General System Description:

The **DTS 800** Dissolution Test System is designed for the fully automated determination of dissolution rate of active materials in tablets and other solid dosage forms in one compact, totally integrated design. The system contains a dissolution tester, which is in compliance to the monographs of the USP <711/724> and EP <2.9.3/4> and a PDA spectrophotometer as well as a pump and integrated 8 way, flow through, sample cell changer. The system control functions are provided by the fully 21 CFR part 11 compliant WinDiss32 Dissolution software package suitable for closed and open system operation.
As all components in the standard version are integrated in the same housing, sample transfer tubing is kept to a minimum and is designed for easy replacement. All connections are “lockable” Luer types for easy and secure connections. The system conforms to the current Pharmacopoeia requirements (USP / EP / JP) for such a test system.

The Dissolution Bath:

The instrument has 6 sample and two auxiliary 1 litre stirred USP vessels, which are maintained at the correct working temperature by a thermostatically controlled water bath. The sample vessels are also numbered and coded. The vessels are self centring in the water bath cover which also supports a motorised synchronous tablet drop magazine for all 8 vessel positions to allow the simultaneous dosing of test tablets into the

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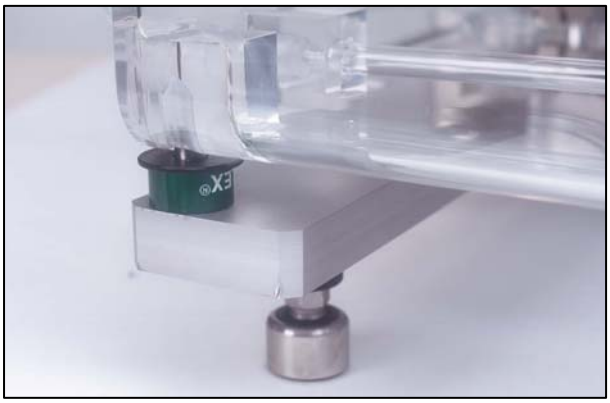
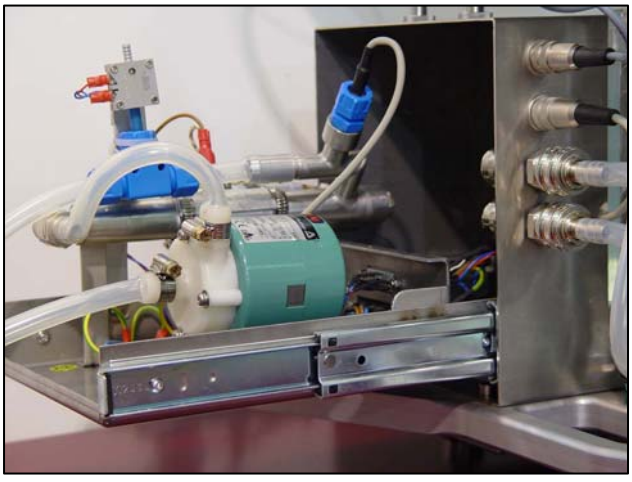
test medium prior to start up of the dissolution tools and the test itself. The 8 tool mono-shafts are made of 316 stainless steel, are coded for positional integrity. Also included are 8 threaded, exchangeable, Apparatus 2 paddle tools made of electro-polished 316 stainless steel. Other stirring tools are available and thanks to the built in pre-calibrated head height adjustment, the user has only to calibrate the first position using the supplied depth gauges, and the other tool positions are automatically available by selecting the appropriate tool number on the menu screen. The tool options are described below.



Additional features….

Specifications for dissolution baths may well be changing in the future, and as you would expect, Pharma Test has introduced some innovations to allow our users to be prepared for these future requirements.

Vibration is a problem, especially in a busy lab environment where mechanical isolation from other pieces of equipment is not always possible. Vibration transmission through the water bath supports and even from water heater / circulating systems does provide a significant contribution to the failure of standard USP Prednisone tests for example. Pharma Test have introduced two features which will greatly reduce the vibration transmission to the dissolution vessel. In the first instance, the pump for the water circulator / heater is mounted on a shock proof, suspended platform which virtually eliminates vibration from this sector. Additionally, the water bath itself is mounted on **vibration absorbing** feet which will remove vibration from sources outside of the instrument housing. This, in effect, isolates the water bath and hence the vessels to a point where vibration plays a minor role.



Servicing and routine maintenance was never this easy….

Regular maintenance and service also plays and important role in providing a trouble-free operational life. Pump tubing may need to be changed or the heater element accessed for routine checks. These two elements have been successfully combined to be accessed through a “Drawer” system located at the rear left side of the instrument. Undo two bolts and the whole assembly may be disconnected (with snap fit connectors) and rolled out for inspection or maintenance. Similarly, the “power” electronic control components are located in a similar position on the right hand side of the instrument for easy access.

Security for your heating system….

The security system built in to all Pharma Test heater / circulation systems has been transplanted into the DTS 800 too. This means that you have three security systems to back up the control thermostat which controls the heater and hence the water bath temperature.

The first is the security sensor which is in-line with the water flow after the heater element. Any temperature above 45°C automatically turns off the heater. Then there is the over temperature sensor on the heater support bracket which turns off the whole heater system should the support plate get too hot. Then there are a series of thermal fuses which will back up the over temperature sensor. If this was not enough we have the additional security of a flow detector for the pump such that if no flow is detected over a period of 5 seconds (forgot to prime the system for example?), then the pump and heater are closed down until the error is confirmed on the front panel, the system checked and the flow restarted. Your security is our priority.

IQ, OQ requirements and instrument log….

All IQ and OQ paperwork for the Dissolution Bath and onboard UV/VIS Diode Array Spectrophotometer is included in the normal scope of delivery. The general requirements for OQ tests are as for other Pharma Test equipment and instrument calibration sets with certified media are available. All IQ and OQ paperwork is FDA compliant. All subsequent OQ's performed after installation may be recorded along with training records in the instrument log book which is also provided as part of the standard paperwork.
Additionally, the instrument can print out a short OQ as well as the instrument log and settings on the built in printer located at the top right hand side of the instrument. This is a useful way to print and store hard copy run time logs of dissolution runs in compliance with current GMP practise.

Dissolution Tester Technical Details….

Rotational Speed Range:	20 - 250 RPM
Accuracy:	± 2%
Stirrer System Security:	Encapsulated tool in bearing minimizes tool vibration
Stirrer Positions:	4 + 4 (all positions numbered)
Remote Control:	Via RS 232C interface
Heater Operational range:	30° - 45°C
Heater Control:	± 0,2°C
Sample introduction:	Automated Tablet Magazine incorporates evaporation proof vessel covers
Sample transfer pump:	Built in 8 channel peristaltic pump, RS-232 controlled
Sample transfer:	System uses EPE-C sampling manifold for all 8 vessels
Sampling positions:	Sampling tubes are either in the vessel full time or lowered in and withdrawn as required
Sample filtering:	Samples filtered on-line to 5 or 10 .
Vessel temperatures:	ITM (Individual Temperature Measurement) module in EPE
Parallel Port:	Use to connect a parallel port printer
Voltage requirements:	230V 50/60Hz - 115V 50/60Hz
System tools:	USP Apparatus 1, 2, 5 (3 variants), cream cell, trans-dermal patch tools Mono-shaft design, exchangeable stirring inserts

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Tool height qualification:	Qualify 1 position (paddle) and all other stirring tool positions are instantly qualified due to Mono-shaft Stirrer Design
Water bath:	U-shaped Plexiglas bath including a polypropylene cover
Pump system:	Pump system located in easy access “drawer” slot
Heater system:	750W heater with thermal protection in easy access “drawer” slot
Thermal protection:	1 in-line security sensor, 1 over-temperature cut out, 1 thermal fuses
Power electronics:	All power electronic control boards in easy access “drawer” slot
Water circulation:	Water circulated through special diffusion system
Circulation Security:	Water flow detector shuts off heater and pump if no flow detected
Test Vessels:	1 litre USP Borosilicate glass vessels supplied with individual number coding
Certification:	All components certified to USP / EP requirements
CE / EMC Certification:	All CE / EMC Certification provided
IQ / OQ :	All paperwork for system qualification provided with instrument
OQ:	Short OQ available as instrument printout, additional to OQ supplied
OQ warning:	OQ warning on screen when OQ is due
Instrument Log:	Log is printable on built in printer
Vibration:	Bath and pump system on vibration-free mounts.
Measurable vibration:	Less than 0.25 µm displacement
Cleaning Assistant:	Plexiglas plate holding 8 cleaning beakers to be used to flush all tubing and cells when test is finished

The Measurement and Media Transportation System….

Included in the instrument housing is a state-of-the-art UV/VIS Spectrophotometer incorporating a SA500 Diode Array Detector. The detector has a single fibre guide which is connected to the sample cell changer located on the left hand side of the instrument. The cell changer operates in a conventional manner, but radiation is transmitted and data collected via fibre optics rather than by traditional parallel or focused light beam sender and receiver.

The media transportation is provided by an Ismatec IPC peristaltic pump with 8 individually adjustable channels. The built-in pump is controlled via its interface to ensure full system control throughout the entire testing time.

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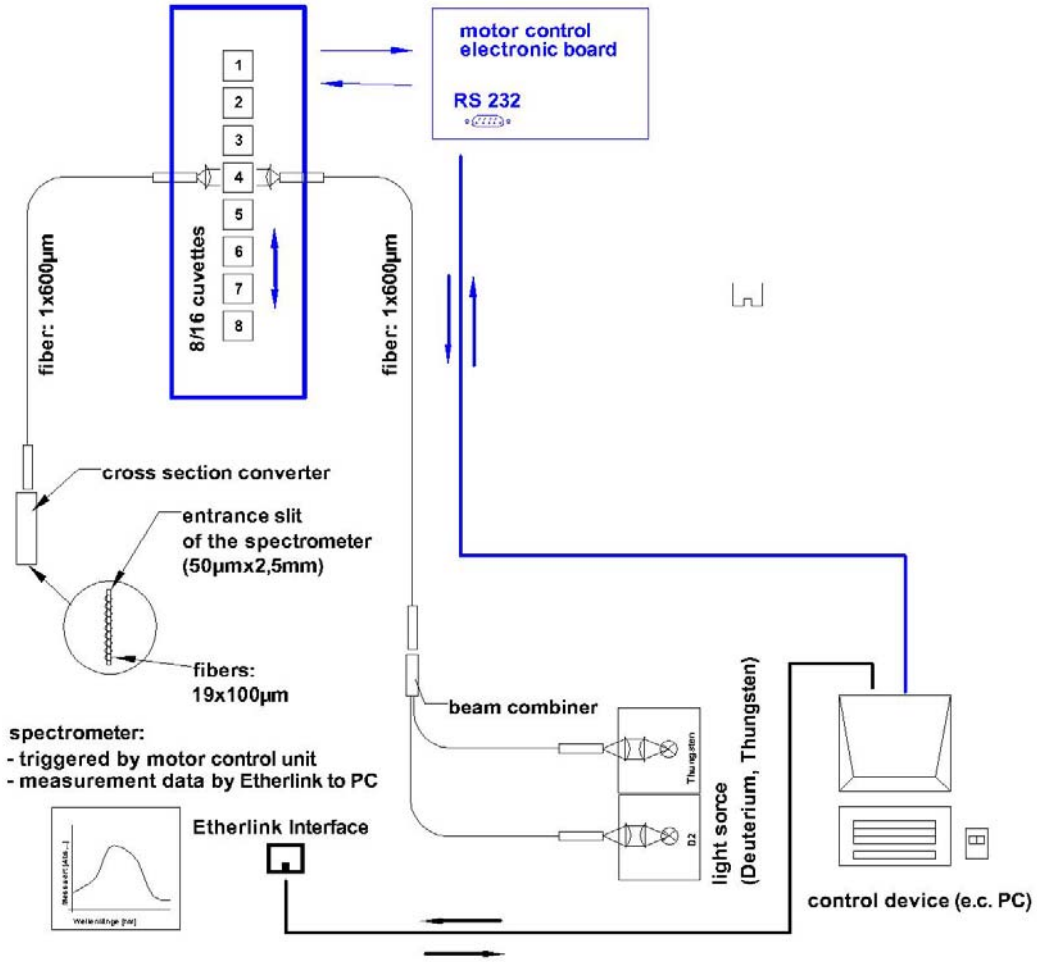
The SA 500 DAD Spectrophotometer Instrument….

A complete new design of detector and optics is implemented inside the DTS 800. The result is a spectrophotometer which is optimized for the use of fibre technology offering state of the art performance.

Combined with 8-place cuvette changer it is possible to acquire data from 8 vessels. The reference measurement for each measurement cycle is done through one cuvette which is defined as reference place. Then the instrument performance is equal to a real double beam spectrophotometer. The cell changer can take flow-cells from 0.1 mm to 20.0 mm pathlength.

With respect to maintenance and service all components are easily accessible. It guarantees highest demands on robustness and reliability. The inbuilt solution inside the DTS 800 reduces footprint and offers highest comfort for complete system validation.

System Setup SA 500 DAD detector



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What are the key Spectrometer USP's?

Complete unit SA 500

- SST, System Suitability Test prior to the start of an analytical sequence.
- Easy access to lamp and power supply - without having to physically move the bath or the housing of the complete test equipment.
- Supports service and maintenance in an efficient way.
- Fast acquisition of 8 cuvettes in less than 100 milliseconds
- Real sequential dual beam operation with reference and intensity compensation
- Significant higher response time, up to 10 times faster compared to existing cell changer systems
- A special highlight is the possibility of high speed kinetic measurements at a free chose able cuvette with up to 50 spectra per second.
- No mechanical moving parts inside the active optical path, the cuvettes in the cell changer are the only moved components in the optical path.
- Up to 10 times better drift and noise behaviour compared to competitive systems
- Short distance between vessels, pumps and the cell changer reduce error and impurity impacts. Faster cycle times are a big advantage!
- No additional space for photometer is required, the footprint of DTS 800 includes all spectrophotometric components and the cell changer
- Cell Changer can handle up to 20 mm Path length Flow-Cells

Spectrophotometer unit:

- Fitted optical construction, calculated not "tried out", providing maximum light gain and thus outstanding signal to noise ratio and drift stability
- UV-resistant aperture adjuster and optimised light fibres, a nearly unlimited possibility to use various types of measuring cells or arrangements
- Multi-layer light filter to suppress second order effects
- High process stability due to ceramic housing with no moving parts for best thermal and mechanical stability, a guarantee for accurate and correct results
- Wavelength stability and reproducibility allows to measure absorbance values also at the slope of the signal. There is no necessity to measure always in the peak maximum.
- Easy handling, maintenance and service, no complicated and time-consuming calibrations necessary for simple validation
- Modern data processing allows unmatchable measurement speed, easy setting of analysis parameters, saving time and money
- High acquisition speed offers fast channel multiplexing or high speed kinetic measurements
- Various interfaces like Ethernet, RS 232, ISA, PCI or PCMCIA available, providing maximum flexibility and future connectivity
- More than 16 year experience in the field of diode array detection in combination with fibre optics (in the spectral range of UV, VIS, NIR)

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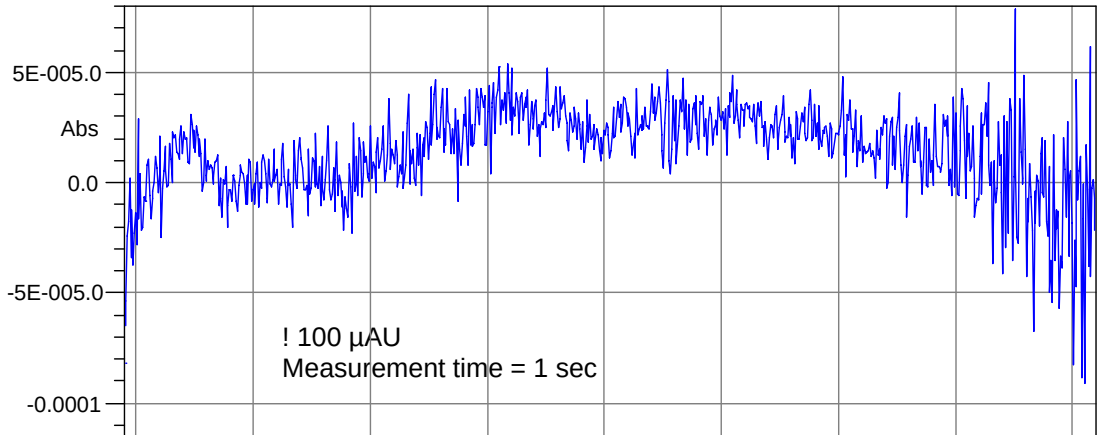
Cell changer unit

- State of the art design and functionality. Produces no additional noise or drift!
- 8 Cell Holder also able to handle flow cells with a path length up to 20 mm!
- The cuvette changer and the shutter are the only moving parts in the system
- The cell changer can switch in less than 100 ms between each cuvette and can address all cuvettes in less than 10 seconds.
- Simple interface via RS 232 and full control by spectrophotometer
- Easy access for service by exchangeable components

Spectral drift and Noise through one cuvette place



Technical Data for the Measurement Instrument….

Diode Array Detector:	TIDAS Detector element with 1024 diodes
Spectral range:	187nm – 1010nm
Spectral resolution:	0.8nm per pixel
Optical grating:	248 L/mm
Baseline noise specification:	Extremely low at < 50 AU peak to peak without smoothing
Wavelength accuracy:	Long term stability < 0.1nm
	Repetitive Accuracy is < 0.1nm
Temperature Drift:	< 0.005nm / °C
Scattered light:	< 0.1% @ 340nm (D2 lamp)
Light sources:	Integrated D2 and Tungsten Lamps
Light source:	Built in light source with light transfer using fibre guides
Lifetime:	D2 lamp has a life of approx. 1500 hours
Data Integration:	Data integration time approximately 100ms per channel
Flow cell compensation:	Work with either absolute or baseline corrected absorption data

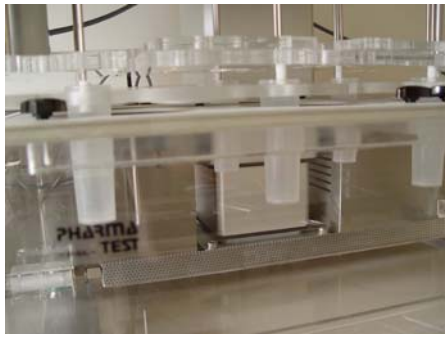
Additional requirements….

As with any system there are some additional requirements which are necessary for system functionality. The two main issues are cell dimensions and control software. All applications are different and so to some extent the measurement capacity of the detection system is dependent on factors such as the flow cell dimensions. The system accepts standard flow

cells which are available from the Pharma Test program. All of the cells are made of quartz glass, have a 15mm centre axis and have a 4mm (wide) window. The connection system is via an M6 threaded screw connector with PTFE tubing to connect to the send and return lines

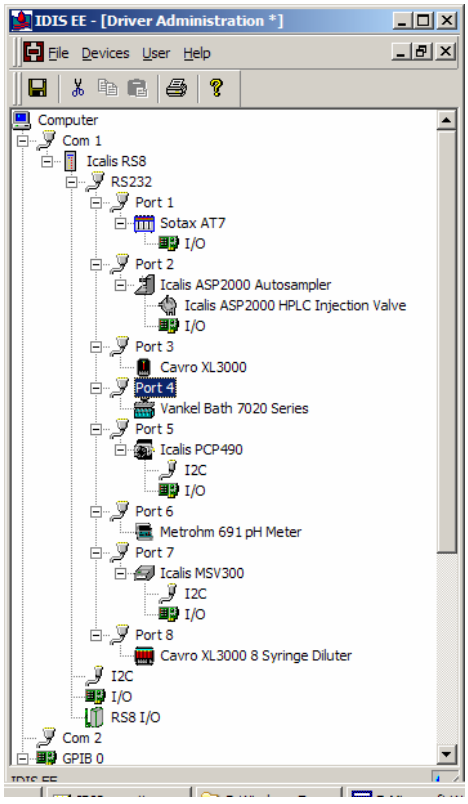
The other principal requirement is that of software and a suitable PC. The WinDiss32 Dissolution Software is supplied by Pharma Test and is able to control all the mechanical functions of the dissolution tester as well as the scanning spectrophotometer and the cell changer.

Tablet Drop Magazine and EPE Auto Sampling System



Tube Cleaning System

The WinDiss32 Software….



The DTS800 System is controlled and integrated into WinDiss32 Dissolution Data management software which is used by the worlds largest Pharmaceutical companies.

Driver Linkage with Unique Solution Path Technology

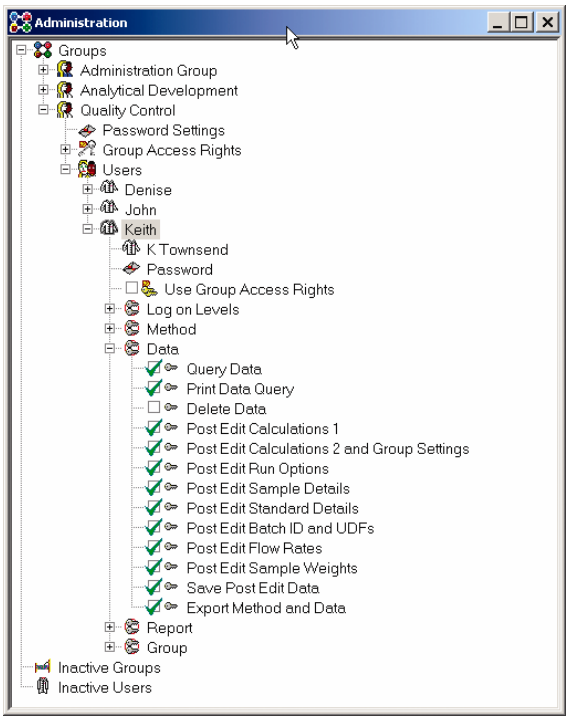
WinDiss32 Supports a wide range of Baths, Autosampler and other UV/VIS Detectors. It uses a Unique Solution Path Technology. Configuration for different analysis requires no additional reprogramming. Support for Closed and Open Loop for UV and HPLC systems. WinDiss32 can operate with USP I, II, III and IV methods.

FDA 21 CFR part 11 Compliance

The WinDiss32 Administration allows the system administrator to enter details of users to access the system. The user Logon name, full name and password are configured for each user with Group or individual access rights.

Individual access to the system is by a unique user name and password and the users full name is displayed whenever the user logs on successfully.

Configurable Centralised Security



The Global Settings allow the administrator to set limits to prevent unauthorised access to the data station, Password expiry, Log Off Times etc for each access level.

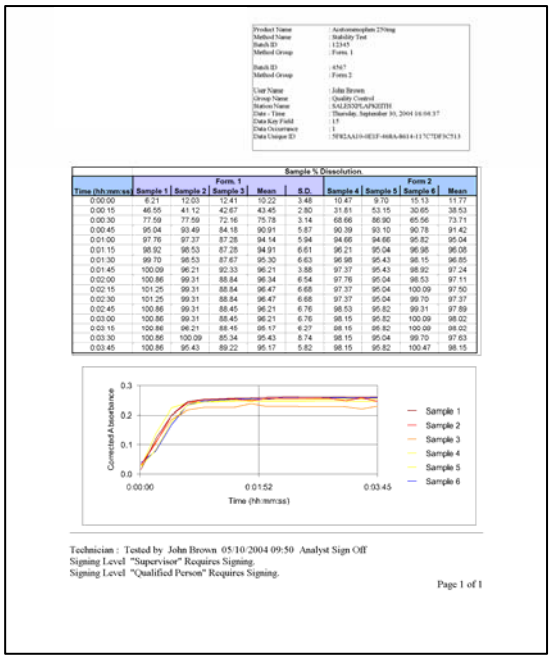
These activities can be performed remotely from any WinDiss32 networked workstation.

WinDiss32 provides the user with total management of the signing process, from start to finish. This includes configuring the number of signing levels, the Users for each level, Signer Activity and Meaning.

Signing and Reporting Signed Records

Once data is acquired in a Group with signing rights, any report generated will show the signing status for all pages of the record shown on the report.

Dynamic Report Editor



The WinDiss32 report organiser allows users to produce customised reports with the right information by selecting from a combination of objects such as Method Header, Data tables, Method parameters, Graphs and the company logo.

These details may include any parameter measured during the test such as bath Temperature, Paddle speed, Time Intervals as well as Absorbance, Concentration and % Dissolved. Any number of pages can be selected with automatic page numbering.

Standard Report Format Graphics Printer

WinDiss32 is supplied with a Graphics Printer that provides compliance with 21 CFR Part 11 requirements for “human readable form”. These reports can be circulated, emailed etc., in the safe knowledge that they are non-editable. This Graphics Printer can capture any report into TIF, BMP or JPG (JPEG) and save them as electronic files. The TIF format can save a multiple page report and the Image Viewer supplied automatically displays the printed file image for verification.

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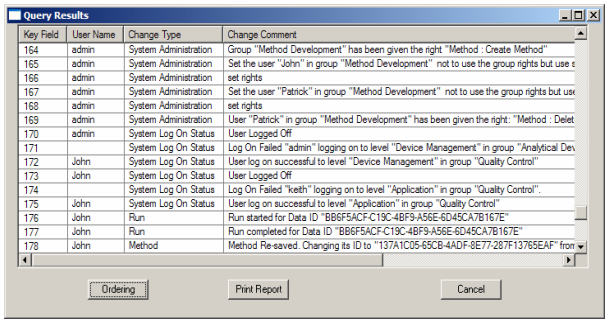
User Queryable Audit Trail

WinDiss32 Audit Trail lists all user activity that creates, deletes or modifies; i.e., from logging on and off to editing of method and data records.

This Audit Trail can be queried to limit the volume of information from a search and the results from any search can be printed.

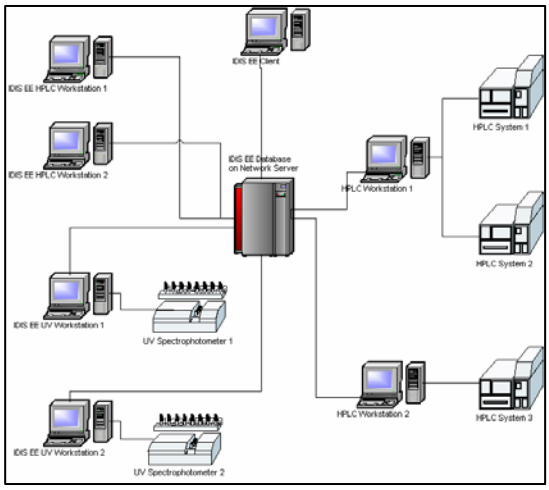


Networking

Our networked system provides a central relational database that contains all data (methods and data records) from all WinDiss32 workstations. Details are accessible from any station linked to the networked database.

Each system runs from a workstation PC, as each hardware configuration can be unique.

This configuration allows Data records to be signed remotely by users from clients. For example, it is now possible for analysts and supervisors or managers to view, sign, print etc away from the laboratory area.



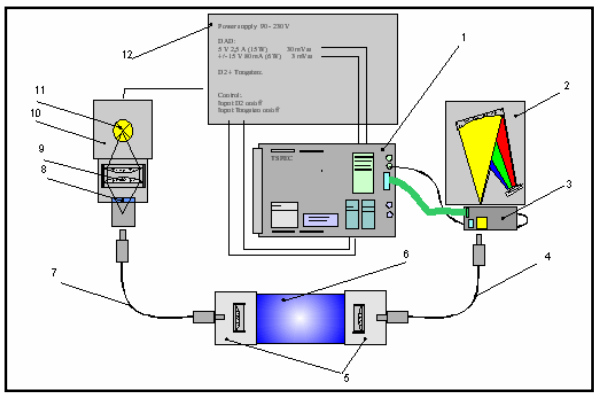
Included Bath Driver: DTS 800

Included Photometer Driver: SA 500 PDA Diode Array Photometer incl. 8-cell changer

Included Pump Driver: Ismatec IPC 8

SA 500 Diode Array Spectrophotometer

The built-in SA 500 uses a very fast RISC Processor and processes the raw spectral data within the unit. All data storage and post processing is then via an external PC.



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Available System Options

- UV light protected vessels
- stainless steel basket inserts to be screwed into the mono-stirrer shafts
- Transdermal testing cylinders and Paddle over Disk assemblies
- flow-through cells 0.1, 0.5, 1,2,5 up to 20 mm path length - micro cells upon request

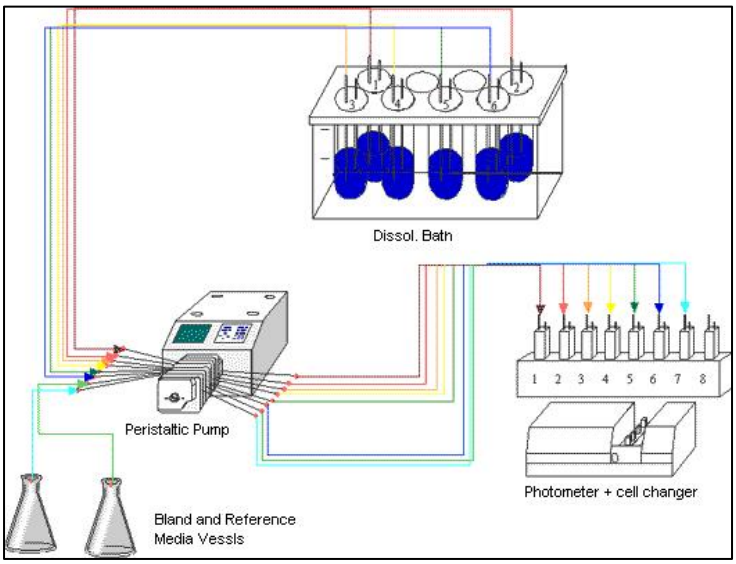
System validation can be done using the USP calibrator tablets and standards. Supply scope includes full IQ/OQ documentation for the Dissolution Bath, Peristaltic Pump and Diode Array Photometer.

Installation and Qualification

System validation can be done using the USP Reference Standard (RS) Tablets and Standards. The dissolution system installation and qualification may be performed at installation by a Pharma Test trained engineer or agent.

The WinDiss32 Software is installed under Windows NT or 2000, XP™ (GB or US Version)

Principle of Operation



The operator describes the operational procedure within the wizard driven software. Then the system will flag when the samples have to be introduced; after this point, the dissolution system works automatically. Prior to the measuring time the pump will be started and circulate the solvent through a 5 or 10 micron filter. During a measurement the pump is stopped temporarily and data is read and stored by the PC. The same is repeated for any programmed measuring cycle. As well as the measured absorbance, speed, temperature and pH-values (optional) are recorded. The selectable option to run a reference standard solvent, (which is measured in each cycle) or the entry of a theoretical maximum absorbance is available. Running a standard offers some advantages as results that may be influenced by a less than optimum light source, evaporation or temperature influences are corrected by the reference measurement. At the end of a run the operator creates his report and chooses which data that he needs to have printed. As all results remain filed within the system, a batch comparison statistical analysis can be performed at any time.

For further information about dissolution automation ask for our WinDiss32 Dissolution software flyer or for demo version.

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Other factors influencing Dissolution Rates.

Below are some interesting statistics covering various things which may influence the results of a typical dissolution test run. Some influences are quite small but others, such as degassing the dissolution medium, are quite dramatic (ask for the PT-DDS Medium Degassing and Preparation Instrument brochure):

Factors affecting the PQ results:

Type	Rating	influence degree
Temperature	not too significant	linear
Speed	**significant**	**10 - 30%**
Vibration	**significant**	**10 - 40%**
Centricity	reasonable	5 - 15%
Dissolved Gas	**significant**	**50%**
Media pH	reasonable	5 - 10%
Media Contamination	**significant**	**20 - 45%**
Sampling Position	not too significant	1 - 3%

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