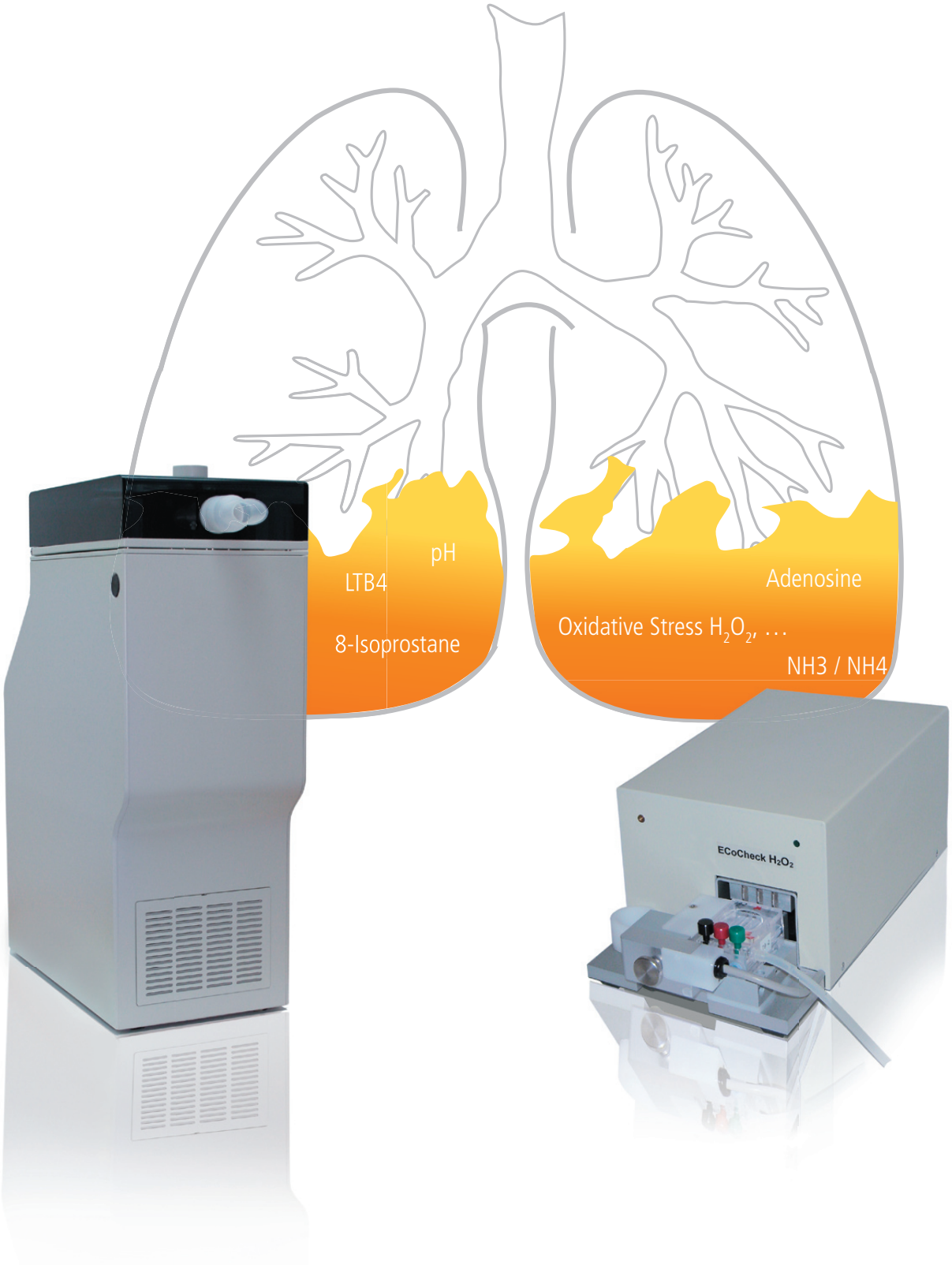
FILT

Airway inflammation Diagnostic

EBC-Collection & analysis



Diagnostic of inflammatory processes in the lung

ECoScreen

EBC-Collector

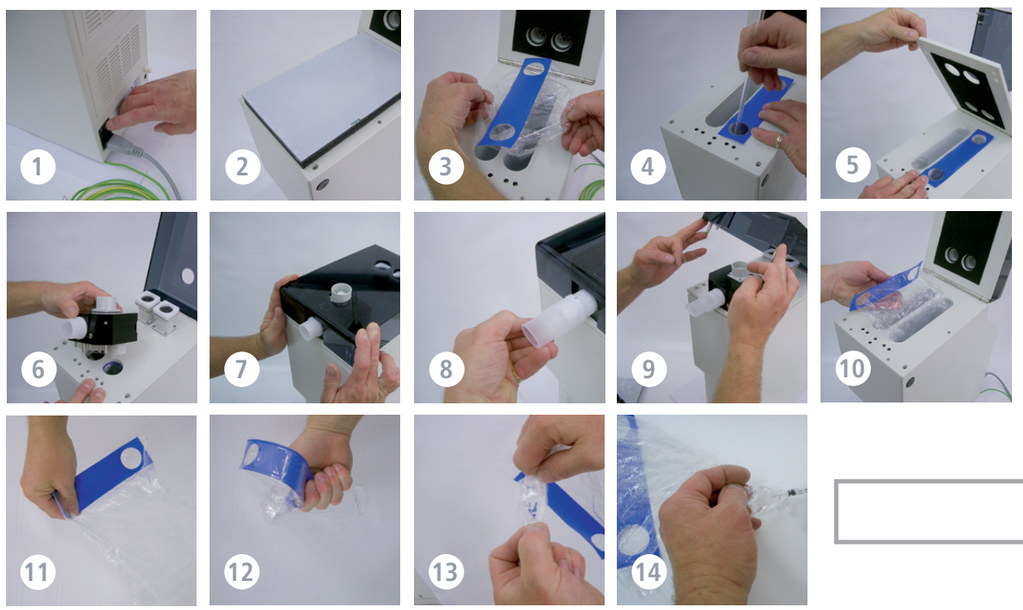
The EBC-Collector is an innovative solution for non-invasive, fractionised collection of exhaled breath condensate (EBC), because of:

- a spirometers, which is built in, allows the measurement of volume and time controlled standardised collection,
- breath controlled collection into two separate chambers makes it possible to collect condensate from different depths of the bronchial system, so that the dead space condensate may be discarded,
- the material of the sampling bags is approved for the collection of exhaled biomarkers:
  hydrogen peroxide, L-lactate, proteins and lipids, like: prostaglandin and leukotrienes.
- H_2O_2 and L-Lactate can be analysed by EBC Analyzer:

oder ECoCheck

Advantages of the EBC Collector:

- fractionised condensate collection
- transportable desktop device
- simple handling
- low noise level
- stable construction



ECoCheck

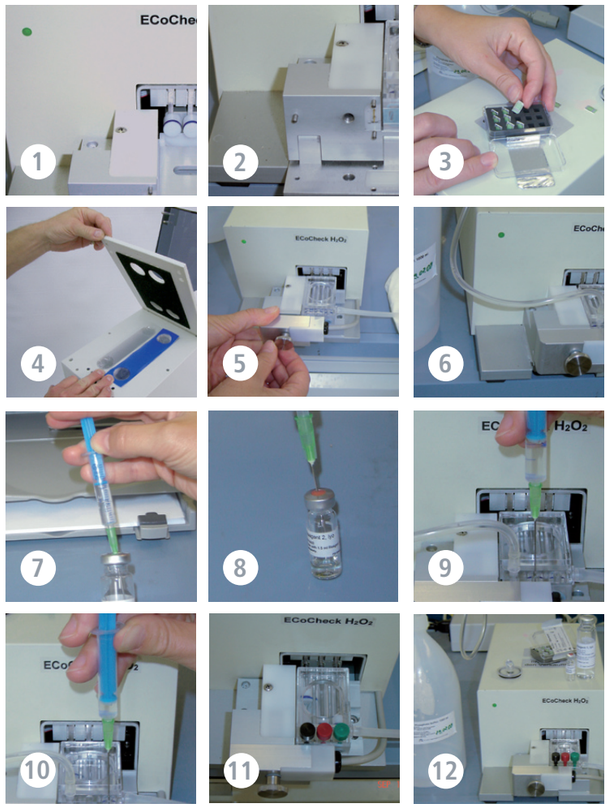
EBC-Analyzer

EBC Analyser is an innovative solution for measurements of H_2O_2 and L-lactate in exhaled breath condensate immediately after collection. The principle of the measurement is a highly specific reaction of the analyse substance with oxidase followed by amperometric detection.

The detection of these biochemical markers has become easier compared to chemiluminescence or fluorescence spectroscopy, because of:

- small amount of needed EBC volume (min. 300 ml),
- high sensitivity of the measurements:
  for H_2O_2 in linear range from 30 up to 3000 nmol/l and
  for Lactate in linear range from 5 up to 150 mmol/l,
- short measuring time (result within 5 min in H_2O_2 case),
- no calibration required (in H2O2 case),
- offline input of ventilation data,
- automatic recalculation of results according to collecting time and total exhaled volume.

The ECoCheck device gives opportunity to simultaneous measurements in EBC of pH and the temperature as well. The measurements are performed with an IsFet pH sensor (pH range from 0 to 14, temperature range from 0 up to 70°C).



EBC collection methode with the EBC Collector F

The EBC Collector F allows the non-invasive collection of non-gaseous contents in exhaled breath air. This includes metabolic products from cells in the airways as well as those from other organs, reaching the lung over the blood streams. Also, all the exhaled substances, which entered the body through the lungs, the alimentary canal or over the skin. The physicochemical features of exhaled substances use different ways into exhalation: as a volatile compounds, steam or aerosol. Therefore, the EBC analysis addresses important research needs by allowing non-invasive assessment of biochemical and inflammatory biomarkers in the airway. Measuring the biomarkers in the breath air is a very attractive approach to monitoring the short-term effect of interventions (i.e. medications) as well as the chronic diseases (i.e. asthma and COPD inflammation). The compounds which the most often identified in EBC are: hydrogen peroxide, isoprostanes, leukotrienes, nitrogen oxides, peptides and various ions. Additionally, the change of the pH level of the breath air is a assumed as a marker of the asthma and COPD.
For collection, these sensitive processes strongly rely on breathing pattern, depth and frequency of breathing. Additionally, for the standardisation of measurements, the time of sampling, exhaled volume and amount of condensate should be monitored during each collection as well. Relating measured substances in exhaled volume and/or collection time allows better intra-individual comparisons. The EBC collection has to characterise a way of sampling of the breath air which can be repeated frequently within only short breaks and with good reproducibility in EBC volume as well as in concentration for tested markers.
These requirements fulfil the EBC-Collector, which has a built-in a spirometer to record breathing volumes and time for standardization. It also controls the splitting of exhalation in up to four fractions. Control of the amylase activity and the viscosity - used to validate the method - show that no contamination of the sample by the saliva is observed.
The measurements can be done with every patient or test person which is capable of spontaneous respiration. Only a constant rest respiration will be required with a duration of 5 to 15 minutes according to sample volume needed. Because of the short time and effortlessly to control the course of the measurements, this method can also be used in the routine analyses and in screening tests where the measurements should be repeatable as much as possible. No change due to the sampling analysis has been observed in the sample compared to the sampling of sputum. Immediate analysis of the collected condensate regarding the measurement of hydrogen peroxide (H2O2), L-lactate and pH may be done immediately after collection for example with the EBC Analyser (ECoCheck) system.

Clinical tests proved that the concentration of the marker H_2O_2 is 2-3 times higher in the central respiratory tract than from the alveolaren periphery.

Procedure of fractionated EBC collection

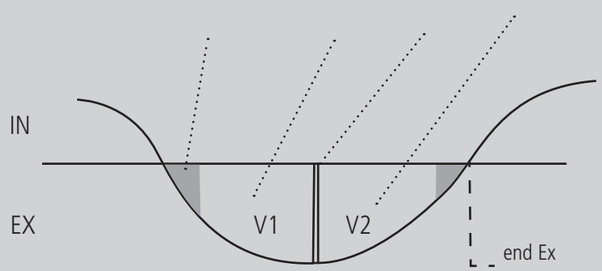
The spirometer controlled collection of EBC can be defined by the following parameters in the setting:
Vges = Total volume of the whole collection of exhalations,
SampleVol per exhalation = Setting for the acustic signal to control patients breathing,
VV1 for wasting dead space and sampleVol1 = SV1,
VV2 for wasting a defined volume, if more peripheral breathing gas is targeted in sample volume2 = SV2.

The diagrams demonstrate the two modes:

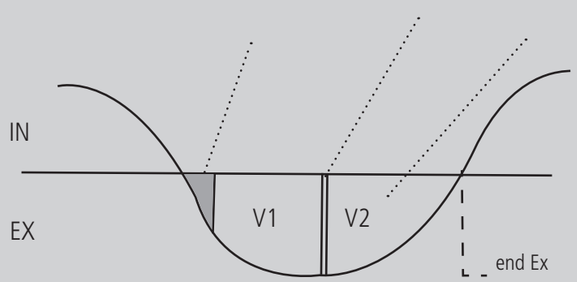
Example1 – Accurate sample volume
The collection happens exactly according SV1+SV2, the rest volume until end exspiration is wasted.
The total volume Vges is exactly the addition of (SV1 + SV2) times exhalation numbers.
SampleVol per exhalation SollV has to be higher than the sum of SV1+SV2.

Example2 – Sample volume until end exspiration
The collection is the accumulated out of SV1+ SV2 until end exspiration.
SV2 has to be higher than SollV.
That means that the sample volume2 is dependent from the differences of the patient exhalation volume and
contains the breathing gas until the end of exspiration.
The total volume Vges is different from the calculated SV1+SV2 times exhalation numbers.

Example1 – Accurate sample volume
Vges: 100L; SollV: 1100mL; VV1: 100mL; SV1: 500 mL; VV2: 0 mL; SV2: 500 mL



Example2 – Sample volume until end exspiration
Vges: 100L; SollV: 1000mL; VV1: 100mL; SV1: 500 mL; VV2: 0 mL; SV2: 1500 mL



Recommended publications of EBC collection and analysis:

Variability of exhaled breath condensate leukotriene B4 and 8-isoprostane in COPD patients
Int J Chron Obstruct Pulmon Dis., Volume 2, 2007, Pages 71-6
Z.L. Borrill, R.C. Starkey, S.D. Singh

Gas chromatography/mass spectrometry analysis of exhaled leukotrienes in asthmatic patients
Thorax, Volume 59(6), 2004, Pages 465-70.
P. Cáp, J. Chládek, F. Pehal, M. Mal_, V. Petr_, P.J. Barnes, P. Montuschi

Influence of condensing equipment and temperature on exhaled breath condensate pH, total protein and leukotriene concentrations (!)
Respiratory Medicine, Volume 102, Issue 5, 2008, Pages 720-725
K. Czebe, I. Barta, B. Antus, M. Valyon, I. Horváth, T. Kullmann

Quantitative Assessment and Repeatability of Chlorine in Exhaled Breath Condensate (!)
Respiration, Volume 72, No. 5, 2005 , Pages 529-536
A. Davidsson, K. Naidu Sjöswärd, L. Lundman, B. Schmekel

Factors influencing breath condensate volume
Pneumologie, Volume 55, 2001, Pages 414-419
C. Gessner, H. Kuhn, H. J. Seyfarth, H. Pankau, J. Winkler, J. Schauer, H. Wirtz

Exhaled breath condensate: An evolving tool for noninvasive evaluation of lung disease
Journal of Allergy and Clinical Immunology, Volume 110, Issue 1, 2002, Pages 28-34 John Hunt

Comparison of Biomarkers in Exhaled Breath Condensate and Bronchoalveolar Lavage
American Journal of Respiratory and Critical Care Medicine, Volume 175, 2007, Pages 222-227
A. S. Jackson, A. Sandrini, Ch. Campbell, S. Chow, P. S. Thomas, D. H. Yates

Effects of breathing pattern and inspired air conditions on breath condensate volume, pH, nitrite, and protein concentrations
Thorax, Volume 59, 2004, Pages 694-698
J. B. McCafferty, T. A. Bradshaw, S. Tate, A. P. Greening, J. A. Innes

Differences in exhaled breath condensate pH measurements between samples obtained with two commercial devices (!)
Respiratory Medicine, Volume 101, Issue 8, 2007, Pages 1715-1720
L. Prieto, A. Ferrer, J. Palop, J. Domenech, R. Llusar, R. Rojas

Method optimization and validation for the simultaneous determination of arachidonic acid metabolites in exhaled breath condensate by liquid chromatography-electrospray ionization tandem mass spectrometry
J Occup Med Toxicol. , Volume 17, 2006, Pages 1-5
L. M. Gonzalez-Reche, A. K. Musiol, A. Müller-Lux, T. Kraus, T. Göen

Biomarker reproducibility in exhaled breath condensate collected with different condensers
Eur Respir J, Volume 31, 2008, Pages 934-942
P. P. Rosias, C. M. Robroeks, A. Kester, G. J. den Hartog, W. K. Wodzig, G. T. Rijkers, L. J. Zimmermann, C. P. van Schayck, Q. Jöbsis, E. Dompeling

Breath condenser coatings affect measurement of biomarkers in exhaled breath condensate
Eur Respir J, Volume 28, 2006, Pages 1036–1041
P.P. Rosias, C.M. Robroeks, H.J. Niemarkt, A.D. Kester, J.H. Vernooy, J. Suykerbuyk, J. Teunissen, J. Heynens, H.J. Hendriks,Q. Jöbsis and E. Dompeling

Multiplex analysis of cytokines in exhaled breath condensate
Cytometry A., Volume 69(3), 2006, Pages169-72.
U. Sack, R. Scheibe, M. Wötzel, S. Hammerschmidt, H. Kuhn, F. Emmrich, G. Hoheisel, H. Wirtz, C. Gessner

Comparison of two methods for exhaled breath condensate collection (!)
Allergy, Volume 61, Issue 8, 2006, Page 1016-1018
O. U. Soyer ,E. A. Dizdar, O. Keskin, C. Lill, O. Kalayci

Validation of a new method to measure hydrogen peroxide in exhaled breath condensate
Respiratory Medicine, Volume 99, Issue 9, 2005, Pages 1132-1137
W. B. Gerritsen, P. Zanen, A. A. Bauwens, J. M. van den Bosch, F. J. Haas

Evaluation of H2O2 and pH in exhaled breath condensate samples: methodical and physiological aspects
Biomarkers, Volume 13(3), 2008, Pages 319-41
H. Knobloch, G. Becher, M. Decker , P. Reinhold

Exhaled breath condensate in patients with asthma: implications for application in clinical practice
Clinical & Experimental Allergy, Volume 38 Issue 4, 2008, Pages 557-565
K. Kostikas A. Koutsokera S. Papiris K. I. Gourgoulianis S. Loukides

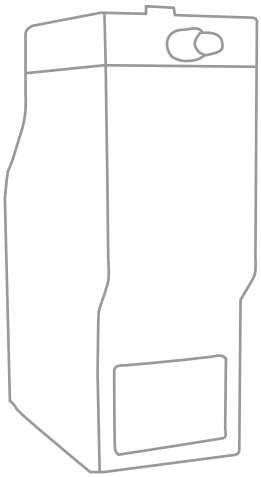
H_2O_2

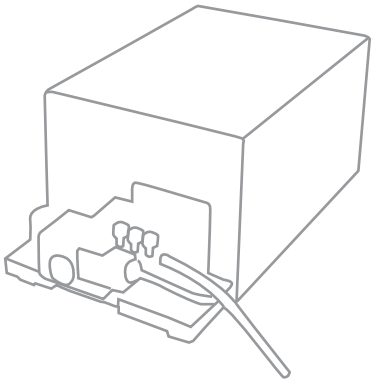
Markers of inflammation and oxidative stress in exacerbated chronic obstructive pulmonary disease patients
Respiratory Medicine, Volume 99, Issue 1, January 2005, Pages 84-90
W. B. M. Gerritsen, J. Asin, P. Zanen, J. M. M. van den Bosch, F. J. L. M. Haas

Exhaled breath condensate: methodological recommendations and unresolved questions
Eur Respir J, Volume 26, 2005, Pages 523–548
I. Horvath, J. Hunt, P. J. Barnes

Exhaled Markers of Pulmonary Disease
Am J Respir Crit Care Med, Volume 163, 2001, Pages 1693–1722
S. A. Kharitonov and P. J. Barnes

Collection of exhaled breath condensate and analysis of hydrogen peroxide as a potential marker of lower airway inflammation in cats
The Veterinary Journal, Volume 169, Issue 3, 2005, Pages 385-396
N. Kirschvink, D. Marlin, F. Delvaux, J. Leemans, C. Clercx, A. Sparkes, P. Gustin





EBC-Collector

ECoScreen 2

Technical Data

Size (H x W x D):	50 x 18.5 x 37 cm
Weight:	approx. 17 kg
Voltage:	220-230 V (115V on request), 50-60 Hz
Power consumption:	150 VA

Ambient specifications

Temperature range:	5-30°C/ 41- 86 °F
-EBC-collection with 2 fractions and exclusion	
-Flow measurement with Venturi principle	
-Flow range:	up to 10 L/s
-Accuracy:	± 5 %
-Temperature control:	± 1 °C

Spare parts
-collection bags one way
-Valve unit
-calibration pump
-below valve
-other please ask

Option
file transfer via USB connection

EBC-Analyzer

ECoCheck

Technical Data

Size:	15,5 x 12,5 x 30 cm
Weight:	3.0 kg
Voltage:	220-230 V (115V on request), 50-60 Hz
Power consumption:	50 VA

Ambient specifications

Temperature range:	5-30°C/ 41- 86 °F
-Storage of H2O2 Sensors:	2 - 8 °C
of Lactat Sensors:	-10 to –25°C
-Storage of Calibration-Kit:	2-8 °C
-Sensitivity:	30 – 3.000 nmol/L
Accuracy:	± 5 %

Spare parts
- H2O2 biosensors
- Lactate biosensors
- pH-probe
- buffer kits,
- Calibration kits

FILT

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