



CLL Pharmaceuticals Analysis Update (Bulletin #11102003_01)

Saturday, October 11, 2003

Dear Quality Assurance Manager,

Choksi Laboratories Limited has just completed a successful installation of TOC - VCSH analyzer (Shimadzu, Japan) at its Vapi Laboratory. This is the first installation in a contract laboratory in India.

With this new addition, CLL is adding a new dimension to its process validation solutions to pharmaceutical manufacturers. It also helps the pharmaceutical manufacturers in meeting stringent regulatory compliance for water quality monitoring.

Regulatory Requirements for TOC:

(a) USP, EP, and JP - TOC testing methods

The organic impurities measuring method employed by United States Pharmacopoeia (USP) and European Pharmacopoeia (EP) has changed from the potassium permanganate consumption testing method to the TOC testing method, and WFI (water for injections) and PW (purified water) can only have up to TOC 0.5mg/L.

The JP explanation document states that the use of a TOC analyzer that can measure water sources (tap water, river water, ground water, etc.) is desirable in certain situations for the monitoring of the manufacturing process for WFI.

(b) GMP water quality monitoring

Water quality monitoring is required for water validation in GMP manufacturing. If TOC is used for this application, organic impurities can be quickly and easily monitored with high sensitivity and superb accuracy.

As the implementation deadline of Schedule M in pharmaceutical units, draws to a close, manufacturers will need to comply with stringent requirements for GMP and its inherent requirement for Water Quality Monitoring.

Technology

CLL's TOC analyzer uses catalytically aided combustion oxidation / non-dispersive infrared detection (NDIR) to measure TOC as per USP, EP, JP or GMP regulations.

The instrument can provide data on all analytes such as TC, IC, TOC, and NPOC, with a sensitivity of upto 4 ppb, much lower than compliance levels of 500ppb.

Equipped with auto-injector and auto sample preparation system, all tasks such as dilutions, acidification, sparging are carried out automatically by the instrument, with a digital readout of the results.

CLL can now provide completely automated, high sensitivity TOC analysis in 3 minutes.

TOC Applications – Pharmaceuticals

Validation of manufacturing water

- Monitoring of water manufacturing systems (validation)
- Monitoring of organic impurities in manufactured pure water
- Monitoring of deterioration in functional materials (ion exchange resin, activated carbon, etc.)
- Monitoring of degeneration and pinholes in ultra filtering modules (enables timely module replacement and equipment maintenance)
- Water source monitoring: Avoidance measures can be taken when there are abnormalities
- Water quality evaluation when restarting a line after a long layoff.

Cleaning validation

- In the case of pharmaceutical manufacturing equipment, this provides scientific validation that residue of previously manufactured products or cleaning agent and externally mixed in matter is at the tolerated limit or below.
- Rinse water sampling
- Final rinse water is taken as a sample and TOC measured
- Swab sampling (Swab: A specific area of the equipment surface is swabbed with swab material. Recommended by the Ministry of Health and Welfare, Japan and FDA.)
- Organic residual matter extracted using water after swab, and TOC treasured.



Choksi Laboratories Limited

Sampling Procedure for TOC Analysis

Sample Quantity: 200 ml.
Sample Container: Amber coloured glass bottle with glass stopper, washed with concentrated HCl or HNO₃ and oven dried.

- (1) Rinse the container 2 -3 times with sample.
- (2) Fill the container upto the brim, leaving no air bubbles or headspace.
- (3) Add 2 – 4 ml (a drop) of 1 Normal HCl in 200 ml sample and store below 4 Deg C till analysis is carried out.
- (4) For transit to lab:
 - (a) Chill sample to 2 – 4 Deg C, cover with gel / ice packs and immediately courier across in a thermally insulated box to laboratory.
 - (b) For sampling and collection facility, contact CLL Lab Managers at any of the following addresses:

Choksi Laboratories Limited

Lab Manager - Vapi
101/8 Gokul Complex
2nd Floor, Behind GIDC Office
GIDC Char Rasta, Vapi – 396 195
Tel: (0260) – 2433488, 2434061, 2432715
Fax: (0260) – 2432728

Lab manager - Baroda
829 GIDC Makarpura
Vadodara – 390 010
Tel: (0265) – 2655 955, 2657 955, 2652 955
Fax: (0265) - 2631714

Lab Manager - Indore (Corporate Headquarters)
6/3 Manoramaganj
Indore – 452001 (MP)
Tel: (0731) 2493 592 /3, 5070019, 2490 592
Fax: (0731) 2490 593

Additional Applications of TOC

TOC, as Humic Acid in Influent and Treated Municipal Water
TOC in Ethanolamine
TOC in Hydrogen Peroxide
TOC in Sludge
TOC in Landfill Leachate

TOC in SeaWater
TOC in Electroplating
TOC in Pharmaceutical Water Quality Monitoring
TOC in Pharmaceuticals - Water for Injections, and Purified Water.

Cut along this line and fax it across to (+91) 260 - 2432728 or email at info@choksilab.com

Name:		Title:	Mr. / Ms. / Dr. / Mrs.
Designation:		Department:	
Organization:			
Address:		City/State/Country:	
		Pincode:	
Telephone (Extn.):		Mobile:	
Fax:		Email:	

Yes, I am interested in TOC analysis (Tick all applicable):

- Please quote for
 - a. One time analysis charges for TOC in Water
 - b. Sampling Charges
 - c. Container Charges
- I am interested in Cleaning Validation project. Please have a CLL representative call / fax / email me.
- I am interested in Annual Contract. Please have a CLL representative call / fax / email me.