh and Start
  - One calibration for all matrices
  - Easy control Software
- **High Productivity**
  - Fast analysis , 6 minutes
  - 40 position autosampler + dual-tray autosampler for a continuous operation
- **Lowest cost of analysis**
  - Eliminates waste disposal
  - Easy maintenance
  - Long Consumables life time
  - Air Compressor
- **Validated results (US EPA and ASTM methods) for solid and liquid matrices**

Introducing the Milestone Connect

The new era in customer support

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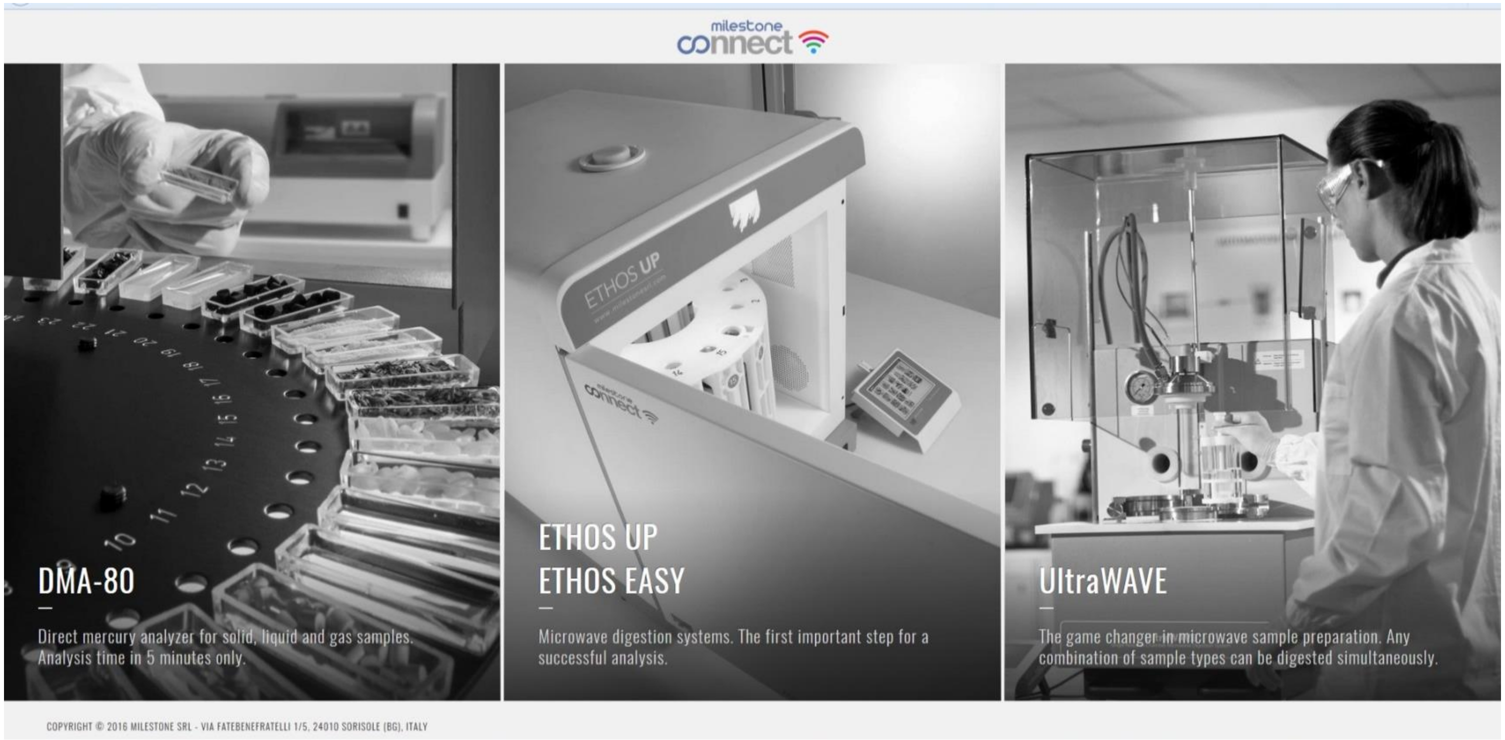
Milestone Connect



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Milestone Connect

Available for Ethos Easy, Ethos UP, UltraWAVE and DMA-80

- Application notes and application reports
- Scientific paper library
- User manual
- Tutorial videos
- Tips and Techniques
- Spare parts and consumables
- Remote control of the system

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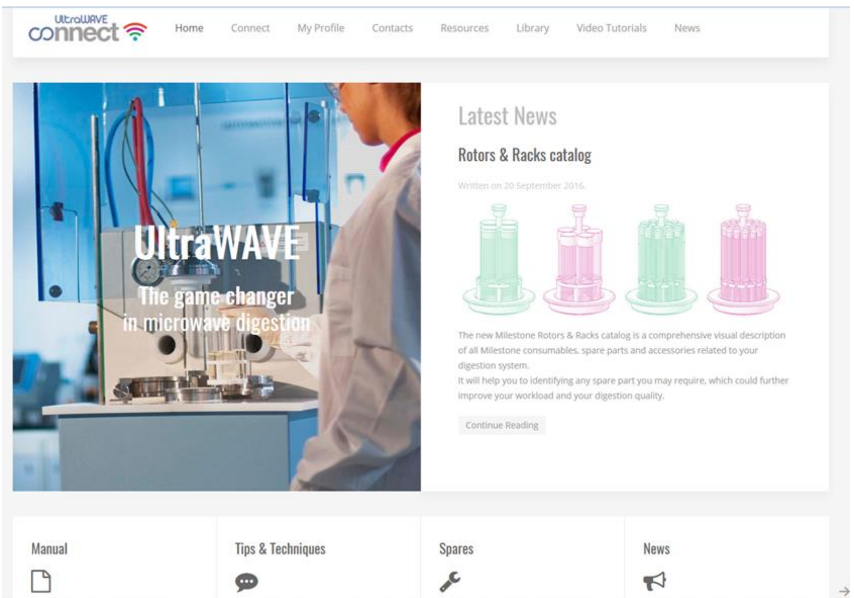
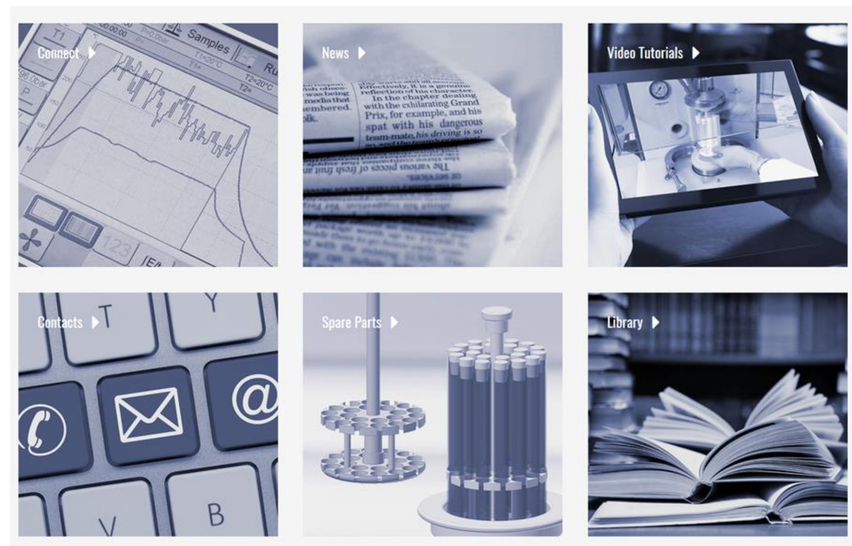
milestone connect





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Thank you for the attention

Questions?

application@milestonesrl.com

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