



ERWEKA[®]

www.erweka.com

Dissolution Catalogue 2010²

Dissolution Testing – The Baths

The DT x 20 generation of ERWEKA Dissolution Baths reflects more than 50 years of experience in the development of high-quality Dissolution Testers. As a result this new generation of ERWEKA instruments sets the benchmark in Dissolution Testing and represents the most advanced, durable and user friendly units available on the market today. This is what we are working for.

SmoothMove® Column

DT 720/820 Dissolution Testers come with the unique SmoothMove® column, which allows for the effortless lifting and lowering of the unit's drive head.

Easy Access

In lifted position the DT 720/820 allows for max. 36 cm space between water bath cover and drive head thus offering easy access to the test-stations for loading and removing the vessels.

External Heater

To eliminate the risk of any vibration transfer, all ERWEKA baths come with a sturdy, high power external flow-through heating system (heating time of water bath: Approx. 12 min. from 20°C to 37°C).

MagniShaft®

DT 720/820 units, as standard, come with the advanced MagniShaft® system (Low-Head use only). This system allows for the assembly / disassembly of Paddles and Baskets by click-in within seconds. No height adjustment is required.

UniShaft®

The optional UniShaft® system uses one shaft for all stirring methods. The stirring heads for each method are securely screwed to the shaft. There is no height adjustment required. Online OQ for correct height adjustment is available for DT 820 units.

High-Head and Low-Head

DT 720/820 units with UniShaft® system offer the flexibility to choose between the evaporation-free Low-Head testing position and the easy to access High-Head testing position on a day-to-day basis.

Vessel Covers

DT 720/820 vessels are automatically covered when moving down the head.

Teflon Shafts and Methods

DT 720/820 Shafts, Paddles and Basket Holders are made from either Teflon or PEEK (MagniShaft®). As standard all parts are numbered.

The DT 820 with "SmoothMove®" Lifter Column, alpha-numeric keypad and 5.7" full graphic display is the ideal unit for advanced stand-alone and offline operations.

The integrated memory allows for the storage of all essential test-run parameters (including offline-system information such as sampling and replacement volumes) of max. 100 products, which later on can be recalled for testing. The product data stored can be transferred to any other DT 820 unit, using a standard USB memory stick.



The integrated OQ Menu supports the performance of a fully menu guided System Suitability Test.

All measurement results may be entered via Keypad. A documentation printout is generated when a printer is connected to the standard USB printer interface.

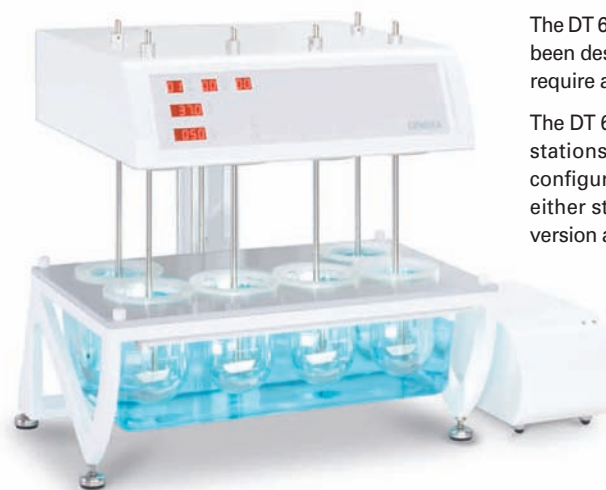
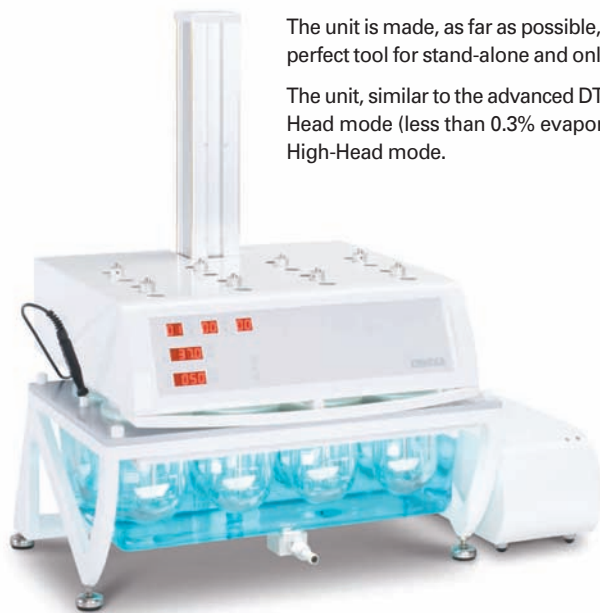
Easy and comfortable access to the test-stations due to a high-opening lifter column (distance between bath and drive-head: max. 36 cm/91 inch).



The DT 720 has been designed for those users, who want to perform dissolution tests with little preparation time rather than clicking through extensive menus.

The unit is made, as far as possible, of non-corrosive materials and represents the perfect tool for stand-alone and online operations with control via an external PC.

The unit, similar to the advanced DT 820, can be operated in low-evaporation Low-Head mode (less than 0.3% evaporation within 24 hours at 37°C) or easy-access High-Head mode.



The DT 626 with fixed drive-head has been designed for those users, who require a durable low-cost unit.

The DT 626 comes with up to 6 test-stations and 6 vessels in U-shape configuration. Stirring elements in either stainless steel or full Teflon version are available.



Membrane sealed low-evaporation vessel covers minimise the media loss for all High-Head operations.



UniShaft (screwed on for staggered test start) and MagniShaft (magnetic system for simultaneous test start) stirrer systems. Stirring elements are made of Teflon (not Teflon coated) or stainless steel.

Water Drain

ERWEKA Dissolution baths come with a water drain for emptying the water bath.

Eas-ur-Dis

You are tired of clicking through extensive menus or small touch-screen buttons while you just want to set rpm and temperature for a quick test? Here come the DT 620 and DT 720 which will fulfill your needs: Easy and understandable programming by just 8 UP/DOWN symbol keys, large and bright individual LE displays for control and START/STOP buttons. We offer minimalism for your comfort.

Sample Delivery System

DT 720/820 units come with a sample delivery system for simultaneous or staggered insertion.

Manual Sample withdrawal

The integrated sample withdrawal openings allow for the insertion of a pipette or syringe into the media through the drive head. This increases the ease of use tremendously compared to the standard operation of 2-row dissolution testers. Sampling syringes with height adjustable holders are available.

OQ Traffic Light

The DT 820 comes with an OQ Traffic Light, which shows the condition of the unit at a single glance. Intervals for System Suitability Tests and calibration e.g. with USP calibrators can be individually defined according to in-house standards.

User Access

User Access to DT 820 units is password protected (3 user levels).

Hard-Copy documentation

Documentation is supported via USB printer interface.

Product Memory

Up to 100 products with all important test-run parameters (including offline-system information) can be stored on the DT 820. The data stored can be easily transferred to any other DT 820 unit via USB memory stick.

Non-corrosive Materials

DT 620/720/820 units are, as far as possible, made of non-corrosive materials.

Dissolution Testing – The Accessories

Vessels

ERWEKA Dissolution baths can be fitted with standard 1000 ml and special 250 ml vessels, which are offered in clear glass, UV-resistant amber glass and polycarbonate. All vessels, as standard, are numbered and optionally available with an individual compliance certificate. 250 ml vessels require a conversion kit, vessels with 2000 ml and 4000 ml capacity require special bath versions.

Shafts

MagniShafts® as well as UniShafts® are made from Teflon (DT 620: stainless steel) and are numbered as standard.

Paddles (Standard/Mini)

Paddles for ERWEKA stirring shafts are generally numbered and made from PEEK. MiniPaddles for use with the 250 ml vessels are made from Teflon coated stainless steel.

Baskets

Baskets are laser-numbered and made from stainless steel or acid resistant gold-plated stainless steel. They are available in versions with 10, 20 or 40 mesh, with or without individual certificate of compliance.

Basket holders for the MagniShaft® system are made from non-corrosive Teflon; basket holders for the UniShaft® system are made from stainless steel.

Felodipine Basket

Stationary Felodipine Baskets are available for all ERWEKA Dissolution Testers.

Discs for USP method 5

125 µm discs are available in either stainless steel or gold-plated stainless steel. Other sizes are available on request.

Filters

Tip filters for automated sampling stations or manual withdrawal syringes are available in porosities of 1 µm, 4 µm, 10 µm (other porosities on request). Membrane filters for double filtration systems and the Automatic Filter Changer AFC 825 are available in porosities of 0.45 µm, 0.7µm, 1.0 µm.

Manual Sampling Tools

ERWEKA offers a wide range of tools for precise manual sample withdrawal, either with a connected syringe (height adjustable acc. to USP requirements) or in combination with an Eppendorf pipette for one-hand operation.



Vessel sizes: 250 ml, 1000 ml, 2000 ml and 4000 ml



Mini Paddle with 250 ml vessel



Vessel materials: clear glass, amber glass and polycarbonate



Glass vessel with attached stand



UniShaft® and MagniShaft® in Teflon finish; PEEK Paddle



Advanced Basket Holder for use with standard Baskets. Due to an integrated rubbering the basket holder can be used without the spring-holder.



Felodipine Basket



USP 5 disc



USP 6 Rotating Cylinder (short and long version)



Enhancer Cell: Teflon cell with adjustable volume for testing of emulsions, suspensions and ointments



Intrinsic Dissolution Kit with 10 mm² surface area. Optional 10 tons hydraulic pressure.



Filters



Manual Sampling manifold with height adjustment



Pipette



Sinkers: "Japanese" type sinkers as well as plastic made "spider" sinkers

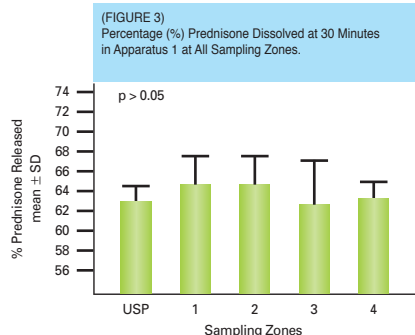
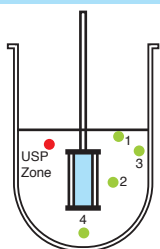


The System-Suitability-Kit, available in standard or certified version, comes with all tools required to check the mechanical parameters of the dissolution tester. Optional tools for the validation of the automated sampling station are available.



The ERWEKA QA Station is a Windows®-based System Suitability Software to which various tools for the measurement of the mechanical parameters of the unit may be attached. All measured data is automatically transferred and cannot be influenced by the user. Each tool comes with a certificate the validity of which is additionally stored in the software. Results may be printed or stored for documentation purposes. The ERWEKA QA station can be used for all kinds of dissolution baths, not only of the ERWEKA brand.

(FIGURE 1) USP Sampling Zone (Red Circle) and Four Sampling Zones (Green Circles) Evaluated in USP Apparatus 1.



Results of official USP study (2007)* about varying dissolution results depending on where the sample has been withdrawn.

The study clearly shows the existence of differences in analytical results between samples withdrawn within the USP Zone (red point) and samples withdrawn within the other (non-compliant) zones.

As a consequence the withdrawal in the correct sampling zone is essential for valid dissolution results.



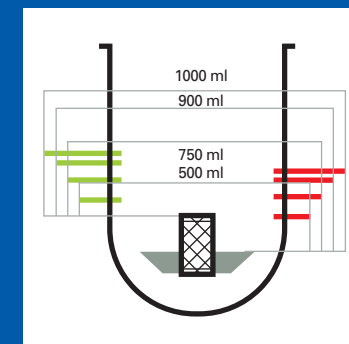
ERWEKA Sampling Station with automatic height adjustment taking into account the method applied and the media volume used.

Similar to manual sampling the tubes (stainless steel or non-corrosive Titanium) are inserted into the media only for sampling and removed afterwards. Since this system adheres to USP requirements, cross-validation is not required.

Sample withdrawal

According to the USP automated sampling systems may be used. But USP clearly specifies that as soon as the USP described parts, such as stirrers, shafts etc. have been modified, cross validation has to be performed.

Therefore ERWEKA has developed a system (patented) which simulates the 100% USP compliant manual sampling process, which in addition assures sample withdrawal at the USP specified sampling zone, midway between the surface of the media and the top of the rotating stirring element, not less than 1 cm away from the vessel wall.



Since there are four different methods (Basket, Paddle over Disc and Rotating Cylinder) as well as four different media volumes (500, 750, 900 and 1000 ml) described in USP and Pharm. Eur., 16 different sampling heights exist. Shown above: Sampling heights for Paddle (red) and basket (green).

*Kikwai-Mutua, Loice, Gang Deng, William Brown, Ronald Manning and Samir Wahab (2007): Evolution of Various Sampling Zones in the USP Apparatus 1 (Basket) and 2 (Paddle) Using USP Lot P Prednisone Tablets Reference Standard, USP Rockville, MD 20852, USA

Dissolution Testing – Media Preparation

Media Preparation

USP 27, NF 22 <711> Dissolution states:

„NOTE – Dissolved gases can cause bubbles to form, which may change the results of the test. In such cases, dissolved gases should be removed prior to testing.“

How to deaerate correctly?

A standard procedure is described in USP 27 NF 22 <711> Dissolution:

„One method of deaeration is as follows: Heat the medium, while stirring gently, to about 41°C, immediately filter under vacuum using a filter having a porosity of 0.45 µm or less, with vigorous stirring, and continue stirring under vacuum for about 5 minutes.“

Automation

Since the deaeration procedure described is quite complicated, USP 27 NF 22 <711> Dissolution also specifies: „Other validated deaeration techniques for removal of dissolved gases may be used.“

MultiPrep

MultiPrep is designed for the preparation up to 18 litres of dissolution media automatically, either from pre-mixed media or deionised water and concentrate/s (up to 6 different concentrations).

Due to its precise mixing and the documentation of the nominal/actual mixing ratio the MultiPrep is the perfect device when using ready-made dissolution media concentrates.

The dosing range (metric) reaches from 50 – 4000 ml, adjustable in 1 ml steps with an accuracy better than ± 1 ml or 1%.

MediPrep 120

MediPrep120 is a bench top degasser for the pre-heating, degassing and dosing of dissolution media. The media is dispensed by weight using a load cell. Dissolution media for 6 test stations can be prepared in less than 10 minutes from cold media storage.

Easy-to-use menus guide the user through each operation making media preparation easier and quicker than ever. Media changes are quick due to the flush routine and flow-through heater (i.e. waiting time for media tanks to heat up is avoided). For the storage of media ERWEKA offers tanks made of Polypropylene or stainless steel.



The ERWEKA MultiPrep is an advanced automated device for the preparation of dissolution media from either pre-mixed solutions or deionised water and concentrate. Recipes for up to 60 media can be stored under the media name and be recalled for preparation.

The MultiPrep offers the combination of deionised water and pre-mixed media as well as the combination of 6 different concentrates or a cleaning solution.

A circulation heater brings the media to the required temperature; deaeration is fulfilled by means of vacuum and stirring. Via a dispense nozzle the media is dosed directly into the dissolution vessels inside the Dissolution Tester. The complete operation for 8000 ml of media (mixing, heating, deaeration and dosing) takes 10 minutes max.

A special washing routine allows for the fully automated cleaning of the system between media preparations.



An integrated printer allows for the documentation of calibration as well as operations.



The ERWEKA MediPrep 120 is the basic economically priced bench-top tool for dissolution media preparation. Pre-mixed media is heated to 37°C and deaerated to less than 5.5 ppm.

Media dispensing is possible from 250 – 1000 ml in 50 ml steps with an accuracy of $\pm 1\%$.

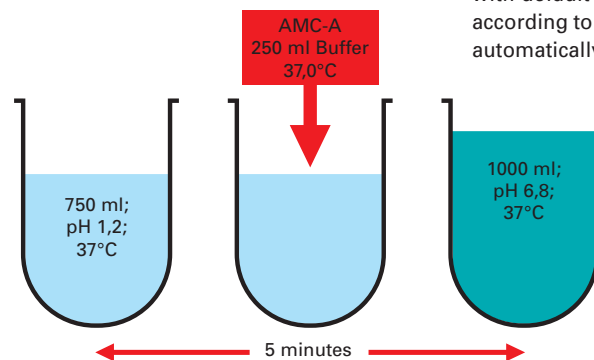


ERWEKA Automatic Media Changer for media changes according to USP method "A", type AMC-A.

The AMC-A is either operated stand-alone or controlled via the DT 820 dissolution bath, into which the time point for media change is programmed.

After a pre-set runtime the stirrers are automatically stopped and heated buffer solution is pumped from the AMC-A into the vessels of the Dissolution Tester.

Upon completion of the media change time (freely selectable with default setting at 5 minutes according to USP) the stirrers are automatically restarted.



Automatic Media Changer

ERWEKA offers a device for the automatic change of media according to USP method "A" (Half-Change for all USP stirring methods), type AMC-A. The AMC-A has 8 vessels with a maximum capacity of 250 ml buffer solution each, which are located in a thermostatically heated water bath. Eight one-channel peristaltic pumps transfer the buffer solution from the AMC-A to each vessel inside the Dissolution Tester within a time range of max. 5 minutes as described in the USP.

In combination with the DT 820 dissolution bath the media change with an AMC-A unit is fully automated: at the set time point the stirrers are stopped, the pre-dosed, heated buffer solution is added and on completion of the pre-set media change time range the stirrers are re-started.

The AMC-A can also be used with other Dissolution Testers. In this case, however, the stirring action has to be stopped / re-started on the Dissolution Tester, and the transfer of the buffer solution must be activated manually on the AMC-Unit.

Detergents Tester (Tergotometer)

The RT 700 is equipped with 7 test stations with 1000 ml or 2000 ml glass vessels and a further station into which the supply of the immersion cooler is integrated. The water bath can be heated up to 45°C or cooled down to 10°C, depending upon test requirements.

Each of the 7 test stations simulates the agitating movement of a washing machine / dishwasher with paddles. The unit can be driven with up to 300 rpm. The direction of rotation can be changed after a freely adjustable break, and thus the washing process is simulated optimally.

Thanks to its freely adjustable test parameters such as temperature, rate of motion and duration of the test, most different test standards currently used by manufacturers of cleaning agents and dishwashers are supported by the RT 700. In each test the structure of the cleaning solution, degree of water hardness, pH value, chloride etc., can be varied.



Detergent Tester RT 700 is a versatile laboratory test equipment, which simulates the washing process of washing machines and dishwashers in order to determine different quality parameters of cleaning agents (tabs).

Dissolution Testing – Offline Systems

Offline Dissolution Systems

The wide range of ERWEKA Offline Dissolution Systems reflects the varying requirements of the different users and their products as well as local specifications. Decades of experience have led to a unique variety of systems, which allows each user to make his individual choice.

All Offline Dissolution Systems are controlled by an upgraded DT 820 Dissolution Bath ("i" version) which supports the storage of the test-run parameters of up to 100 different products. This configuration does not require a PC or any software and therefore saves space, money and last but not least software validation work.

FRL 700/800 Offline Kits

Modified gas-tight glass/Teflon Hamilton® syringes offer precision dosing, elimination of absorbance and, when required, easy exchange. The syringes are offered in 10 ml version as standard or in 25 ml version for higher volume withdrawal and upgrade possibility to a UV-VIS Off-/Online system.

In contrast to other Syringe Pumps the ERWEKA SP 840-S includes sturdy mechanical 4-way valves with enlarged admission diameter and motor forced switching. Minimum sampling interval: 2 min. Cleaning of the complete system is performed automatically by the cleaning menu of the DT 820 bath.

FRL 704/804 Offline Kits

Dosing is performed by 3-way solenoid valves incorporated into the Fraction Collector. Similar to the FRL 700/800 system the FRL 704 Kit offers sampling only, while the FRL 804, additionally offers media replacement and HPLC membrane piercing. The FRL 704/804 Kit in combination with a piston pump supports the use of the Automatic Filter Changer, type AFC 825. This system allows for filtration (membrane filters) down to 0.45 µm (with Peristaltic- and Syringe Pump down to 1.0 µm) and exchange of the filters for each sampling interval (max. 25 times for each test station).

Racks

For the drawer platform of the the ERWEKA Fraction Collectors different racks are offered:

- 24 x 8; 10 ml glass tubes
- 16 x 8; 25 ml glass tubes
- 24 x 8; 1.5 ml HPLC vials
- 24 x 8; 4.0 ml HPLC vials



Up to 24 sampling intervals of 2 min. may be stored into 1.5/4.0 ml sealed/unsealed HPLC vials or 10/25 ml glass tubes using the FRL 700/800 Offline Kit.

In contrast to the basic FRL 700 Kit, which allows for sample storage only, the FRL 800 Offline Kit, in addition, offers media replacement, dilution (max. 1:10) and HPLC membrane piercing. Additionally, the FRL 800 Kit may handle the sampling operations of up to two independent dissolution baths.

ERWEKA Offline Systems are controlled by the DT 820 Dissolution Tester ("i-version"), not only to reduce cost and lab-space required but also to eliminate software validation.



The heart of this system is the 8-channel Syringe Pump with sturdy mechanic 4-way valves, which generates a dosing accuracy of typically ± 0.1 ml (10 ml syringes).



Optional high-precision, high-pressure piston pump, type PVP 820



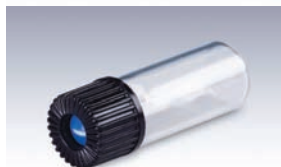
The FRL 704/804 Offline Kit comes with a Peristaltic or high precision/high-pressure Piston Pump.

Dosing with accuracy better than $\pm 5\%$ (Peristaltic Pump), respectively better than $\pm 2.5\%$ (Piston Pump) is performed by solenoid valves.

The FRL 704/804 systems offer fast sampling intervals and, in combination with the Piston Pump, the use of the Automatic Filter Changer, type AFC 825, for membrane filtration down to 0.45 µm.



The racks (various versions available) are placed on a platform with drawer mechanism. This mechanism allows for the easy loading, removal or exchange of the rack.



FRL 800/804 may store samples into sealed HPLC vials (1.5 and 4.0 ml capacity).



Heated reservoir for replacement media to connect to FRL 800 and FRL 804 Fraction Collectors.



Peristaltic Pumps for automatic refilling of the media replacement- and dilution containers inside the FRL 800/804 Fraction Collectors.

Dual Offline System

The FRL 800 Offline Kit with just one Syringe Pump can handle up to two DT 820 Dissolution Testers simultaneously (max. 12 sampling intervals each). To avoid cross-contamination between the two testers it is recommended to run both units with the same product and dissolution media. Minimum sampling interval (sampling, media replacement, system cleaning): 15 minutes.

Heated Replacement Media

In some cases, especially when low quantity of media is used or a high volume of media is withdrawn and replaced, adding unheated media can lead to a temperature drop which causes non-compliance with the regulations. To eliminate this problem ERWEKA offers a heated replacement media reservoir in combination with a special fast refill system inside the Fraction Collector.

Ultra Filtration (below 1.0 µm)

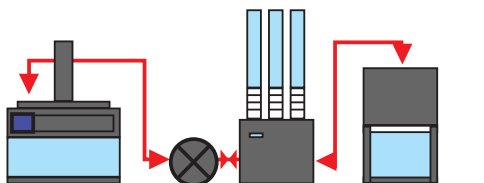
For HPLC analysis (but also to fulfil the regulations of the Japanese and Russian Pharmacopoeia) filtration below 1.0 µm has to be performed. Since filters below 1.0 µm porosity usually are blocked after use they have to be exchanged after each sampling interval.

ERWEKA has developed the AFC 825 Filter Changer, which automatically exchanges the used membrane filters (brands on request) for new ones. The AFC 825 can be used in Offline Systems (controlled via the DT 820 Dissolution Tester) as well as in UV-VIS On- and UV-VIS Off-/Online Systems (controlled via the ERWEKA Dissolution Software).

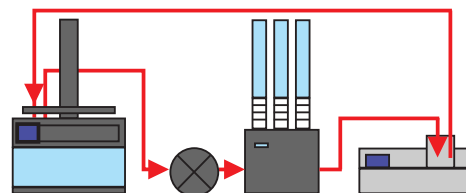
Filtration down to 0.45 µm is possible in combination with the high-pressure PVP 820 Piston Pump (1.0 µm in combination with Syringe- and Peristaltic Pumps).

Filters can be exchanged either after each test-run or after each sample withdrawal interval.

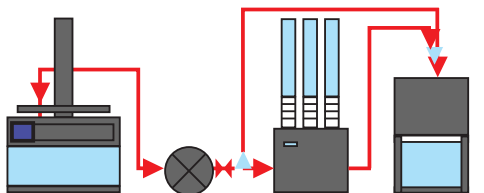
AFC 825 automatic 8-channel filter changer with max. 25 filters/channel.



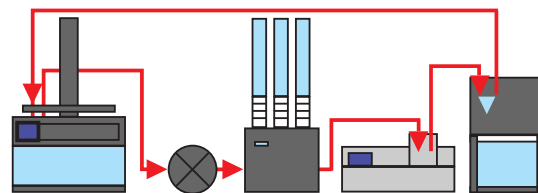
Dissolution Offline System; media replacement only when filters are exchanged.



Dissolution Online System



Dissolution Offline System; media replacement via bypass around the membrane filter.



Dissolution On-/Offline System.

Dissolution Testing – Online Systems

Dissolution Systems

Due to a unique patented sample withdrawal system (see page 05) all ERWEKA Systems fully comply with USP/Pharm.Eur./JP specifications. As a consequence no cross-validation is required.

Having the user in mind, ERWEKA offers a wide range of Dissolution Online Systems, custom-fitted to the various special requirements involved.

The ERWEKA UV-VIS Systems can be configured a) Inline, i.e. the sample after analysis is returned to the vessel not to decrease the media volume level or b) Online, i.e. the sample is rejected after analysis and the effect eliminated by calculation.

Further, a wide selection of Sample Transfer Pumps is available: a) an economic 8-channel Peristaltic Pump with absorption-free Verderprene tubing, b) a precise 8-channel Glass/Teflon Syringe Pump and c) a high-pressure 8-channel Piston Pump (required for filtration below 1.0 μm).

The ERWEKA software DSS controls UV-VIS Spectrophotometers of Analytik Jena® (Specord 205/215), Perkin Elmer® (λ 25/35) and Shimadzu® (1700/1800).

The DSS software further handles other devices implemented into the standard UV-VIS Online-/Inline System such as Automatic Media Changer, type AMC-A and Automatic Filter Changer, type AFC 825. While the AMC-A supports fully automated media pH changes according to USP method "A" (half change) without user interaction, the AFC 825 allows for the incorporation of membrane filters down to a porosity of 0.45 μm in the sample transfer line thus eliminating any particles.

The ERWEKA DSS software package supports the use of 8 temperature sensors for media temperature documentation in each individual vessel. For further details on the ERWEKA DSS software package see page 12.

Dual UV-VIS Inline System

This system not only reduces cost (compared to two standard UV-VIS Inline Systems) it also reduces the use of lab space and eliminates the validation of a second PC/software.

ERWEKA® UV-VIS Online/Inline Dissolution System



Due to a unique patented sample withdrawal system ERWEKA UV-VIS Dissolution Inline-/Online Systems fully comply with USP/Pharm.Eur./JP standards and therefore do not require any cross-validation (see page 05).

Different brands of UV-VIS Spectrophotometers are available. In addition to the standard configuration, ERWEKA Inline-/Online Systems can be fitted with the Automatic Media Changer type AMC-A (half change acc. to USP method "A", see page 07) and Automatic Filter Changer, type AFC 825 (see page 09), for membrane filtration down to 0.45 μm porosity.

ERWEKA® Dual UV-VIS Online Dissolution System



Due to two individual Sample Transfer Pumps (Peristaltic-, Syringe- or Piston Pumps) and a 16-position cell changer ERWEKA Dual UV-VIS Inline Systems support the operation of two completely independent Dissolution Baths with varying products, dissolution media and even sampling intervals without any risk of cross-contamination. Only one UV-VIS Spectrophotometer is required.



Peristaltic Pump

ERWEKA Dissolution Systems are available with Syringe-, Peristaltic- and Piston Pump for Sample Transfer.

ERWEKA® UV-VIS Off-/Online Dissolution System



The ERWEKA Off-/Online Dissolution System offers total flexibility due to a combination of a) an Offline-System, based on which samples are collected (media replacement and HPLC membrane piercing available) and later manually transferred to e.g. a HPLC unit and b) an UV-VIS Online-System, which allows for the withdrawal of samples to be directly analysed and then returned to the vessels not to lower the media volume.

ERWEKA® UV-VIS On-/Offline Dissolution System



This system allows a) to collect samples into glass tubes or sealed/unsealed HPLC vials and replace the withdrawn volume by fresh media, b) to analyse the samples in the Spectrophotometer and then to return the samples into the vessels not to lower the media volume or c) to analyse the samples in the UV-VIS Spectrophotometer first and then to store the analysed samples in the Fraction Collector and replace the withdrawn sample volume by fresh media (in case the Fraction Collector is installed after the UV-VIS Spectrophotometer).

ERWEKA offers the connection of up to two DT 720/820 Dissolution Testers with fully USP compliant automated sampling station to one HPLC System e.g. Agilent, Waters, Shimadzu, VWR-Hitachi ... For sampling the HADs uses an innovative flow-through system of sealed PEEK-vials. HADs can be used as sample collection device, HPLC Online System, Online UV-VIS system as well a combination of all. The system offers Video analysis of the dissolution process in time laps mode with overlaying real time dissolution curve to identify disturbances such as coning etc.

ERWEKA® Dissolution HPLC Online System



UV-VIS Off-/Inline System

In addition to the Dissolution Tester with automated sampling station the system comprises the 8-channel syringe pump SP 840-S/25, the Fraction Collector FRL 800 and a Perkin Elmer® UV-VIS Spectrophotometer.

Complete control, display and storage of results is offered by the ERWEKA Dissolution software DSS.

UV-VIS On-/Offline System

In case of the On-/Offline System (in contrast to the above mentioned Off-/Online System) Sample Transfer Pump (Peristaltic or Precision highpressure Piston Pump), Fraction Collector FRL 804 and Perkin Elmer® UV-VIS Spectrophotometer are installed in-line.

The On-/Offline System, in combination with Piston Sample Transfer Pump, type PVP 820, further allows to include the Automatic Filter Changer, type AFC 825, for filtration down to 0.45 µm into the sampling line.

Complete control, display and storage of results are offered by the ERWEKA Dissolution software DSS.

HPLC Online System

In combination with an HPLC system it is recommended to use the double filtration system with membrane filters (filtration down to 0.45 µm, depending on the pressure created by the Waters® pump).

Control of the HPLC system and Sample Withdrawal Pump are performed by the Waters® Alliance software package while the Dissolution Tester is handled by its own keypad and display simultaneously.

„HADS

The highest degree of automation and flexibility is offered by the new Half-Automated-Dissolution System.

It is prepared for UV-VIS-, HPLC analysis, fraction collection as well a combination of all with up to two dissolution tester.

That's the breakthrough for method development in R&D as well for highest flexibility and throughput in QC."

Dissolution Testing – The Software

ERWEKA's DSS software represents today's state-of-the-art in dissolution testing.

The program has been designed to support a wide variety of configurations in dissolution testing – both simple and complex. It follows the validation lifecycle and complies with global regulatory standards.

DSS has been developed using the most advanced technologies such as MS.net and is fully functional both in a networking environment as well as stand-alone.

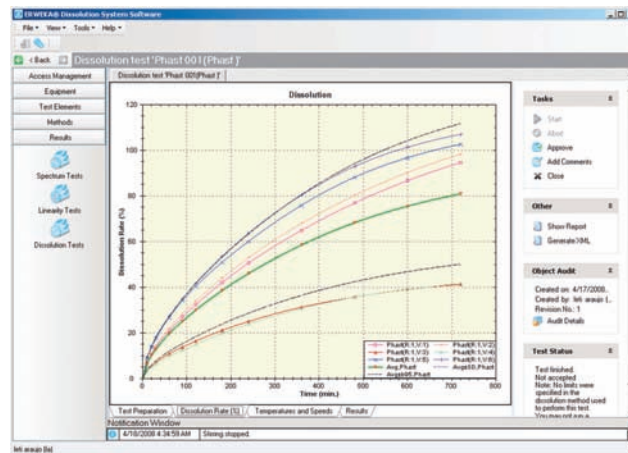
DSS relies on a transactional database (MS SQL) and therefore complies with audit trail requirements on the highest level. In particular it offers the possibility to manage user-privileges in great detail. Based on a .Net generator a large variety of reports can be generated easily.

According to 21 CFR 820 the software is fully documented by user requirement specification, functional specification and design specification. It therefore enables any user to start the validation process immediately after the installation of the software.

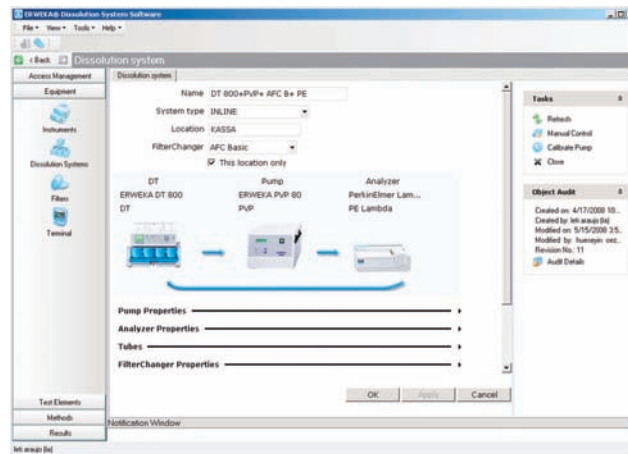
On the operational level DSS supports all relevant state-of-the-art routines in dissolution testing such as the analysis of drugs with up to 4 active ingredients, automated pH-changes (full change and half change) and auto cleaning and flushing routines between, before and after the run.

In order to grant maximum convenience of documentation, the DSS software not only offers a compact analytical report (default report with all relevant data fits on two A4 pages) but also comprises method data, calibration data and raw data (one A4 page each in default setting).

Last but not least – and unlike any other dissolution software available on the market – the DSS software supports the GMP conform correction of data input after the measurement. As a consequence, the loss of valuable measurement data due to data entry mistakes are a thing of the past. All corrections made are documented and included in the report.



DSS is the most advanced dissolution software available on the market today. It supports the calculation and monitoring of dissolution profiles with different values like E1%, EE, C/AU, spectra, calibration lines and online standards as well as the analysis of standards with different concentrations for up to 4 active ingredients.



In the dissolution settings mode a wide variety of configurations for online, offline and on-/offline systems can be easily defined and controlled. DSS supports all major models of UV-VIS spectrophotometers of various brands.

The screenshot shows the 'Audit Trail' window, which provides a detailed log of all system activities. It includes a search filter for 'User' (set to 'huiseyin oezcan') and a table with columns for 'Date/Time', 'Performed by', 'Operation', 'Host', and 'Status'. The table lists various operations such as 'Login', 'Logoff', 'Run of dissolution', and 'Dissolution metho' performed by the user 'huiseyin oezcan' on the host 'KASSA'.

Date/Time	Performed by	Operation	Host	Status
5/16/2008 1	letl araujo (lo)	Login	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	Logoff	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	Run of dissolution	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	Dissolution test cr	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	Dissolution metho	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	Dissolution metho	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	[AuditOp:UpdateF]	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	Run of dissolution	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	Dissolution test cr	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	Dissolution metho	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	Dissolution metho	KASSA	
5/15/2008 5	huiseyin oezcan (ho)	[AuditOp:UpdateF]	KASSA	

The DSS dissolution software complies with all relevant regulations. In particular it supports the full audit trail required by 21 CFR Part 11 including date & time stamp, user ID, events, database back-up and restore feature etc.

The DRT chewing gum tester is designed for the in vitro release of substances from a medicated chewing gum into a surrounding liquid medium (artificial saliva) during the mastication process. The test equipment is available with 1 to 6 test stations.

Vertical up- and down-strokes of the lower jaw in combination with a revolving movement of the upper jaw simulate the mastication of the sample and provide the adequate agitation of the test medium within the test cell (cuvette with a volume of 20-70 ml).

To facilitate data acquisition, the DRT can be equipped with an optional tool to measure, monitor and record pressures and torque (twisting of upper jaw) during mastication testing.

This NEW design can be used for testing tablets with the cuvette (dissolution) or in dry form (crushing).



Chewing Gum Dissolution Tester

The cuvette of the DRT is double-walled and made of glass in order to enable the visual inspection during the testing process. It is temperature controlled by a water circulation system, which can be regulated from 25 to 45°C.

For manual sampling, emptying and cleaning, the lower jaw together with the cuvette can be positioned at its lowest point to allow full access. The entire apparatus is built on an aluminium mobile cart for maximum mobility and can be built without the aluminum cart for stationary installations.

When testing with force monitoring, first the final gap (distance between upper and lower test jaws) must be set with gauges. The force level required to achieve the gap spacing during the stroke cycle is measured by the system. Throughout the process, data is recorded and stored for evaluation.

CALEVA® USP 3 and 7 BioDis, type RRT 9



The CALEVA BioDis complies with USP method 3 (Reciprocating Cylinder) and method 7 (Reciprocating Holder).

This enables the user to change the type of media (i.e. varying pH values) of media up to 6 times (6 rows, each 6+2 vessels).

The design guarantees easy access and visibility of the vessels and fast exchange of complete rows of vessels as well as easy handling by the numeric keypad. Method-storage and user-management with password protected access is standard.

The optional CALEVA USP 7 conversion kit allows for the changing from USP method 3 to 7 within one unit, which gives it a unique cost-advantage compared to other systems.

Dissolution Testing – RoboDis®

With RoboDis® ERWEKA sets the benchmark in the high-end of automated dissolution testing. The system has been developed in close cooperation with Bayer Healthcare® and therefore reflects state-of-the-art operational know how acquired in over 15 years of process optimization and automation in method development and quality control laboratories.

2-in-1

RoboDis® includes two 8-station Dissolution Testers which are operated by an industrial 6-axis Robot. Based on the configuration with 2 Dissolution Testers the throughput in comparison with other automated dissolution testers is significantly increased.

Vessel Filling

In its standard configuration RoboDis® offers volumetric filling of the vessels. The actual filling level of each vessel is controlled and documented by control weighing. Optionally a medium selector is available, which allows for the use of various kinds of media. To increase the throughput of the system simultaneous vessel filling is available in combination with the ERWEKA MultiPrep (see page 6).

pH change

RoboDis® supports the automated pH change according USP method "A" (half-change) and method "B" (full change).

Cleaning

On completion of the test-run the media is removed from the vessels by vacuum (no valves in the vessel). Remaining tablet debris (matrix) can be dissolved by cleaning solution or be removed by increased vacuum. After use the complete system is rinsed with hot water or a combination of cleaning solution and water.

Used media can be separated into standard waste water and contaminated waste water based on a valve system.

Methods

The RoboDis® is designed for the fully automated performance of up to 20 dissolution tests according to the latest USP/Pharm.Eur./JP requirements. It supports the following methods and processes:

- Performance of tests with USP Apparatus 1, 2 and 5
- Automated change of method from apparatus 1 to 2 and vice versa
- USP compliant Basket start routine
- Use of "Japanese Sinkers"



RoboDis® performs up to 20 test-runs automatically. To increase the throughput the system comprises two 8-station Dissolution Testers which are completely handled by the integrated Robot. As a consequence system performance is significantly improved compared to conventional automated dissolution testers.

RoboDis® combines the flexibility of a Robot (USP methods 1, 2 and 5; media change according to USP methods "A" and "B"; insertion and removal of Japanese Sinkers etc.) with the speed of an automated Dissolution Tester (simultaneous operation of volumetric media filling, tablet drop and sample withdrawal).

Analysis can be performed either by Fibre Optics, UV-VIS or HPLC.

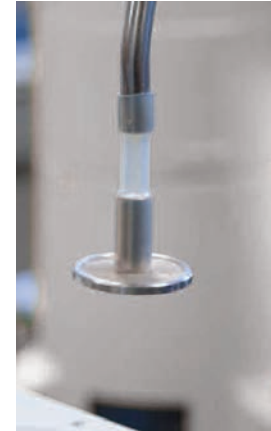
Robot arm with UV-optrode (Fibre Optics) taking measurement inside the vessel



Insertion of sample with Japanese sinker/Removal of Japanese sinker



Robot arm with different “hands” for media filling, tablet/pellet/ Japanese sinker insertion, optic measurement and media and sinker removal



Robot arm performing method change from Paddle to Basket

Removal of disc according to USP method 5

Sampling station with PT 100 temperature sensors (optional)



Video recording of the dissolution process. Dissolution results may be shown as overlapping real-time dissolution curve to show and document unexpected effects such as coning etc.

Filtration

Filtration can be performed by either Tip or Membrane Filters (min. 0.45 µm), depending on the Analysis system used.

Analysis

RoboDis® offers maximum flexibility concerning the analytical method applied as well as full visual supervision of the dissolution process:

- UV-VIS “in-vitro” measuring based on fibre optics (no Multiplexer required due to sequential measuring)
- Online measuring based on UV-VIS and/or HPLC analysis
- Sampling into a fraction collector for offline operations
- Measuring of calibration and control standards in case of online operations

System Control

- 21 CFR Part 11 compliant Windows®-based software package
- Online control of rpm and temperature in each individual vessel and in the bath

Video Controlling

As an additional feature RoboDis® offers video analysis of the dissolution process in time-lapse mode with overlapping real-time dissolution curve to identify disturbances such as coning etc.

Compliance

RoboDis® is compliant with all relevant regulatory standards in the pharmaceutical industry such as:

- 21 CFR Part 11
- GAMP (current edition)
- CGMP (FDA)
- GMP Guidelines of the EU
- EMC directive according to EN 61010
- Guidelines of US Pharmaceutical Manufacturer’s Association (PMA) concerning the qualification and computer validation of equipment

Dissolution Testing – USP 4 method – The Basics

Langenbucher Flow-Through-Cell

The USP method 4 is the solution for those products, which are not suitable for the standard stirrer type dissolution baths.

The Langenbucher Flow-Through-Cell can handle:

- long duration test-runs
- samples, which need a high volume of media to dissolve (Open-Loop System)
- samples which need a low amount of media to dissolve, e.g. 27 ml per test-station (Closed-Loop System)
- Implants, stents, suppositories etc.

In addition, USP method 4 testers are ideal for easy multiple media changes (up to a maximum of four).

The ERWEKA Flow-Through-Cell is offered in two different configurations:

- “Open-Loop” system, in which fresh media is pumped from a reservoir through the cells in a continuous flow;
- “Closed-Loop” system, in which the media for each test station is stored in a thermostatically heated beaker glass with integrated stirrer (Media Transfer Station, Type LMT 700) from where it is pumped in a closed circle through the cell.

Both systems are optimized for different purposes: While the “Open-Loop” system uses a high volume of media to dissolve the drug, the “Closed-Loop” system only requires a minimal volume (from 27 ml).

The basic “Open-Loop” system consists of 2 units: (1) the USP 4 compliant 7-channel Piston Pump, type HKP 720, and (2) the 7 test-station Flow-Through-Cell Dissolution Tester, type DFZ 720. The basic “Closed-Loop” system additionally requires the Media Transfer Station, type LMT 720.

USP 4 compliant pump

To fulfil the requirements for the media transfer a special low-footprint piston pump has been designed, which allows for transfer flow rates of 2.0 to 32.0 ml/min. at 120 strokes/ min. at an accuracy better than $\pm 5\%$.

The ERWEKA pump has a valve-free design and deaerates the pump heads (Teflon/ceramics) automatically.

Volume adjustment is easier than ever: Just select the required flow rate via the membrane keypad, press >Enter< and start the test-run.



The low-footprint DFZ 720 Flow-Through-Cell, in combination with seven 3-way valves, has been developed with R&D requirements in mind and therefore offers an individual opening / closing mechanism for each individual cell.

The USP 4 pump, type HKP 720, allows for automatic flow volume adjustment (2.0 – 32.0 ml) with an accuracy of better than $\pm 5\%$, without the need for permanent re-calibration.

System cleaning is extremely easy since the complete base plate, with cell holders, media warming spindle and tubing can be removed from the water bath.

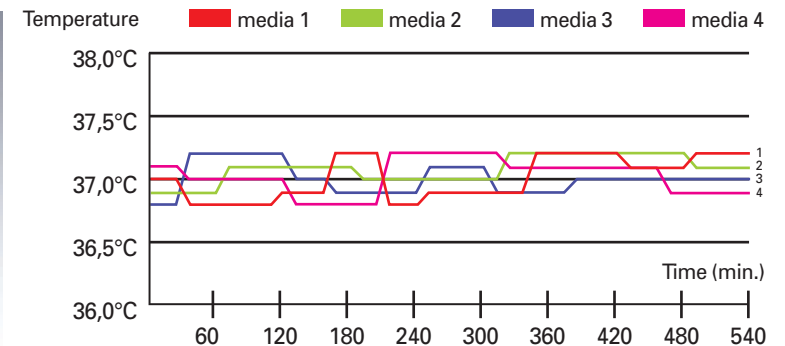


Cell-Blockage Controller

The Control Box, type SE, in combination with the DFZ 720T Flow-Through-Cell, displays the individual media temperatures prior to entering the cell. Via the standard printer interface test-run parameters, incl. media temperatures, may be printed.

In addition the SE controls the automatic media switch, type MS 40, for changing the kind of media up to 4 times – without any user interaction.

The SE controls all types of USP 4 Offline-Systems, “Open-Loop” and “Closed-Loop”.



Display of temperature of up to 4 different media prior to entering the cell.



The unique feature of seven 3 way-valves (available as an option) allows for the individual control (opening / closing; start / stop) of each test-station.



USP design tablet holders against floating.



USP 4 Dissolution Tester

The ERWEKA DFZ 720 was designed having in mind the needs of R&D laboratories. Unlike other units the DFZ 720, in combination with seven 3-way valves, supports the opening and closing as well as the activation and deactivation of each individual cell.

As an additional feature the DFZ 720T allows for the measurement of the actual media temperature at the inlet of each cell. Via the Control Box, type SE, the individual temperatures are displayed and may be printed.

As standard the DFZ 720 comes with a Cell-Blockage-Controller: In case a cell is blocked, the media is directed back to the media reservoir before entering the cell.

System cleaning is easy since the base-plate with attached cell holders, media warming spindles and tubing can be removed from the water bath.

Media Transfer Station

The Media Transfer Station LMT 720 is required to build a "Closed-Loop" USP 4 system. It consists of seven 1000 ml beaker glasses with integrated magnetic stirrers, which are positioned inside a water bath to supply the media.

Online Media Deaeration

A device for online dissolution media deaeration can be incorporated into the media line ("Open-Loop").

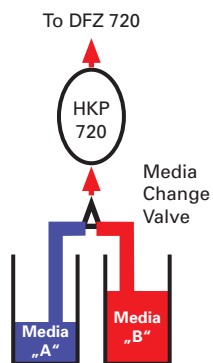
Media Change

"Open-Loop" Flow-Through-Cell systems are ideal for media changes. ERWEKA offers two different units for media change:

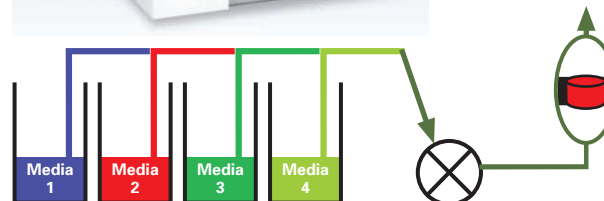
- 1) The manual media switch valve MS 10 for changing the media one time;
- 2) The automated media switch valve MS 40 for up to 4 different types of media within one test-run. The MS 40 is connected to the Control Box, type SE, where the media change times are programmed.

Control Box, type SE

The Control Box allows for the programming of the test-run parameters of up to 40 different products. Additionally, the Control Box displays the actual media temperatures prior to entering the cell (DFZ 720T), sets the required temperature of the Flow-Through-Cell-/Media-Transfer-Station's heater and controls the Media Switch, type VS 40.



Media Change Systems:
 Left: manual media switch for one media change.
 Right: automated media switch (controlled by SE Control Box) for max. 4 media changes.



“Open-Loop” Systems

Offline-System

Instead of manual sampling, which requires the presence of a user during the complete test-run, a USP 4 Offline Dissolution System can be used.

A Fraction Collector with split valves, type FRL 704, is integrated into the media line behind the outlet of the cells. These split valves allow for the collection of an average of the media-flow for analysis.

Racks for 24 collection intervals (10 ml collection capacity) or 16 collection intervals (25 ml collection capacity) are available and can be placed on a platform with drawer mechanism. This mechanism offers to load, remove or exchange the rack very easily.

The complete system, including the split calculation of the valves, media changes (up to 4), flow rate setting (2.0 – 32.0 ml at 120 strokes/min.) and media temperature display for each cell, is controlled by the Control Box, type SE. The SE Control Box supports the storage of up to 40 product test-run parameters.

Via the printer interface of the Control Box test-run parameters including individual media temperatures can be documented.

UV-VIS Online System

The “Open-Loop” UV-VIS Online System integrates a UV-VIS Spectrophotometer with cell changer into the media outlet line of the DFZ 720.

The media inside the flow-through-cells of the Spectrophotometer is measured continuously staggered and a dissolution graph is calculated and displayed by the DSS software.

The complete system, including media temperature recording, media changes (up to 4) and the flow rate is controlled by the Windows®-based software package DSS.

Results may be stored or printed.

Dissolution Testing – USP 4 method – The Systems



“Open-Loop” USP 4 Offline System, to eliminate the need of permanent user presence during long-term test-runs.

Complete system control, incl. up to 4 automated media changes, flow rate and temperature setting as well as media temperature display for each cell by the Control Box, type SE. Storage of the test-run parameters for up to 40 different products.

A test-run parameter print-out is available via the Control Box’s printer interface.



“Open-Loop” USP 4 UV-VIS Online-System for the direct analysis of the media-flow. Ideal for long-term studies, since no user-intervention is required during the complete test-run.

Complete System control by the Dissolution Software DSS, including standard dissolution graph.



“Closed-Loop” USP 4 Offline System with sample withdrawal from stirred media reservoirs located in the thermostatically heated water bath of the Media-Transfer-Station, type LMT. The system includes a Sample Transfer Pump and collects the samples into glass tubes or sealed / unsealed HPLC vials inside the FRL 704/804 Fraction Collector. In a configuration with the FRL 804 Fraction Collector the withdrawn sample volume can be replaced by fresh media automatically.

Sample Transfer Pump and Fraction Collector are controlled by the Control Box, type SE, which additionally supports the storage of up to 40 product test-run parameters.



“Closed-Loop” USP 4 UV-VIS Online System for the automated analysis of the media by a connected UV-VIS Spectrophotometer. After analysis the withdrawn samples are returned to the media reservoir inside the Media-Transfer-Station in order not to decrease the volume of media available for dissolution.

The ERWEKA Dissolution Software DSS controls the Sample Transfer Pump and the UV-VIS Spectrophotometer. Analytical results are shown in a standard dissolution curve and can be printed and stored.

“Closed-Loop” Systems

Offline-System

The USP method 4 “Closed-Loop” Offline-system withdraws the sample from the stirred media reservoir located inside a thermostatically heated water bath (LMT 720). The sample is then transferred by a Sample Transfer Pump (Peristaltic or Piston Pump) to the Fraction Collector for storage.

While the FRL 704 Fraction Collector only can store samples (implying the reduction of the media volume in the media reservoir) the FRL 804 supports the replacement of the withdrawn media with fresh media after storage in order to keep the media volume inside the LMT’s media reservoir stable. This function is very important for those applications, which require only a very small quantity of media for testing (min. 27 ml).

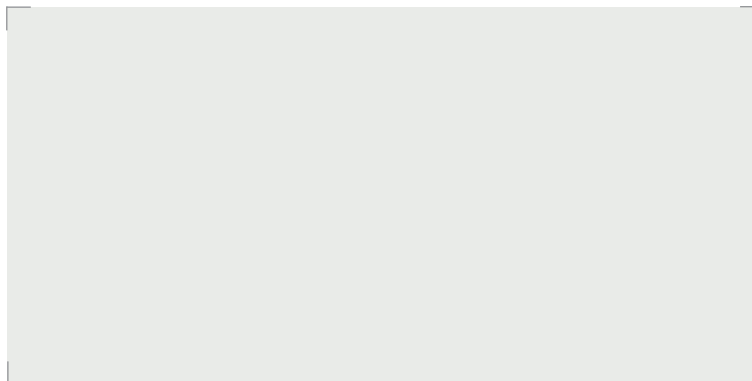
In addition, the FRL 804 offers HPLC membrane piercing to store the withdrawn sample in sealed HPLC vials (1.5 or 4.0 ml).

Online-System

The “Closed-Loop” UV-VIS Online System, similar to the above-mentioned Offline-System, withdraws the samples from the LMT’s media reservoirs and transfers them into the cells of the UV-VIS Spectrophotometer for analysis. After the analysis the samples are transferred back to the media reservoirs not to decrease the media level available for dissolution.

The ERWEKA Dissolution Software DSS controls the Media Transfer Pump as well as the UV-VIS Spectrophotometer. Results are displayed in the format of a regular dissolution curve and can be printed and stored.

presented by



ERWEKA®

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www.erweka.com

Germany
Switzerland/Austria

ERWEKA®

GmbH
Ottostraße 20-22
63150 Heusenstamm
Phone: +49-61 04-69 03-0
Fax: +49-61 04-69 03-40
Email: sales@erweka.com

International Sales

ERWEKA®

International AG
Peter Merian-Str. 58
CH-4052 Basel
Phone: +41-61-735 90-50
Fax: +41-61-735 90-55
Email: sales@erweka.com

USA/Puerto Rico

ERWEKA®

America Corp.
70, Church Street, Suite 102
Flemington, NJ 08822
Phone: +1-908-788-4666
Fax: +1-908-788-4667
Email: sales.usa@erweka.com

France

ERWEKA®

France
Saint Martin du Parc
27 800 Le Bec Hellouin
Phone: +33-23243-2254
Fax: +33-23243-2585
Email: sales.france@erweka.com

Poland/Czech Rep./Slovakia

ERWEKA®

Poland Sp. z o. o
ul. Bitwy Warszawskiej 18/9
02-366 Warszawa
Phone/Fax: + 48-22-66888-30
Phone/Fax: + 48-22-66888-91
Email: erweka@erweka.pl

Hungary/Slovenia/Croatia

ERWEKA®

Magyarország Kft.
Öntő u. 22.
2030 ÉRD
Phone: +36-23-5237-97
Fax: +36-23-5237-96
Email: erweka@erweka.hu

Asia-Pacific

ERWEKA®

30./F., 99 Hennessy Road
Wanchai, Hong Kong, China
Phone: +852-2291-6300
Fax: +852-2291-6311
Email: asia-pacific@erweka.com

India

ERWEKA®

India PVT LTD
502, Mahalay
Off C.G.Road
Ahmedabad-380009
Phone: +91-79-2-6560-629
Fax: +91-79-2-6560-702
Email: sales.india@erweka.com