Excellence in Pharmaceutical TOC Water Testing and Vaccine Quality Control

multi N/C pharma Series

analytikjena

An Endress+Hauser Company

multi N/C pharma Series

The multi N/C pharma series offers tailored solutions for TOC cleaning validation, extractables testing from packaging materials, ultrapure water control and total protein analysis in pharmaceutical aqueous solutions.

Enhanced software features ensure full data integrity and 21 CFR part 11 compliance. A complete service package including system qualification and software validation provides you with maximum comfort in operating your analyzer.

Your benefits:

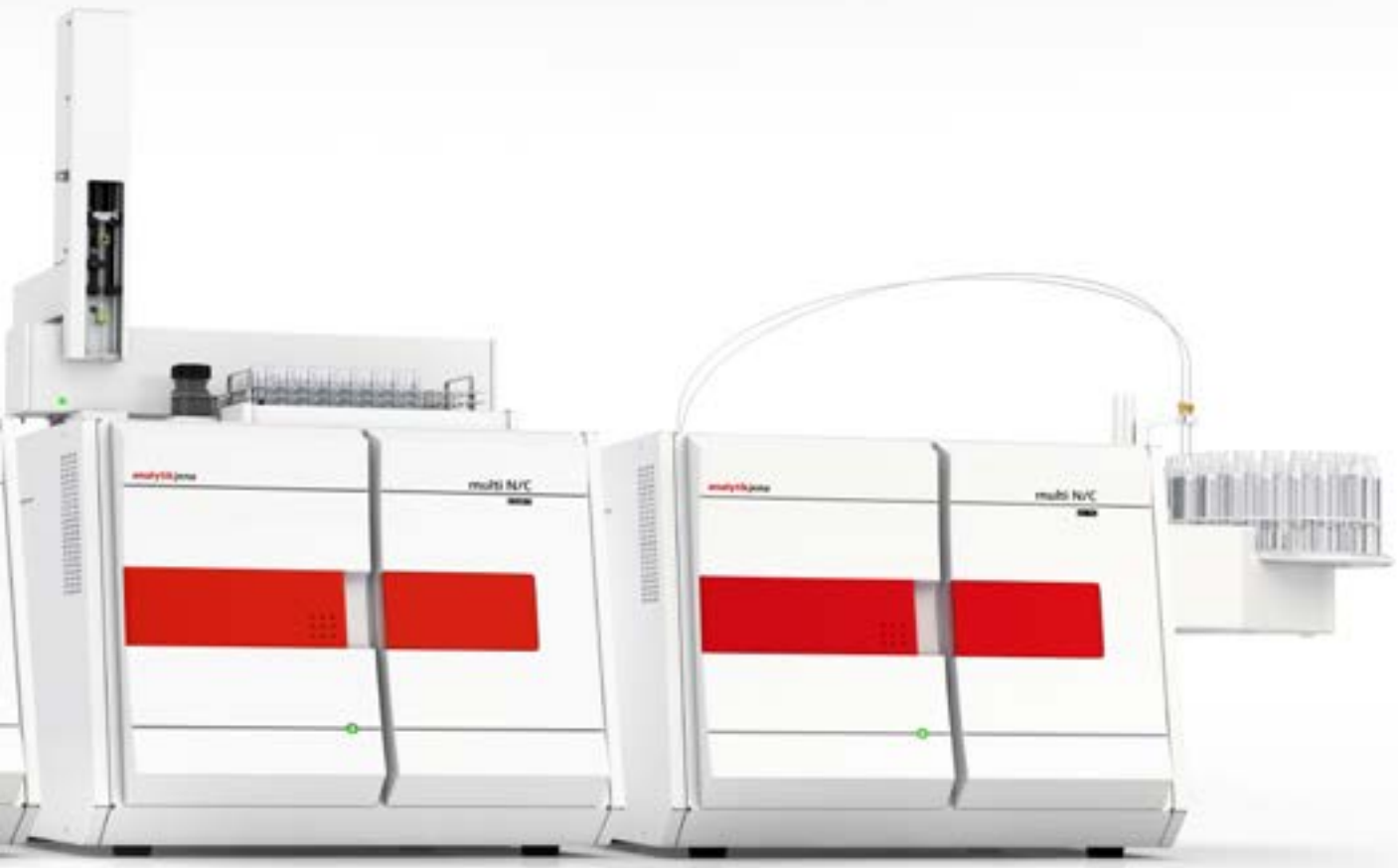
- Compliance with international pharmacopoeia methods guaranteed
- Exceptional reliable long-term and cost-effective operation
- High sensitivity
- Individual systems tailored to your needs

multi N/C series – Features

- **Focus Radiation NDIR Detector**
  Highest radiation density for highest sensitivity and precision
- **VITA Flow Management System**
  Continues to work where classical TOC analyzers reach their limits
- **Easy Cal**
  Calibration has never been so easy
- **High-power, long-life UV reactor**
  Convincing performance in wet chemical oxidation

multi N/C pharma Series

Excellence in pharmaceutical TOC water testing and vaccine quality control



multi N/C pharma UV
Highly sensitive TOC ultra-trace analysis using wet chemical UV digestion

multi N/C pharma HT
Sensitive TOC ultra-trace and TN analysis using catalytic high-temperature combustion

multi N/C 3100 pharma
High-throughput TOC trace and TN analysis in a wide concentration range using catalytic high-temperature combustion

multi N/C 2100S pharma
Wide range total protein analysis via catalytic high-temperature combustion and CLD detection

multi N/C pharma – A Perfect Match for your Application

Tailored solutions for pharmaceutical industries

TOC ultrapure water testing according to USP <643>

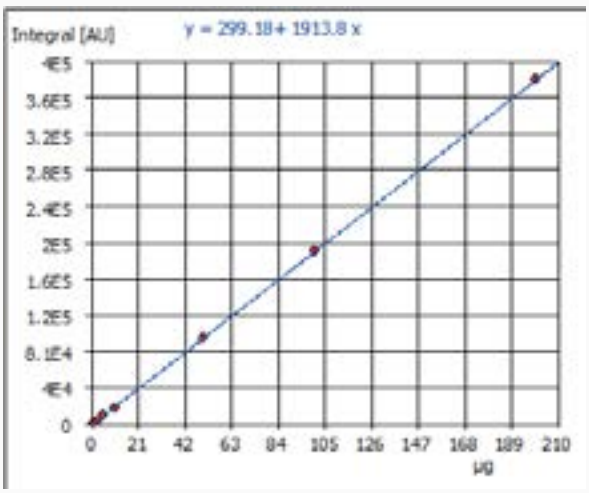
The TOC parameter is used for quality control in ultrapure water analyses, in particular for the analysis of water for injection (WFI) and purified water. USP <643> represents the general monograph for TOC testing in pharmaceutical applications and provides guidance on how to qualify the analytical technique for use as well as guidance on how to interpret instrument results for use as a limit test, e.g., the 500 ppb limit for bulk water like WFI or the 8 ppm limit for sterile water. The analysis can be performed using high-temperature combustion or wet-chemical/UV oxidation. Generally the UV digestion method provides the better sensitivity in the trace range and reduced cost of ownership, whereas the high temperature combustion method provides also access to the total nitrogen parameter besides TOC.

TOC cleaning validation

The TOC analysis plays a major part in in cleaning validation since it provides a non-substance specific method, which allows for the measurement and quantitative determination of total organic residues of active ingredients (API), additives, break-down products and detergents in the trace range. Therefore, it is used as a worst-case screening parameter for cleaning validation testing of production equipment according to the established TOC monographs, e.g. USP <643>, Ph.Eur. 2.2.44 or JP 17, section 2.59. The instruments of the multi N/C series allow for a TOC cleaning validation analysis in the post-final rinse as well as swab test after elution or via direct high-temperature combustion. The particular advantage of aqueous rinse samples or swab eluates is that ultrapure water testing and cleaning validation of samples can be processed in a single TOC device using the same measuring method. In addition, the high-temperature combustion devices allow simultaneous total nitrogen (TN) cleaning validation when coupled with a chemiluminescence detector for NO detection.

TOC testing for extractables from plastic packaging materials according to USP <661.1> and <661.2>

The characterization of the materials for pharmaceutical packaging systems is important to further improving the product safety of pharmaceuticals. TOC testing of water-based extracts is the preferred method for detecting organic leachables and is specified in the USP chapter <661>, addressing "Materials of Construction" USP <661.1> and "Plastic Packaging Systems for Pharmaceutical Use" USP <661.2>. For the analysis, purified water extractions from polymer packaging materials have to be tested for TOC according to USP <643>.



With their high oxidation power and advanced detection, the instruments of the multi N/C pharma series exceed the required specifications of the USP <661.1> and <661.2>:

- Linear dynamic range of 0.1–20 mg/L (required 0.2–20 mg/L)
- Detection limit <0.005 mg/L (USP max. 0.05 mg/L)

Total protein analysis in vaccines via total nitrogen measurement according to USP <1057>, Method 7.2

The assay determination of protein is immanent for intermediate and finished products in pharmaceutical vaccine production. The determination is used to control the level of antigens by quantifying attenuated or devitalized viruses or bacteria via total protein contents. In allergenic vaccine production it is even possible to use one and the same total nitrogen test method (TN) for testing of raw materials such pollen lyophilisates as well as very different dosage forms of drug product like injectables for desensibilization, prick test solutions or subligual applications. The application range of this TN method in the biopharmaceutical industry is as well very broad.

Since total protein and TN correlate via well-established conversion factors, the method of catalytic high-temperature combustion with subsequent chemiluminescence (CLD) detection of the NO molecules is one of the methods described for in total protein assay in pharmacopoeia. It offers several advantages over other methods:

- Fast and accurate results thanks to a high degree of sensitivity and selectivity
- No carry over risk thanks to direct and septum-free sample injection via microliter syringe
- Broad linear working range from 0 up to 200 µg/mL TN
- High degree of automation with up to 112 HPLC vials per sequence
- Reduced sample consumption requiring volumes of less than 2 mL for multiple injection

The Perfect Solution for Your Requirements

No matter what your requirements and preferences are, the multi N/C pharma series provides a suitable device for all TOC/TN applications in the pharmaceutical industry.

multi N/C pharma UV

The highly sensitive analyzer for uncompromised TOC determination in the ultra-trace range using wet chemical UV digestion:

- TOC determination in direct NPOC mode with no blank interferences for the highest sensitivity
- Injection volume up to 20.0 mL
- TOC detection <1 ppm requiring no oxidation reagent
- Low operating costs – no catalyst or combustion tube, no expensive reagent cardridges, no frequent UV-lamp exchange (3-year warranty)
- Extension of working range up to 10,000 ppm using oxidation reagent that can easily be prepared by the user

Fields of application

- Ideal for WFI and purified water applications
- Ideal for TOC cleaning validation for last rinse samples and swab extracts
- Ideal for testing organic leachables from plastic packaging materials

multi N/C pharma HT

The flexible and sensitive instrument for TOC ultra-trace analysis with the best reproducibility using catalytic high-temperature combustion, including a TN option:

- TOC determination in direct NPOC mode for highest degree of accuracy in the ultra-trace range
- Injection volume up to 3.0 mL
- High-temperature combustion up to 950 °C
- Upgrade available for direct swab combustion for TOC cleaning validation
- Optional TN cleaning validation

Fields of application

- Ideally suited for analyzing WFI and purified water
- TOC/TN cleaning validation of last rinse samples, as well as swab extracts
- TOC cleaning validation via direct swab combustion for water-insoluble or hardly soluble contaminants

multi N/C pharma UV

multi N/C pharma HT

multi N/C 3100 pharma

The high-throughput TOC analyzer for pharmaceutical applications requiring a broad concentration range using catalytic high-temperature combustion, including a TN option:

- TOC determination in direct NPOC mode for high accuracy in the ultra-trace range
- Injection volume up to 1.0 mL
- Covering a TOC concentration range of 0–30,000 ppm
- High sample throughput with parallel purging and analyzing
- Highdegree of automation with automatic sample acidification and an effective reverse rinse function that prevents sample carry over in case of changing concentrations

Fields of application

- Ideal for TOC cleaning validation for last rinse samples and swab extracts
- Ideally suited for testing for organic leachables from plastic packaging materials
- Suited for analyzing WFI and purified water
- Optional TN cleaning validation

multi N/C 3100 pharma

multi N/C 2100S pharma

The dedicated total protein analyzer for aqueous pharmaceutical samples using high-temperature combustion in combination with septum-free direct injection via microliter syringe:

- Minimum sample consumption with a typical injection volume of 50–200 µL (max. 1.8 mL) that saves costs for expensive products e.g. in vaccine quality control
- Broad working range of 0–200 ppm TN
- High degree of automation for large sample sequences (up to 112 sampling positions for HPLC vials)
- Unattended 24/7 operation thanks to Self Check System
- No sample carry over due to direct injection principle via microliter syringe and effective rinse regime

Fields of application

- Ideal for total protein analysis in vaccine or biopharmaceutical production to monitor antigen levels
- Ideal for TN cleaning validation

multi N/C 2100S pharma - the total protein analyzer

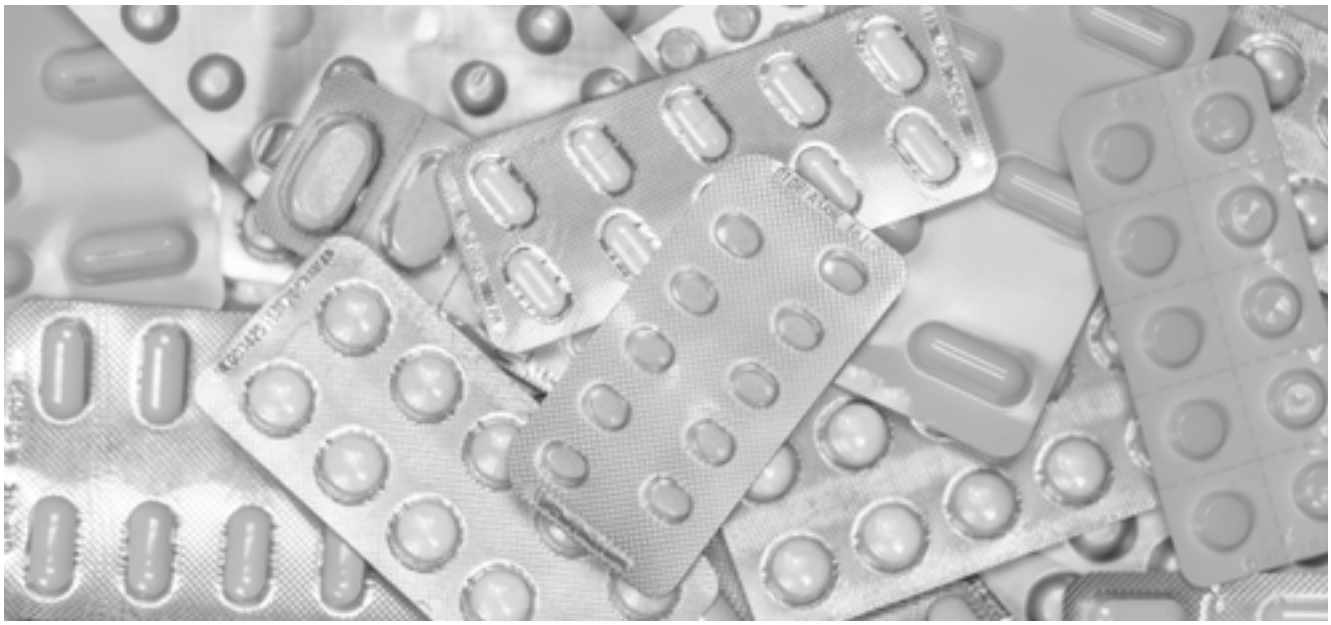
Data Integrity and Reliable System Operation

Enhanced software features ensure full data integrity and 21 CFR part 11 compliance. A complete service package offers you maximum convenience for operating your analyzer.

Compliance with pharmacopoeia

The multiWin software fully complies with the requirements of FDA 21 CFR part 11 and EudraLex Vol. 4 Annex 11. The user management of the software offers different user levels and a personalized service and administrator logon so that users can be given different access rights. Individual passwords of adjustable complexity and expiration times guarantee that no unauthorized person has access to the system. All important events, such as logon/logoff, measurements, calibrations, electronic signatures as well as the messages generated by the Self Check System (SCS), are recorded in the audit trail.
All relevant information is protected. For example the method and the calibration which have been used to generate the respective measurement results have both to be checked and authorized via electronic signatures and cannot be changed afterwards.

Individual electronic signatures are implemented in the multiWin software according to 21 CFR part 11 requirements for signing methods, calibration reports and analysis reports of measurement data produced in a three-stage process: created, examined and authorized. This process establishes the principle of dual control.
The multiWin software allows for LIMS import and export of data, as well as an idividually customized manual or automatic PDF or CSV data export.



System suitability test

The system suitability test (SST), which is mandatory as per pharmacopoeia regulations (e.g. USP <643>, EP 2.2.44 or JP 17, section 2.59), is an integrated function of the multiWin pharma software. Sucrose, p-benzoquinone and the water used to prepare these check solutions are measured by simply selecting the SST function, which is integrated directly in the user interface. The respective SST result report is generated instantly. It offers relevant information like the SST quotient and individual measurement results of the test solutions. SST tests are also logged in the audit trail.

The Self Check System (SCS) provides valuable services at a pharmaceutical lab

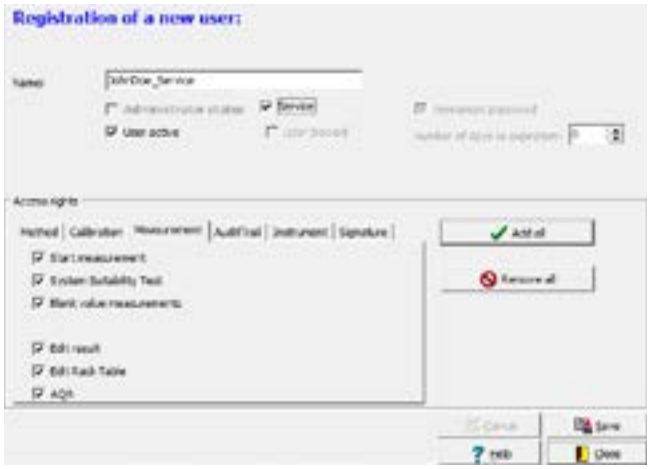
As an intelligent combination of hardware components and software functions, the SCS automatically ensures the smooth operation of the entire analytical system. Important parameters, such as gas flows, temperatures, pressures, system tightness, detector status, baseline stability, etc. are constantly checked and any deviations are recorded in the audit trail.

DQ, IQ, OQ, PQ and software validation – a reliable package!

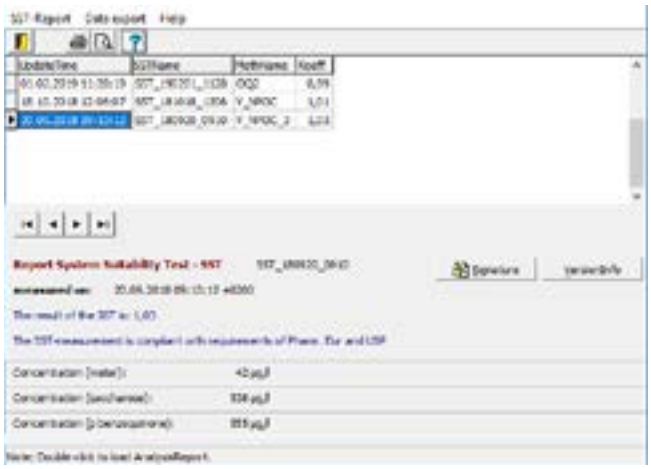
Analytik Jena provides assistance in design qualification, optimized and detailed installation qualification and operational qualification protocols are used for initial qualification or re-qualification after servicing or maintenance. Guidelines for performance qualifications are offered as well as software validation services according our customized protocols.

Comprehensive Service – IQ, OQ, software validation and more

Analytik Jena offers various services including maintenance, software updates and validation as well as system calibration from a single source.



multiWin user management permits granting of individual access rights, e.g., a personalized service logon



Structured presentation of the measurement results in the SST report

Highest Precision Meets Outstanding Stability and Robustness

High accuracy in the TOC trace range

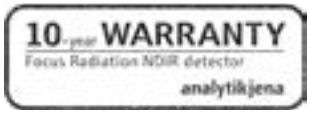
Advanced detector technology – Focus Radiation NDIR Detector

A combination of high-quality optics and the latest detector technology provide a detection system of unchallenged performance. High-energy IR radiation is focused on the micro detector by means of integrated optics. The obtained radiation density exceeds conventional detectors and guarantees higher sensitivity and precision over a measuring range from 0 to 30,000 mg/L TOC without sample dilution.

Since the detector uses corrosion-free materials and an electronically pulsed radiation source instead of classic, mechanically moving components, the detector is extremely stable, even when working with aggressive samples.

Focus Radiation NDIR Detector – Your benefits

- High measurement sensitivity and precision
- Large range of detection: undiluted measurements from 0–30,000 mg/L TOC
- 10-year long-term warranty*



Efficient gas management – VITA Flow Management System

The VITA Flow Management System continues to work where conventional TOC analyzers reach their limits. It allows for the quick injection of large sample volumes in high-temperature TOC devices and to obtain flow-independent measurement curves. This significantly improves both the precision of measurement results and sensitivity in the trace range.
VITA also guarantees highest operating safety and reliable analysis results via continuous internal tests in combination with the Self Check System (SCS), such as the automatic leak check.

VITA Flow Management System – Your benefits

- Quick injection of large sample volumes: Increase of sensitivity
- Compensation of carrier gas fluctuations for maximum precision
- Permanent leak test
- Enables the use of Easy Cal and thus minimum calibration effort with maximum long-term stability

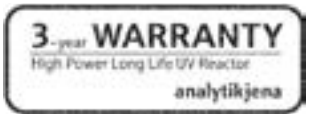
Calibration made easy – Easy Cal

Calibrations with VITA can be carried out based on a single standard using different injection volumes. The obtained calibration curves are independend of flow. The calibration remains stable! This technique is ideally suited for calibration in the trace range.

Reliable sample digestion using durable technology

Both digestion techniques used in the multi N/C pharma series provide efficient digestion of the samples.
The proven TOC furnace technology of the high-temperature combustion devices allows for the complete oxidation of the most stable organic compounds and makes simultaneous TN determination.
The high-power, long-life UV reactor of the multi N/C pharma UV uses the radiation of two wavelengths, 254 nm and 185 nm, which are particularly rich in energy, for UV-supported wet chemical digestion. This allows for fast and complete oxidation of the most stable organic compounds.

For both techniques, we offer a long-term warranty that guarantees stable performance and reliable analyses for many years.



* according to our warranty conditions: www.analytik-jena.com

multi N/C pharma Series – Specifications and Recommended Fields of Application

multi N/C pharma series	multi N/C pharma UV	multi N/C pharma HT	multi N/C 3100 pharma	multi N/C 2100S pharma
				
Sample digestion principle	UV/Persulfate	HTC	HTC	HTC
Injection principle	flow injection	flow injection	flow injection	direct injection
Measuring range [mg/l] TC/TOC/NPOC/TIC	0–10,000	0–30,000	0–30,000	-
Measuring range TN [mg/l] (CLD)	-	0–200	0–200	0–200
Highest injection volume [µL]	20,000 µL	3000 µL	1000 µL	500 µL
Best precision in the TOC trace range	x	x	(x)[1]	-
Highest automation comfort for NPOC (automatic acidification)	x	-	x	-
Extra rinse function (best carry over prevention)	x	-	x	x
Self Check System / VITA / Easy Cal	x	x	x	x
Best suited for following application				
WFI, purified water	x	x	(x)[1]	-
Extractables (TOC) from packaging materials (USP 661)	x	x	x	-
TOC cleaning validation (last rinse / swab extracts)	x	x	x	-
TOC cleaning val. (direct swab combustion)	-	x	-	-
TN cleaning validation	-	x	x	x
Total nitrogen in vaccines / aqueous protein solutions	-	-	-	x

1) Suited for side application

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Subjects to changes in design and scope of delivery as well as further technical development!

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