COPLEY SCIENTIFIC

Creams and Ointments

Powders

Suppositories

Tablets and Capsules

Transdermal Patches

2007 Edition

Quality Solutions for the Testing of Pharmaceuticals

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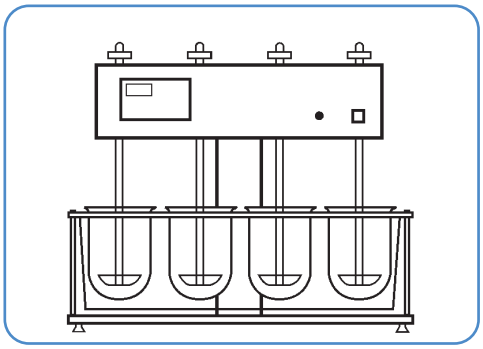

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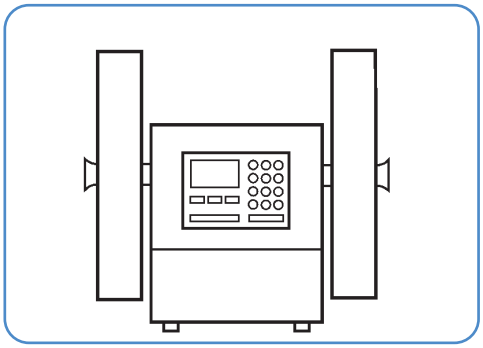

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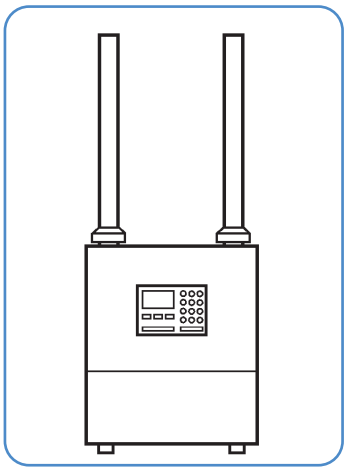

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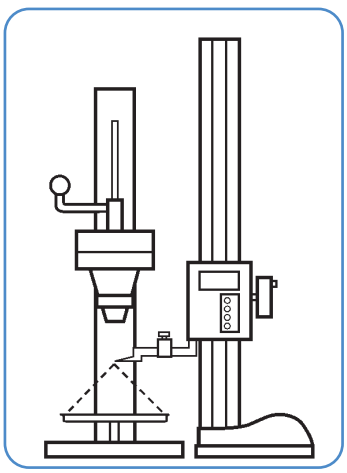

POWDERS - ANGLE OF REPOSE

INTRODUCTION

1. REGULATORY BODIES

In Europe, the ultimate responsibility for the regulation of medicines lies with the **European Medicines Agency (EMEA)** in the form of the **Committee for Medicinal Products for Human Use (CHMP)**.

In the USA, this function is performed by the **Food and Drug Administration (FDA)** through two centers, the **Center for Drug Evaluation and Research (CDER)** in respect of medicines and the **Center for Devices and Radiological Health (CDRH)** in respect of medical devices.

2. DRUG SAFETY AND EFFICACY - THE PHARMACOPOEIA

As with the regulatory organisations, the main Pharmacopoeia lie with the European, Japanese and US bodies.

The main role of the Pharmacopoeia is to lay down suitable quality standards, requirements and tests to ensure the safety and efficacy of the various drugs and excipients used in modern medicine.

This is no easy task for the compendia and the companies involved with supplying the instrumentation for carrying out the tests taking into account the myriad of medicines on the market and the variety of methods by which they can be administered to the body.

3. THE CLASSIFICATION OF MEDICINES

One of the clearest taxonomic guides for the categorisation of pharmaceutical dosage forms is to be found in *Pharmaceutical Forum. 2003;29: Pages 1742-44* under the title "Development of a compendial taxonomy and glossary for pharmaceutical dosage forms".

This proposes a three tier system with the first tier being based on the region of the body to which the drug is to be administered, i.e., **gastrointestinal** (oral), **mucosal membrane** (rectal, vaginal, oropharyngeal, opthalmic, otic and urethal), **skin surface** (topical, transdermal), **injections** incl. infusions or **lungs** (pulmonary).

It is this first tier classification which has been used as the basis for the **Equipment Selection Guide** to be found on the facing page. This lists the dosage form and test parameter concerned, the chapter relating to that test parameter in both European and US Pharmacopoeia (where applicable) and, in the final column, the page number in this catalogue where a description of the test instrumentation concerned can be found.

4. COPLEY SCIENTIFIC

Copley Scientific has been supplying test equipment to the pharmaceutical industry since 1946.

The pharmaceutical industry of today demands instrumentation that is not only precise and accurate but simple and easy to use as well as being robust and rugged in operation.

The Copley philosophy is that the ability to discern between changes in product and the accuracy and reproducibility of results can only be achieved from **"quality by design"** and thereafter through the rigorous application of close tolerances, the use of qualified components, unambiguous adherence to production protocols and regular check of dynamic parameters.

It is this philosophy that is applied to the manufacture of all of our instruments that guarantees you, the user, an instrument of the highest quality and reliability.

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Dosage Form	European Pharmacopoeia	United States Pharmacopoeia	Page No. (in this brochure)
GASTROINTESTINAL - Tablets & Capsules - Disintegration	Chapter 2.9.18	Chapter 701	Pages 5 - 8
GASTROINTESTINAL - Tablets & Capsules - Dissolution	Chapter 2.9.3	Chapter 711	Pages 9-22
GASTROINTESTINAL - Tablets & Capsules - Friability	Chapter 2.9.7	Chapter 1216	Pages 23 - 24
GASTROINTESTINAL - Tablets & Capsules - Hardness	Chapter 2.9.8	Chapter 1217	Pages 27 - 32
GASTROINTESTINAL - Tablets & Capsules - Weight & Thickness	Chapter 2.9.5	Chapter 905	Page 32
GASTROINTESTINAL - Powders - Bulk & Tapped Density	Chapter 2.9.15 (Apparent Volume)	Chapter 616	Pages 33 - 34
GASTROINTESTINAL - Powders - Flowability	Chapter 2.9.36	Chapter 1174	Pages 35 -38
GASTRONINTESTINAL - Granules & Pellets - Friability	Chapter 2.9.41	-----	Pages 25 - 26
MUCOSAL MEMBRANE - Rectal & Vaginal - Drug Release	Chapters 2.9.2 & 2.9.22	-----	Pages 39
MUCOSAL MEMBRANE - Oropharyngeal, Opthalmic, Otic & Urethal	Outside the scope of this brochure		
SKIN SURFACE - Creams & Ointments - Drug Release	-----	-----	Pages 43 - 44
SKIN SURFACE - Transdermal Patches - Drug Release	Chapter 2.9.4	Chapter 724	Page 17
INJECTION - Injections & Infusions	Outside the scope of this brochure		
LUNGS - Inhalers & Nebulisers	Chapters 0523 & 0671	Chapters 601 & 1151	See separate brochure
NASAL - Inhalers & Sprays	Chapter 0676	Chapter 601	See separate brochure
ANALYTICAL INSTRUMENT QUALIFICATION - Guidelines	-----	Chapter 1058	Page 45

DISINTEGRATION TESTER DTG 1000

DISINTEGRATION TESTER DTG 2000

DISINTEGRATION TESTERS SERIES DTG

The Disintegration Tester Series DTG is the result of over 50 years experience in the field of pharmaceutical testing.

They have been specifically designed for use in the quality and production control of normal, plain coated and delayed release coated tablets, and gelatine capsules in accordance with the specifications as laid down in European, United States and associated Pharmacopoeia.

The series is available with one (DTG 1000), two (DTG 2000), three (DTG 3000) or four (DTG 4000) test stations. Each individual test station is capable of accepting one batch of six tablets or capsules.

Foremost in the design specification were those features that you, the user, identified as being essential to the **'ideal'** disintegration tester.

PHARMACOPOEIAL COMPLIANCE AND QUALIFICATION

The most critical factors in the design of any disintegration tester are (a) that it complies with the respective Pharmacopoeia, (b) that this compliance can be proved or qualified and (c) that both compliance and qualification are documented.

Copley offer a three tier approach to address these points:

- **Certificate of Compliance to USP/Ph.Eur.:** Provided free of charge with each unit. Written statement that the product, by design, complies with the current pharmacopoeial specifications.
- **Laser Numbering and Certification:** Identification and measurement of critical components to provide **documented verification** of compliance with current pharmacopoeial specifications. Available as an optional service.
- **IQ/OQ/PQ Qualification Documentation:** Comprehensive documentation to guide the user through the installation, operating and performance checks of the equipment in its operating environment, using specified test protocols. It provides a comprehensive record of the suitability of the equipment to perform its specified task, to be created and archived.

Please see the ordering information for further details on our verification and qualification services.

DESIGN AND CONSTRUCTION

All of the DTG series feature a motor drive operating at a fixed speed of 30 rpm (+/- 1) and a stroke of 55 mm (+/- 1).

Depending on the model, the DTG has the capacity of testing one, two, three or four different tablet batches of six tablets/capsules simultaneously, under identical test conditions.

The control of all models is provided by a membrane keypad linked to a 4-line 20 character back-lit LCD screen which together with the electronics is mounted in the head of the instrument so as to avoid any accidental spillages in the test area.

Particular attention has been given to the design of the basket rack assembly in respect of its removal and cleaning.

The **novel 'quick-release' basket design** not only provides a firm and rigid location for the basket during operation but also allows the basket to be removed from the instrument for rapid cleaning.

Another unique feature of the basket design is the use of **thumb screws** to hold the various components together.

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DISINTEGRATION TESTERS SERIES DTG

This means that if it is necessary to disassemble the basket before cleaning, this can be done very quickly and without the use of any specialised tools.

A common problem associated with fabricated water baths, used for warming the media, is that of leaks.

This problem has now been eliminated through the use of a **one-piece water bath** vacuum formed in rigid PETG. This construction not only eliminates any possibility of leaks but also makes it far easier to clean because of its rounded corners. The bath is fitted with a sturdy 8 mm clear view lid and secured to the base by four easily removed thumb screws.

The temperature of the warming solution is controlled by means of an **independent heater/circulator** to an accuracy of **+/- 0.2 degrees C**. This has two advantages: firstly, it removes the necessity for priming and secondly, it can be removed for cleaning without dismantling the whole disintegration tester. A **low-water level alarm** indicator is built into the unit as standard.

OPERATION

Considerable attention was paid to the design of the DTG series to ensure that the number of actions necessary to perform a test are kept to a minimum.

The membrane keypad allows for the selection of test run times up to **99 hours 59 minutes 59 seconds**. Thereafter, it is only necessary to press the START key to automatically lower the basket rack assemblies into the test media and begin or repeat a test.

During the test, the time elapsed from the start of the test (or if you prefer, time remaining to the end of the test) is displayed on the LCD screen.

At the end of the test, **the basket rack assemblies are automatically removed from the test media** and an audible alarm alerts the user that the run is completed.

Bath and beaker temperatures can be constantly monitored using the **PT100 temperature probe** provided for this purpose. Temperature is critical to the test and is displayed permanently on the LCD screen as soon as the unit is switched on.

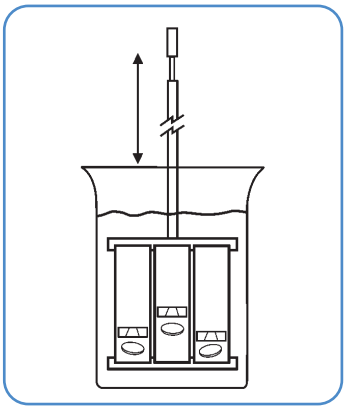
Ordinarily, temperature calibration can prove to be a time consuming and inaccurate process involving the use of iced water. This is not the case with the DTG series. Available as an option, the **electronic temperature calibration kit** comprises two UKAS certified test keys (0 and 37 degrees C) which you simply plug into the PT100 socket to perform the calibration.

Dimensions (mm):
DTG 1000/2000 = 450 mm (W) x 450 mm (D) x 720 mm (H)
DTG 3000/4000 = 700 mm (W) x 450 mm (D) x 720 mm (H)

Cat. No.	Description
1201	Disintegration Tester Model DTG 1000 (1 Station)
1202	Disintegration Tester Model DTG 2000 (2 Station)
1203	Disintegration Tester Model DTG 3000 (3 Station)
1204	Disintegration Tester Model DTG 4000 (4 Station)
1205	Extra for Numbering and Certification (per basket)
1206	IQ/OQ/PQ Documentation Pack
1207	Electronic Temperature Calibration Kit

DISINTEGRATION TESTER DTG 3000

DISINTEGRATION TESTER DTG 4000



'QUICK-RELEASE' BASKET ASSEMBLY

DISINTEGRATION TESTER DTG 2000 IS

100 mL PACK OF AQUA-STABIL

DISINTEGRATION TESTERS SERIES DTG

The Disintegration Tester Series DTG described on the preceding two pages is ideal for quality control and R & D where it is important that the testing is carried out under identical test conditions.

As previously stated, the series offers the user an unparalleled number of standard features including:

- Conforms to all current Ph.Eur. and USP specifications
- Choice of 1, 2, 3 or 4 test baskets
- 'Quick-Release' basket design combines stability with easy removal
- Automatically lowers and raises the baskets at the start and finish of the test
- Easy-to-clean vacuum formed water bath eradicates leaks
- Independent heater/circulator: no priming and easy to remove
- Low liquid level sensor
- Membrane control panel: easy to use
- 99 hour test programme permits delayed release as well as normal testing
- Acoustic signal at the end of the test
- PT100 temperature sensor as standard
- Constant monitoring of time and temperature via LCD screen
- Electronic temperature calibration kit (option)
- Certification and IQ/OQ/PQ documentation packs available (option)

DISINTEGRATION TESTER DTG 2000 IS

There are however certain occasions when it is useful to have **independent control over each of the test stations.**

This is particularly helpful in research and development when the user is comparing one formulation directly against another, or one formulation under varying conditions, or in the case of delayed release or enteric coated tablets where it is necessary to immerse the sample for specified periods of time in different media.

Alternatively, there are times in QC operations when it is more convenient to carry out tests at different times e.g. when one disintegration tester serves to support two tablet presses.

The **DTG 2000 IS** is a two station unit which has been specifically designed for these types of tests. It has all of the features of the standard DTG series mentioned above.

However, on this unit, **each basket rack assembly** can be controlled, started and stopped **individually** using seperate membrane keypads**.**

Cat. No.	Description
1208	Disintegration Tester Model DTG 2000 **IS**
1205	Extra for Numbering and Certification (per basket)
1206	IQ/OQ/PQ Documentation Pack
1207	Electronic Temperature Calibration Kit

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DISINTEGRATION ACCESSORIES

STANDARD ACCESSORIES

Copley Scientific offers a complete range of accessories for use with the DTG series, from complete basket rack assemblies to individual tubes, discs and sieve meshes.

All parts are manufactured to tolerances that are equal to or better than those quoted in the respective Pharmacopoeia and carefully checked prior to despatch.

BASKET RACK ASSEMBLY COVER FOR HARD & SOFT GELATIINE CAPSULES (as per USP Chapter <701>)

Converts standard basket to special cover version for testing hard or soft gelatine capsules according to USP Chapter <701>.

USP specifies that, when testing hard or soft gelatine capsules, the top of the basket rack assembly should be covered by a further sieve mesh (2 mm x 0.63 mm).

Comprises basket cover with integral sieve meshes, plus central locking device for easy assembly.

SPECIAL BASKET RACK ASSEMBLY FOR LARGE TABLETS & CAPSULES (as per Ph.Eur. Chapter 2.9.1 Test B)

Special basket rack assembly for large tablets, capsules and boluses according to Ph.Eur. Chapter 2.9.1 Test B.

In this version, the six standard tubes (21.85 mm i.d.) are replaced with three tubes having an i.d. of 33 mm.

Supplied complete with the special cylindrical discs specified in the Pharmacopoeia.

Can be supplied with Certificate of Compliance on request.

HYGIENE: ANTI-BACTERIA/ALGAE SOLUTION

Keep your water bath free of bacterial, algal or slime growth.

The addition of just 1 mL of Aqua-Stabil per litre of water, per month, will prevent the build-up of bacteria and algae keeping the water in your bath clear, safe and odour free.

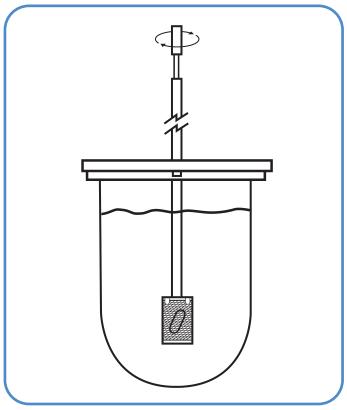
Available in 100 mL packs.

Cat. No.	Description
1210	Standard Basket Rack Assembly
1205	Extra for Numbering and Certification (per basket)
1211	Set of 6 Glass Tubes
1212	Set of 6 Polycarbonate Discs
1213	Set of 6 Sieve Meshes
1214	1000 mL Beaker
1215	Basket Rack Cover for Hard & Soft Gelatine Capsules
1216	Extra for Numbering and Certification (per cover)
1217	Special Basket for Large Tablets (as per Ph.Eur. Test B)
1218	Extra for Numbering and Certification (per basket)
1372	100 ml Pack of Aqua-Stabil

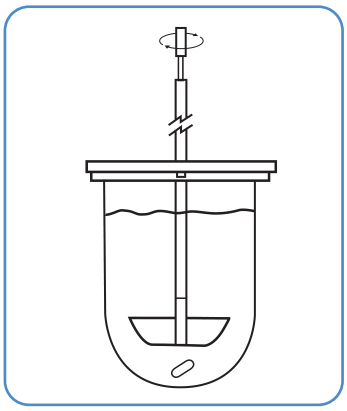
Glass Tubes, Guided Discs & Sieves

Basket Fitted with Special Cover

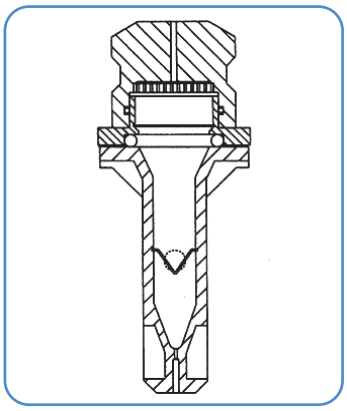
Special Basket for Large Tablets



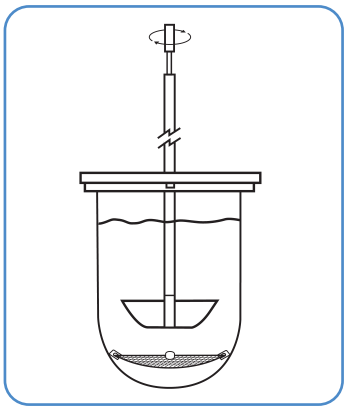
APPARATUS 1 - BASKET



APPARATUS 2 - PADDLE



APPARATUS 4 - FLOW THROUGH CELL



APPARATUS 5 - PADDLE OVER DISC

INTRODUCTION TO DISSOLUTION TESTING

Tablets or capsules taken orally remain one of the most effective means of treatment available.

The effectiveness of such dosage forms relies on the drug dissolving in the fluids of the gastrointestinal tract prior to absorption into the systemic circulation. The rate at which the tablet or capsule dissolves is therefore critical to its therapeutic efficiency.

One of the problems facing the pharmaceutical industry is to optimise the amount of drug available to the body i.e., its '**bioavailability**'. Inadequacies in bioavailability can mean at best that the treatment is ineffective and at worst potentially dangerous (toxic overdose).

Drug release in the human body can be measured '**in-vivo**' by measuring the plasma or urine concentrations in the subject concerned. However, there are certain obvious impracticalities involved in employing such techniques on a routine basis. These difficulties have led to the introduction of official '**in-vitro**' tests which are now rigorously and comprehensively defined in the respective Pharmacopoeia.

The principal function of the dissolution test may be summarised as follows:

- Optimisation of therapeutic effectiveness during development and stability assessment
- Routine assessment of production quality to ensure uniformity between production lots
- Prediction of '*in-vivo*' availability i.e., bioavailability (where applicable)
- Assessment of 'bioequivalence' (production of the same biological availability from discrete batches of products from one or different manufacturers) and its application in Scale-Up and Post Approval Changes (SUPAC).

Whether or not its numbers have been correlated 'in-vivo', the standard dissolution test is a simple and inexpensive indicator of a product's physical consistency.

Initially developed for immediate release (IR) and then to extended / delayed release oral dosage forms, the role of the 'dissolution test' has now been expanded to the 'drug release' of various other forms such as suppositories, topical and transdermal systems.

The term '**dissolution test**' is normally used to describe the testing of those forms such as IR oral tablets or capsules intended to dissolve rapidly in the test medium.

For non-oral dosage forms such as suppositories, topical and transdermal systems, the term '**drug release**' is normally employed.

From a regulatory perspective, the **Food and Drug Administration (FDA)** has published four Guidances for Industry relating to dissolution:

- Dissolution Testing of Immediate Release Solid Oral Dosage Forms, August 1997
- Extended Release Solid Oral Dosage Forms: Development, Evaluation and Application of In Vitro/In Vivo Correlations, September 1997
- Waiver of In Vivo Bioavailability and Bio-equivalence Studies for Immediate Release Solid Oral Dosage Forms based on a Biopharmaceutics Classification System, August 2000
- Bioavailability and Bioequivalence Studies for Orally Administered Drug Products - General Considerations, October 2000

A similar function is provided by the **European Medicines Agency (EMEA)** in the form of the **Committee for Medicinal Products for Human Use (CHMP).**

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PHARMACOPOEIAL REQUIREMENTS

The main role of the Pharmacopoeia is to lay down suitable quality standards, requirements and tests to ensure the safety and efficacy of the various drugs and excipients used in modern medicine.

As with the regulatory bodies, the main Pharmacopoeia lie with the European, Japanese and US bodies.

The value of the 'dissolution test' or perhaps more correctly, 'drug release' as a tool in pharmaceutical development and quality control is reflected in the number of chapters bearing direct or indirect reference to it in the compendia.

In the **United States Pharmacopoeia (USP)**, for example, there are no less than nine general chapters referencing dissolution:

<711> Dissolution
<724> Drug Release
<1058> Analytical Instrument Qualification (proposed)
<1087> Intrinsic Dissolution
<1088> In Vitro and In Vivo Evaluation of Dosage Forms
<1090> In Vivo Bioequivalence Guidances
<1092> Dissolution Procedure: Development & Validation
<1225> Validation of Compendial Procedures
<1226> Verification of Compendial Procedures

A similar situation exists as far as test methods are concerned with seven methods currently listed:

- Apparatus 1 - Basket <711> Dissolution
- Apparatus 2 - Paddle <711> Dissolution
- Apparatus 3 - Reciprocating Cylinder <711> Dissolution
- Apparatus 4 - Flow-Through Cell <711> Dissolution
- Apparatus 5 - Paddle over Disk <724> Drug Release
- Apparatus 6 - Cylinder <724> Drug Release
- Apparatus 7 - Reciprocating Holder <724> Drug Release

Attention should also be drawn to the **Vertical Diffusion Cell (Franz Cell)** whose inclusion in the Pharmacopoeia is currently under review for testing the in-vitro release rate of semi-solid dosage forms such as creams, gels and ointments.

The **European Pharmacopoeia (Ph.Eur.)** categorises its Dissolution Chapters in a similar manner, thus:

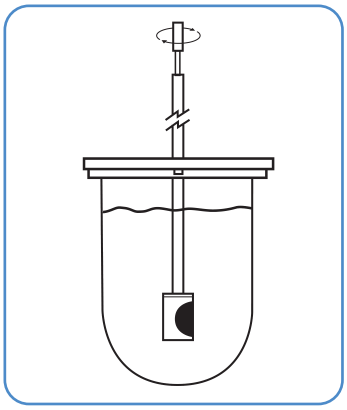
2.9.3 Dissolution test for solid dosage forms
2.9.4 Dissolution test for transdermal patches
2.9.25 Dissolution test for medicated chewing gum
2.9.29 Intrinsic Dissolution
2.9.42 Dissolution test for lipophilic solid dose forms (suppositories)
2.9.43 Apparent Dissolution (powders and granules plus various monographs on dosage forms

At first sight, this proliferation of equipment and procedures can appear confusing. Suffice it to say however that the drug release of all but the most specialised of dosage forms can be tested with a combination of the following three apparatus :

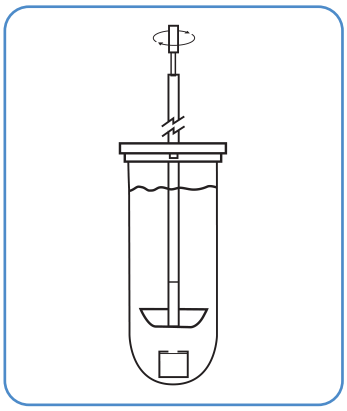
1. Apparatus 1 - Basket Method
2. Apparatus 2 - Paddle Method (plus appropriate accessories)
3. Vertical Diffusion Cell

This includes tablets, gelatine capsules, oral suspensions, orally disintegrating and chewable tablets, transdermal patches, semi-solids such as creams, gels and ointments and suppositories.

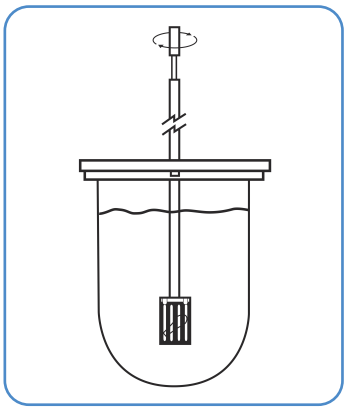
Please contact our technical staff for advice on your application.



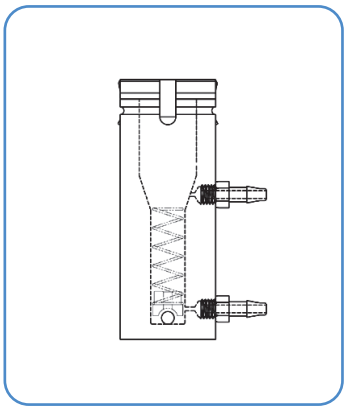
APPARATUS 6 - CYLINDER



SPECIAL OINTMENT CELL



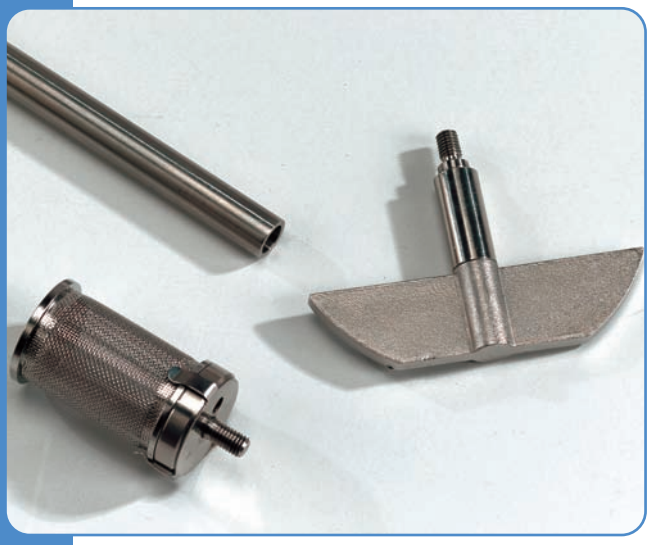
SPECIAL SUPPOSITORY BASKET



VERTICAL DIFFUSION CELL (FRANZ CELL)

DISSOLUTION TESTER DIS 8000

COMPLIANCE AND QUALIFICATION



INTERCHANGEABLE BASKETS/PADDLES

DISSOLUTION TESTER DIS 8000

The Dissolution Tester Series DIS represents the very latest in tablet testing technology. CNC production techniques combined with modern microprocessor design guarantee the highest standards of performance and reliability.

All Copley Scientific dissolution testers meet the latest specifications as laid down in the European, United States and associated Pharmacopoeia.

Efficient and extremely compact, the **Tablet Dissolution Tester DIS 8000** is a rugged 'no-nonsense' unit having **eight stirred** test vessels and **simple, easy-to-use controls**. It is ideal for both R&D and routine quality control applications.

The design of the unit has been based on those features that you, the user, advised us as being essential to the **'ideal'** dissolution tester:

PHARMACOPOEIA COMPLIANCE AND QUALIFICATION

The most critical factors in the design of any dissolution tester are (a) that it complies with the respective Pharmacopoeia, (b) that this compliance can be proved or qualified and (c) that both compliance and qualification can be documented.

Copley offer a three tier approach to address these points:

- **Certificate of Compliance to USP/Ph.Eur.:** Included with each unit. Written statement that the product, by design, complies with the current pharmacopoeial specifications.
- **Laser Numbering and Certification:** Identification and measurement of critical components to provide **documented verification** of compliance with current pharmacopoeial specifications. Available as an optional service.
- **IQ/OQ/PQ Qualification Documentation:** Comprehensive documentation to guide the user through the installation, operating and performance checks of the equipment in its operating environment, using specified test protocols. It provides a comprehensive record of the suitability of the equipment to perform its specified task, to be created and archived.

Please see the ordering information for further details on our verification and qualification services.

DESIGN AND CONSTRUCTION

In common with the rest of the series, the DIS 8000 has been specifically designed to reduce clutter and maximise visibility and access in the critical sampling area above the water bath.

Particular emphasis has been placed on those factors affecting eccentricity, alignment and centring in order to reduce the number of parts used and hence keep the machine variables at a minimum.

BASKETS, PADDLES AND ROTATING CYLINDERS

All of the DIS series are equipped with precision ground drive shafts that will accept any of the baskets, paddles or rotating cylinders described in the respective Pharmacopoeia.

Individual clutches enable each individual basket/paddle to be raised, lowered or engaged independent of the drive head. This feature is particularly useful in the case of staggered starts, and at the end of the test allows the baskets/paddles to be pushed upwards to gain maximum accessibility to the vessels.

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DISSOLUTION TESTER DIS 8000

All stirring elements can be laser numbered and certified on request.

The construction of the **baskets and paddles** are such that they are completely **interchangeable**. Simply screw in the appropriate element, with no further height adjustment necessary.

All of the elements can be supplied with a 2.5 micron coating of gold for additional protection against aggressive media, if necessary.

VESSELS, VESSEL CENTRING AND LIDS

All Copley dissolution testers are supplied with USP/Ph.Eur. compliant vessels and feature the unique **'Easy-Centre'** system to ensure that the vessels are perfectly centred every time.

The 'Easy-Centre' system is based on a standard 1000 mL borosilicate glass vessel with a rim that has been precision ground and then centred accurately within a two-part acetal ring.

The acetal ring is provided with three bayonet fittings which locate in recesses provided in the vessel support plate. When turned clockwise these fittings lock the vessel into the correct position, relative to the drive shafts.

The fixture is designed such that once secured, the vessels will not become loose or float, even when empty.

All vessels can be numbered and certified on request. UV-resistant amber vessels are also available for those products sensitive to UV.

All vessels are supplied as standard with clear view acrylic lids. Special membrane-sealed two-part lids are available on request, where losses caused by evaporation may be an issue.

CONTROL AND MONITORING OF SPEED AND TEMPERATURE

All of the DIS series of dissolution testers have a speed range of 0-200 rpm.

The electronic speed control is provided with its own digital closed loop circuitry which guarantees an accuracy of **+/- 2%** by automatically checking and compensating for any drift from the nominal speed.

In the case of the DIS 8000, the temperature of the warming solution is controlled by means of a **self-priming 1200 W external heater/circulator**, which allows for rapid heating of the test media from ambient to the desired temperature.

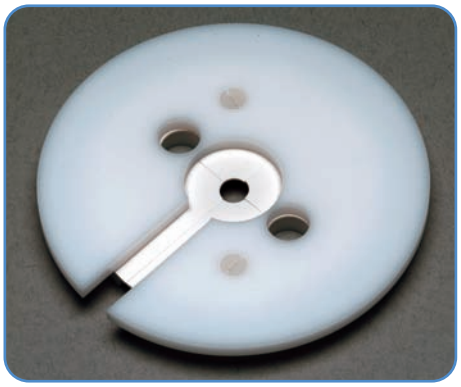
The heater/circulator has an accuracy of **+/- 0.5 degrees C** thus ensuring a constant and even distribution of heat throughout the bath. It is fitted with an **adjustable over-temperature cut-out** and alarm indicator, in addition to a **priming warning indicator** if there is insufficient water available.

The one-piece vacuum formed water bath is constructed in rigid PETG and has been specifically designed to eliminate leaks and to make it easier to clean. A fill-line is provided on each bath to indicate the level to which the bath must be filled.

The water bath and the easy-to-clean teflon-coated 316 stainless steel vessel support plate are supported by means of four stainless steel pillars and secured by four thumb screws.

The bath and vessel temperatures can be constantly monitored using the **PT100 temperature probe** provided for this purpose. Provision is made for logging the actual speed and temperature at user-defined intervals throughout the test for subsequent printing.

'Easy-Centre' Vessel Location

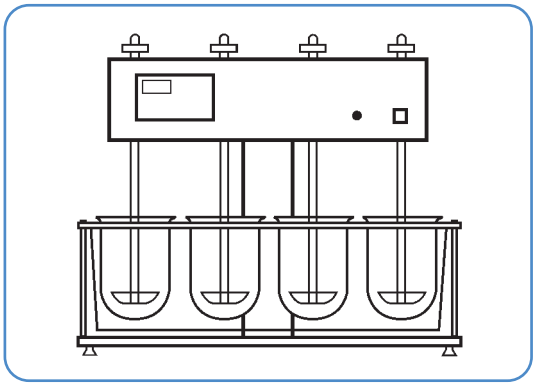


Two Part Membrane-Sealed Lid

External Heater/Circulator

CONTROL PANEL AND DISPLAY

TEMPERATURE CALIBRATION KIT



DISSOLUTION TESTER SCHEMATIC

DISSOLUTION TESTER DIS 8000

OPERATION

The control of all models is provided by a membrane keypad linked to a 4-line 20 character back-lit display, which together with the electronics is mounted in the head of the instrument so as to avoid any accidental spillages in the test area.

Many users have criticised the fact that their existing dissolution testers are overly complex with unnecessary software functionality for day-to-day use. For this reason, considerable attention was given in the design to ensuring that the number of actions necessary to perform a test was kept to a minimum.

Once the test sequence has been initiated, all that is necessary to start the test is to input the nominal rpm and nominal temperature, together with the duration of the test and the report interval (the time interval during the test at which the actual rpm and temperature is logged and subsequently reported), introduce the samples and press START.

During the test the following information is shown on the display:

- Nominal and actual rpm
- Nominal and actual temperature
- Preset test duration and time elapsed

An audible alarm alerts the user that the test is completed.

The dissolution tester is provided with a parallel printer connection as standard for print-out of time, date, bath i.d., serial number and date of calibration, together with the speed and temperature at operator selectable time intervals during the test.

CALIBRATION

Routine calibration is an essential part of your operation. Therefore a special calibration menu guides the user through the various functions and provides a printed report at the end of the operation.

One unique feature in this respect is the **electronic temperature calibration kit**. Ordinarily, temperature calibration can prove to be a time consuming and inaccurate process involving iced water. Available as an option, the electronic temperature calibration kit comprises two UKAS certified test keys (0 and 37 degrees C) which are simply plugged into the PT100 temperature probe socket to perform the calibration.

We offer a wide range of tools for calibrating your dissolution tester. Please see the appropriate information in the Dissolution Accessories section on page 20.

AUTOMATION

Manual dissolution testing is extremely time consuming and tedious. For this reason, many users are turning to complete automated systems to fulfill their requirements. In most cases, the software involved also controls the dissolution tester. Needless to say, this presents no problem for the DIS 8000.

The DIS 8000 has a bi-directional RS232 interface on the back panel which allows for communication with external devices and incorporation into automated systems.

DIMENSIONS

The DIS 8000 measures 650 mm (W) x 450 mm (D) x 640 mm (H) and the Heater/Circulator measures 260 mm (W) x 300 mm (D) x 150 mm (H).

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DISSOLUTION TESTER DIS 8000

SUMMARY OF KEY FEATURES

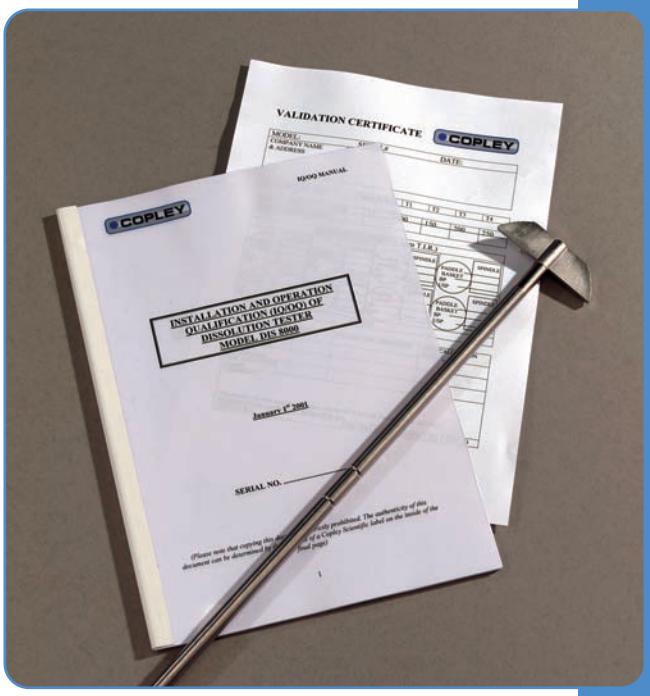
Standard

- Rugged, compact and easy-to-use
- Conforms to all current Ph.Eur. and USP specifications
- User friendly operating procedure via membrane keypad and 4-line LCD screen
- Screw-in baskets/paddles allow method changes in seconds such that no further adjustments are necessary
- Individual clutches allow each basket/paddle to be raised, lowered and engaged independent of the drive head
- Uncluttered design allows maximum access to working area
- 316 stainless steel teflon coated vessel support plate
- 'Easy-Centre' vessel centring dystem
- One piece PETG water bath; no leaks; easy to remove and clean
- Independent digital heater/circulator with over-temperature cut-out and indicator. Easily removed for maintenance
- Full printed test report on completion of the run (user selectable)
- RS232 bi-directional interface and parallel printer port
- Menu guided calibration procedure (with print-out)

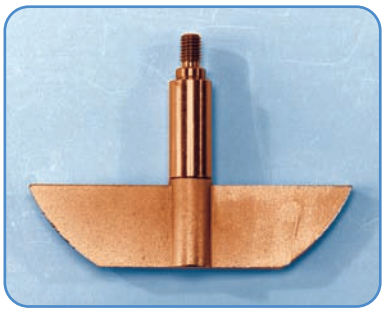
Options

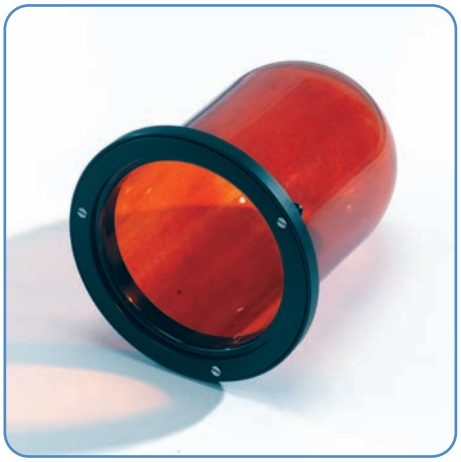
- Laser numbering, certification and IQ/OQ/PQ documentation
- Gold-plated baskets/paddles for aggressive media
- Amber coated UV-Resistant vessels and lids
- Low evaporation membrane sealed vessel lids
- Electronic temperature calibration kit

Cat. No.	Description
1301	Dissolution Tester DIS 8000 (incl. 8 Drive Shafts)
1302A	Set of 8 Baskets (Ph.Eur./USP Method 1)
1303A	Extra for Laser Numbering & Certification of above (8)
1304A	Set of 8 Paddles (Ph.Eur./USP Method 2)
1305A	Extra for Laser Numbering & Certification of above (8)
1306A	Extra for Numbering & Certification of Vessels (Set of 8)
1307	Printer
1308	Electronic Temperature Calibration Kit
1309	IQ/OQ/PQ Documentation Pack



IQ/OQ/PQ Documentation


Gold Plated Paddles


Amber Coated Vessels

DISSOLUTION TESTER DIS 6000

TEMPERATURE CALIBRATION KEY

HEATER/CIRCULATOR EMPLOYED ON THE DIS 6000

DISSOLUTION TESTER DIS 6000

In many laboratories, bench space is at a premium. The **DIS 6000** has been designed as a direct response to this problem. With a footprint of just 650 mm (W) x 450 mm (D) x 640 mm (H) the DIS 6000 is one of the most compact dissolution testers available on the market today.

The unit has **six stirred test vessels** arranged in two rows of three.

Heating is provided by an **independent 1250 W heater/circulator**, which obviates the need for priming and can be quickly removed for cleaning, without compromising the whole tester.

The heater/circulator is fitted with a special **low vibration impellor** which in comprehensive tests has proved to be equal to or less, in terms of vibration measurements than an independent heater/circulator. **A low water-level and over-temperature cut-out** is provided as standard.

A common complaint from customers is that their existing tester is overly complex with unnecessary software functionality for day-to-day use. For this reason, considerable attention was given in the design to ensuring that the number of actions necessary to perform a test was kept to a minimum.

Once the test sequence has been initiated, all that it is necessary to start the test is to input the nominal rpm and nominal temperature required, together with the duration of the test and the report interval (the time interval during the test at which the actual rpm and temperature is logged and subsequently reported), introduce the samples and press START.

During the test the following information is shown on the display:

- Nominal and actual rpm
- Nominal and actual temperature
- Preset test duration and time elapsed

An audible alarm alerts the user that the test is completed.

The dissolution tester is provided with a parallel printer connection as standard for print-out of time, date, bath i.d., serial number and date of calibration together with the speed and temperature at operator selectable time intervals during the test.

A bi-directional RS232 Interface on the back panel allows communication with external devices and incorporation into automated systems. In all other respects, the Dissolution Tester DIS 6000 is similar in construction to the DIS 8000 described on the preceding pages.

Cat. No.	Description
1311	Dissolution Tester DIS 6000 (incl. 6 Drive Shafts)
1302B	Set of 6 Baskets (Ph.Eur./USP Method 1)
1303B	Extra for Laser Numbering & Certification of above (6)
1304B	Set of 6 Paddles (Ph.Eur./USP Method 2)
1305B	Extra for Laser Numbering & Cetification of above (6)
1306B	Extra for Numbering & Certification of Vessels (Set of 6)
1307	Printer
1308	Electronic Temperature Calibration Kit
1309	IQ/OQ/PQ Documentation Pack

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AUTOMATIC TABLET DROP

The first procedure at the start of any dissolution test is to drop the samples into the individual vessels.

This function can be performed manually if desired: indeed, when using the DIS series of dissolution testers, this is relatively easy since the baths have been deliberately designed to reduce clutter and maximise visibility and access in the critical sampling area above the water bath.

However, this approach does mean employing a staggered start since it is very difficult to introduce all the samples simultaneously. For this reason, a correction factor has to be applied to the final results in order to take into account the time-lag between introducing the samples.

In order to obviate this problem, the dissolution tester can be fitted with an automatic tablet drop system.

With this system, the tablets are placed in a series of chambers on the dissolution vessel lids and ejected into the vessels simultaneously at the start of the test.

Cat. No.	Description
1312 A	Automatic Tablet Drop (DIS 8000)
1312 B	Automatic Tablet Drop (DIS 6000)

AUTOMATIC TABLET DROP

SAMPLING

Four different dissolution sampling systems are available according to user requirements.

The simplest method is to sample from each vessel using a **manual sampling cannula**.

The manual sampling cannula has a **luer fitting** to accept a 20 ml syringe (available as an optional extra) and is bent at the top to allow for easy positioning in the dissolution vessel.

Alternatively, we can offer **resident probes** designed to fit directly into the dissolution lid. Resident probes are designed to be left 'in-situ' in the dissolution vessel for the duration of the test - they can, of course, be removed between tests for cleaning.

All of the resident sampling probes are height adjustable to take into account the differences in sampling position required by the differing methods described in the Pharmacopoeia.

Two types of resident sampling probe are available:

1. For manual sampling (with **luer fittings** for manual sampling)

2. For automated systems: fitted with **'Omnifit' fittings** and used in conjunction with the return line inserts for use in automated systems.

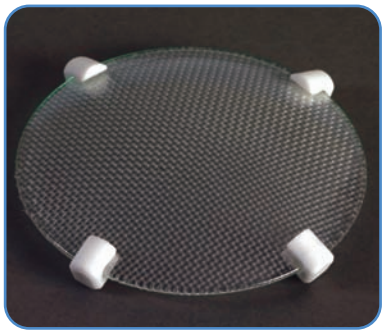
Note: See Page 20 for probe filters

Cat. No.	Description
1313	Manual Sampling Cannula Assembly (each)
1314	Resident Probe with Luer Fitting (each)
1315	Resident Probe with Omnifit fitting (each)
1316	Return Line Insert (each)
1317	Syringe for use with Cat.No.1313

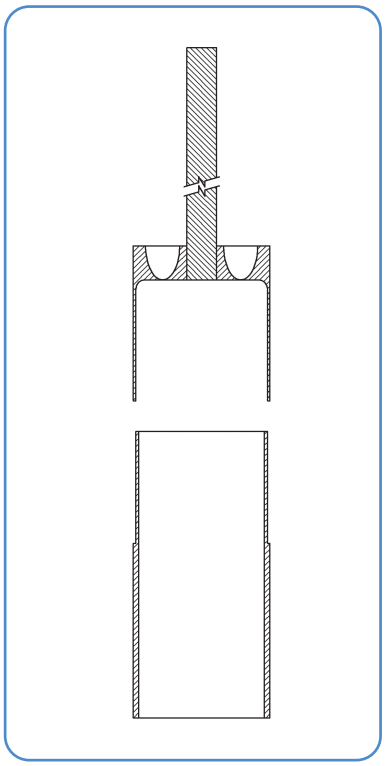
MANUAL SAMPLING CANNULA

RESIDENT PROBES AND RETURN INSERTS

PADDLE OVER DISC



WATCHGLASS/PATCH/PTFE ASSEMBLY



ROTATING CYLINDER

TRANSDERMAL PATCH TESTING

PADDLE OVER DISC

The 'Paddle over Disc' is a modified version of Method 2 (Paddle Method) and is used for the determination of the drug release rate of **transdermal patches**.

It is described in the United States Pharmacopoeia (USP) under Chapter <701> as Method 5 and in the European Pharmacopoeia (Ph.Eur.) under Chapter 2.9.4.1 as 'Disc Assembly Method'.

The **standard disc** comprises a 35 mm o.d. sieve having a pore size of 125 microns mounted in a stainless steel holder having a diameter of 41.2 mm and is designed to hold the transdermal patch at the bottom of the vessel.

It is suitable for all transdermal patches up to a maximum of 16 mm o.d. The transdermal patch is mounted on the disk release side up using a suitable adhesive (Hollister Medical Adhesive or equivalent).

A second and larger version of the disc comprising a 90 mm diameter **watchglass-patch-PTFE** assembly is available to accommodate larger patches. It is this second and larger disc assembly that is normally considered the method of choice since experimentation dictates that this procedure gives almost identical results with that of other, more complicated apparatus.

The assembled disc is placed at the bottom of the vessel parallel with the bottom edge of the paddle and the height of the paddle adjusted such that its bottom edge is 25 mm from the surface of the disc assembly.

The following parameters are normally considered representative of skin conditions 'in-vivo': -

* Media pH : 5 to 6
* Media Temperature : 32 degrees C
* Paddle Speed : 100 rpm

Cat. No.	Description
1384	Disc according to USP Method 5
1384A	Watchglass-patch-PTFE Assembly to USP Method 5
1385	Hollister Medical Grade Adhesive (90 gm spray)

ROTATING CYLINDER

An alternative method for the testing of **transdermal patches**, USP Method 6 (Ph.Eur. Method 2.9.4.3) employs the same dissolution equipment as Method 1 simply substituting a cylinder stirring element in place of the standard basket. The element is designed to accept various sizes of patches.

The protective liner of the transdermal patch is removed and the adhesive side placed on a piece of inert, porous cellulosic material (Cuprophan Type 150) that is not less than 1 cm larger on all sides than the system.

Using a suitable adhesive to the exposed borders of the Cuprophan support, attach the assembled system to the exterior of the cylinder such that the long axis of the system fits around the circumference of the cylinder. Employ the same conditions as Method 5 (above).

1386	Cylinder Stirring Element (USP Method 6)
1387	Cuprophan Flat Membrane 150 pm (10 Sheets)

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SPECIAL APPLICATIONS

SPECIAL BASKETS

Some dosage forms have a tendency to block the standard 40 mesh basket and may require the substitution of a basket having a coarser mesh. The mesh size selected should be sufficient to retain the dosage form in the basket whilst allowing solvent penetration without clogging.

Cat. No.	Description
1361	Basket only in 316 Stainless Steel (20 Mesh)
1362	Basket only in 316 Stainless Steel (10 Mesh)

SPECIAL BASKET (10 MESH)

BASKET FOR THE DISSOLUTION OF SUPPOSITORIES

Oil based suppositories give unacceptable and unreproducible results utilising the standard 40 mesh stainless steel dissolution basket, since the suppository base has a tendency to block the filter mesh.

The special basket for suppositories has the same basic basket specification as the standard USP basket but is constructed from polyurethane. The standard sieve mesh is replaced by 12 linear slots of 2.5 mm width providing a porosity of approx. 52% (approximately equivalent to the 10 mesh).

Cat. No.	Description
1363	Special Suppository Basket

SPECIAL BASKET FOR SUPPOSITORIES

MINI- PADDLE SYSTEMS / OINTMENT CELLS

Various conversion kits comprising special low volume vessels with appropriate mini-paddles are available for low dose formulations (100, 200 mL, etc.)

One version of the mini-paddle and vessel is used with the ointment cell, a variation on USP Method 5 suitable for topical preparations such as liquids, suspensions, gels and ointments.

Mode of operation is extremely simple: fill the cell reservoir with the transdermal preparation to be tested and secure with a suitable membrane (excised or artificial skin). Adjust the volume of the cell to ensure that contact between the sample and the membrane is maintained. Place the assembled cell into the bottom of the dissolution vessel and operate the paddle in the normal manner.

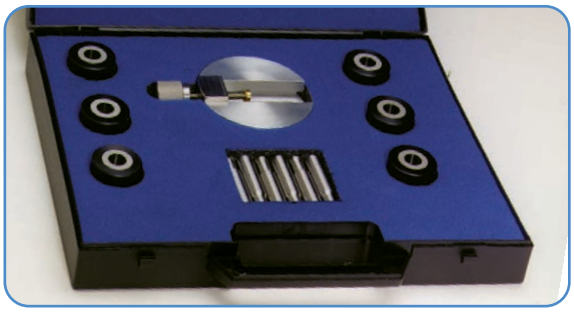
Cat. No.	Description
1371	Conversion Kit for Small Volumes (please specify)
1388	Ointment Cell

MINI-PADDLE SYSTEM / OINTMENT CELL

INTRINSIC DISSOLUTION

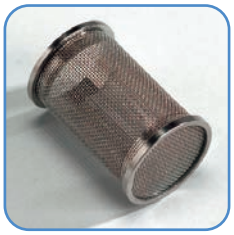
Intrinsic dissolution may be defined as the dissolution rate of a substance under the condition of constant surface area and is normally measured in terms of 'mg per minute per square centimetre'. It differs from the more conventional dissolution methods in that **only one 5 mm surface is exposed to the solvent** (dissolution media). The kit for intrinsic dissolution studies is based on the same principles as the apparatus described in USP Chapter <1087>.

Cat. No.	Description
1364	Kit for Intrinsic Dissolution Studies



KIT FOR INTRINSIC DISSOLUTION STUDIES

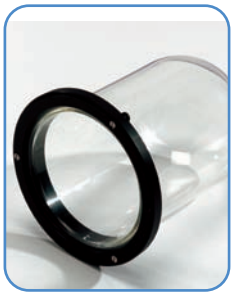
DISSOLUTION DRIVE SHAFT

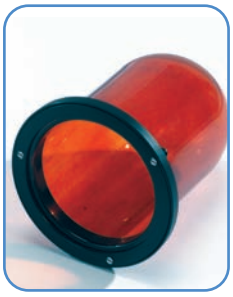


316 SS & GOLD PLATED BASKETS

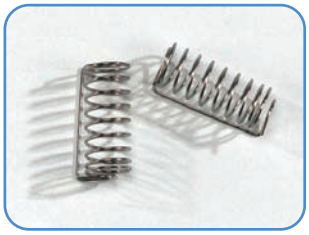
3 PRONG SPRING & BASKET HOLDER

316 SS & GOLD PLATED PADDLES

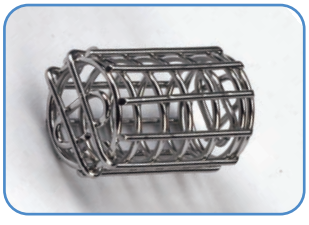




STANDARD & AMBER COATED VESSELS



316 SS & PLASTIC SINKERS



USP/PH.EUR. ALTERNATIVE SINKER

SPARE PARTS AND ACCESSORIES

Cat. No.	Description
	DISSOLUTION DRIVE SHAFTS
1329	316 Stainless Steel Drive Shaft only
1331	Extra for Laser Numbering and Certification
	BASKET STIRRING ELEMENTS (USP Method 1/Ph.Eur.)
1302	Basket **only** in 316 Stainless Steel (40 Mesh)
1303	Extra for Laser Numbering and Certification
1338	Basket Holder complete with Retention Spring (316)
1340	Extra for Laser Numbering and Certification
1336	3-Prong Retention Spring in 316 Stainless Steel
1333	Basket Stirring Element **complete** with Drive Shaft
1334	As above but gold-plated (2.5 micron)
1335	Extra for Laser Numbering and Certification
	PADDLE STIRRING ELEMENTS (USP Method 2/Ph.Eur.)
1304	Paddle **only** in 316 Stainless Steel
1305	Extra for Laser Numbering and Certification
1341	Paddle Stirring Element **complete** with Drive Shaft
1342	As above but gold-plated (2.5 micron)
1343	As above but **TEFLON** coated
1344	Extra for Laser Numbering and Certification
	VESSELS
1346	Vessel, 1000 mL, **with 'Easy-Centre'**
1347	Extra for Numbering and Certification
1349	Amber Vessel, 1000 mL, **with 'Easy-Centre'**
1350	Extra for Numbering and Certification
	VESSEL COVERS
1351	Vessel Cover, **Standard**
1352	Vessel Cover, **Standard**, UV Resistant
1353	Vessel Cover, Two-part Membrane Sealed
1354	Vessel Cover, Two-part Membrane Sealed, UV resistant
1355	Plug for Evaporation Cover
	CAPSULE SINKERS AND WEIGHTS
1356	Set of 6 316 Stainless Steel Sinkers
1357	Set of 6 Plastic Sinkers (3-Prong)
1345	USP/Ph.Eur. Alternative Sinker
1348	Wire, 316 Stainless Steel (50 ft length)

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SPARE PARTS AND ACCESSORIES

PERFORMANCE VERIFICATION TESTING (PVT)

These standardised drug forms supplied by USP (Rockville, Maryland, USA) have been formulated to produce reproducible results under standard dissolution test conditions. Thus, if the results using the reference standards prove satisfactory, it can be assumed that the physical and mechanical variables of the system are within the specified limits and that any anomalies are due to dosage form under test.

Cat. No.	Description
1373	Pack of 30 Prednisone Tablets - USP disintegrating
1374	Pack of 30 Salicylic Acid Tabs - USP non-disintegrating
1375	Prednisone Reference Standard (250 mg pack)
1376	Salicylic Acid Reference Standard (125 mg pack)

USP Reference Standards

CALIBRATION TOOLS

Cat. No.	Description
1377	Wobble Checker
1378	Height Checker
1379	Level Checker (Spirit Level)
1380	Temperature Checker (Digital Thermometer)
1381	Speed Checker (Tachometer)
1382	Centricity Checker
1383	Calibration Tool Kit complete
1367	Vibration Meter (not included in above)

Calibration Tools

HYGIENE: ANTI-BACTERIAL/ALGAE TABLETS

Bacterial or algal growth in dissolution tester water baths can be hazardous, malodorous and inconvenient. The addition of just one mL of Aqua-Stabil per month will prevent the build-up of bacteria and algae keeping the water clear, safe and odour free. Each pack contains 100 mL of Aqua-Stabil to maintain the clarity and quality of your water bath systems.

Cat. No.	Description
1372	100 mL Pack of Aqua-Stabil

FILTERS (ULTRA HIGH WEIGHT POLYETHYLENE)

Cat. No.	Description
1358	Pack of 50 Filters (20 Micron)
1359	Pack of 50 Filters (10 Micron)
1360	Pack of 50 Filters (4 Micron)

Aqua-Stabil & 20 Micron Filters

SUNDRIES

Cat. No.	Description
1365	Carrying Case for 6 Baskets and Paddles
1366	Carrying Rack for 6 Vessels
1367	Pack of 8 Peristaltic Pump Tubes (Green/Green)
1368	Pack of 8 Peristaltic Pump Tubes (Purple/White)
1369	8-Channel Colour Coded Ribbon Tubing (per metre)
1370	Pack of Connectors

Case for Baskets and Paddles

AUTOMATION

INTRODUCTION

The acceptance criteria quoted in the USP Chapters on Dissolution and Drug Release mean that a minimum of 6 and possibly up to 24 individual tests may be required per batch of formulation in order to meet pharmacopoeial requirements. Furthermore, the increasing use of extended and delayed-release preparations means that such tests may extend over 12, 24 hour or longer periods.

These demands together with the rise in multi-point testing brought about by the need for in-vivo/in-vitro correlation means that the dissolution or drug release test has now become one of the most common analyses employed in the pharmaceutical industry.

Manual dissolution testing is time consuming and labour intensive. As a result, an increasing number of laboratories are turning to automated tablet dissolution systems as a means of improving efficiency and reproducibility.

The advantages of automated systems are well documented i.e., improved methodology, accuracy, reproducibility and throughput, better use of human resources, etc.

One should balance against these advantages the costs involved in setting up, programming, validating, operating and most importantly maintaining the automated system concerned, for example, in the event of catastrophic breakdown.

Semi-automated systems that sample, filter, collect or UV/HPLC analyse can provide a valuable trade-off between manual and fully automated systems.

These can be classified into three categories: -

1. 'OFF-LINE' SYSTEMS (COLLECT ONLY)

Normally comprises a sample collector containing test tubes or vials, a peristaltic pump to provide the motive force to transport the samples from the dissolution tester to the collector and a PC and interface box to control the system during operation.

The principle of operation is simple - media from each of the dissolution vessels is circulated via an 8-line peristaltic pump through 8 switching valves prior to being returned to the dissolution vessel.

At user defined intervals the valves operate, diverting a preset volume of sample into the sample collection lines whereupon the samples are dispensed into either test tubes or open HPLC vials (or injected directly into sealed septum vials by means of an electrically operated vial piercing head provided for that purpose).

The pump is then reversed to clear the sampling lines prior to the next sampling interval whereupon the operation is repeated. The whole operation is controlled and monitored by a PC. The exact status of the test at any given time can be determined from the software.

In the case of test tubes, the samples must be handled manually, for example by presenting them to the "sipper" accessory of a suitable spectrophotometer. HPLC vials containing samples can be removed at any time and placed directly into an HPLC Autosampler.

This version is particularly useful where analytical techniques other than UV/VIS or HPLC are employed or where the samples require a degree of manipulation, for example to be diluted or mixed with a reagent prior to analysis.

TYPICAL 'OFF-LINE' SYSTEM INCLUDING DISSOLUTION TESTER DIS 6000 AND PUMP

TEL: +44 (0)115 961 6229 • FAX: +44 (0)115 961 7637

AUTOMATION

2. 'ON-LINE' DISSOLUTION SYSTEMS (UV/Vis)

Traditionally based on 'continuous flow' methods, 'on-line' dissolution systems incorporating UV/Vis analysis are understandably the most popular approach to automated dissolution testing.

Such systems are simple, clean, easy to set up and maintain.

In this technique, media from each individual test vessel is circulated continuously through each of a series of flow cells (nominally 6-8) located in the cell compartment of a suitable UV/Vis Spectrophotometer by means of a peristaltic pump.

A cell changer mechanism moves each cell in turn into the light beam of the spectrophotometer and the absorbance of each solution is measured. Measurements are made at user-specified intervals. The whole system is controlled by an external PC whose software collects and analyses the results. For highly absorbing drug formulations, the systems can be supplied with 1, 2 or 5 mm pathlength flow cells in place of the standard 10 mm giving effective dilution ratios of 10:1, 5:1 and 2:1 respectively.

The choice of spectrophotometer will depend to a large extent on cost and the degree of sophistication required i.e., single beam, double beam, etc.

Most UV/Vis continuous flow systems come 'ready-to-run' and are particularly easy to use; the operator being guided throughout the performance of the test by a series of on-screen prompts.

3. 'ON-LINE' DISSOLUTION SYSTEMS (HPLC)

Although UV is suitable for the analysis of the high proportion of drugs which exhibit active chromopore activity, in the case of certain dosage forms this approach is not practical. Furthermore, many formulations, for example, contain multiple components or excipients or coatings that interfere with UV analysis.

In these cases, **High Pressure Liquid Chromatography (HPLC)** may well provide the solution. The excellent specificity of HPLC makes it more sensitive than UV/VIS techniques for the analysis of sustained release products and of low dosage formulations.

However, these techniques tend to bring a new set of problems. Many of these problems emanate from the fact that the samples are collected in multiples of 6, 7 or 8 simultaneously, whereas the HPLC detector will only accept samples one at a time.

Furthermore, the time taken to perform the test may prohibit the immediate 'on-line' HPLC analysis of the collected samples, that is to say, there is insufficient time between the dissolution sampling intervals to allow for the analysis of 6-8 samples.

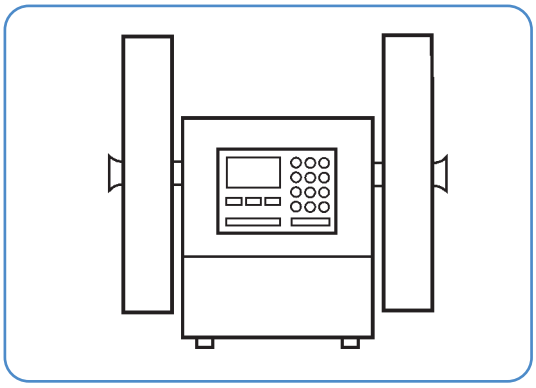
Modern 'on-line' HPLC systems are specifically designed to meet this eventuality in so much that the sampling station acts simply as a temporary storage vehicle for the dissolution samples; the collected samples are then aspirated sequentially to the appropriate detector.

Such systems provide for maximum flexibility in the sample/inject control sequence allowing separate timing of sample withdrawal and analysis whilst optimising throughput.

Our technical staff will be happy to discuss the various options available to you.

Typical 'On-Line' Dissolution System (UV/Vis) including DIS 8000 and Pump

FRIABILITY TESTER FR 1000



FRIABILITY TESTER SCHEMATIC

FRIABILITY TESTER FRV 2000

FRIABILITY TESTER SERIES FR & FRV

INTRODUCTION

Based on an original design by Roche, the friability tester has now become an accepted standard throughout the pharmaceutical industry for determining the resistance of uncoated tablets to the abrasion and shock experienced in manufacturing, packing and shipping operations.

Such stresses can lead to capping, chipping, abrasion or even breakage of the tablets.

Whilst the basic design remains unchanged, considerable advances have been made in terms of reliability and ease of usage which have now been incorporated into current units.

PHARMACOPOEIAL COMPLIANCE AND VALIDATION

In order to meet your individual requirements, Copley provide a three tier approach to regulatory compliance and validation.

- **Certificate of Compliance to USP/Ph.Eur.:** Included with each unit. Written statement that the product, by design, complies with the current pharmacopoeial specifications.
- **Laser Numbering and Certification:** Identification and measurement of critical components (i.e. the friability drum) to provide **documented verification** of compliance with pharmacopoeial requirements. Available as an optional service.
- **IQ/OQ/PQ Qualification Documentation:** Comprehensive documentation to guide the user through the installation, operating and performance checks of the equipment, in its operating environment, using specified test protocols. It provides a comprehensive record of the suitability of the equipment to perform its specified task, to be created and archived. Available as an optional service.

Please see the ordering information for further details on our verification and IQ/OQ/PQ services.

DESIGN AND CONSTRUCTION

Designed in accordance with the specifications as laid down in **Eur.Ph. Chapter 2.9.7** and **USP Chapter <1216>**, the FR Series forms the basis of our range of friability testers.

The standard FR Series operates at a **constant speed of 25 rpm +/- 1.** It is available in two variants, that is to say, with either **one (Model FR 1000) or two test drums (Model FR 2000)**.

Similar in construction to the fixed speed FR Series, the **Friability Series FRV** differs only in having **variable speed between 20 and 60 rpm**. The speed is controlled via the membrane keypad in steps of 1 rpm. The variable speed allows the operator to subject the tablets under test to varying stresses and therefore determine an optimum for each type.

As on the FR Series, the duration of the test can be selected in either revolutions of the drum (1-999,999) or time (up to 99 hours, 59 minutes, 59 seconds).

During the test run, the nominal test duration and remaining test duration, in either revolutions or time, is indicated on the LCD screen, together with the selected speed.

The control of all models is provided by a membrane keypad linked to a 4-line 20 character back-lit LCD screen.

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FRIABILITY TESTER SERIES FR & FRV

DRUMS

The friability drum has been designed for testing the rolling and impact durability of tablets and has a single curved baffle which allows the tablets to be tested to rise and then drop through a distance of approx. 156 mm. Premature fracture or sign of wear at the edges indicates that such tablets may not withstand the rigours of transportation.

All friability drums are now fitted with an aperture such that **it is no longer necessary to remove and open the friability drum in order to load and remove the samples**. At the start of the test, the drum automatically revolves until the aperture(s) faces the operator so that the tablets can be loaded. On completion of the test, the drum stops and then reverses automatically emptying the contents of the drum into the waiting collection tray(s). All friability drums are completely **interchangeable,** i.e. they will fit either side of the tester.

Abrasion drums for carrying out tests into attrition are also available as an optional extra. The Abrasion drum comprises of a drum 20 cm diameter with a series of baffles which carry the tablets to a predetermined height before sliding off and reproduces the action of the tablets rubbing against each other during transport.

All testers can be equipped with a choice of either USP friability drums and/or abrasion test drums. Dual drum units can for example be fitted with one friability and one abrasion drum thus allowing comparisons to be made between the two parameters under identical test conditions.

OPERATION

Considerable attention was paid to the design of the FR and FRV series to ensure that the number of actions necessary to perform a test are kept to a minimum. Consequently, once the method (number of revolutions or time) has been selected and the test duration set, it is only necessary to press the START key to initiate the test.

The standard test procedure is to take a sample of 10 tablets (a sample equivalent to 6.5 grams should be taken if the tablets weigh less than 650 mg), the weight of which has already been determined (W1). The tablets should be de-dusted prior to weighing.

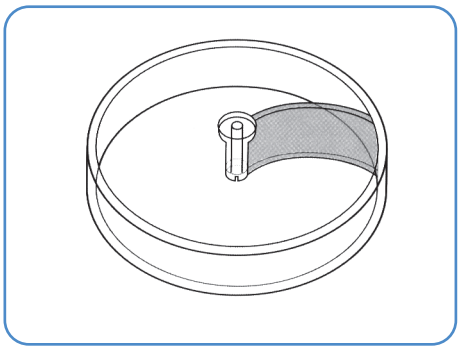
The tablets are then placed into the test drum and allowed to rotate 100 times. The tablets are then re-weighed (W2) having first removed any accumulated dust and the results calculated in terms of % weight loss utilising the formula (W1-W2) x 100 divided by W1.

In general, a maximum weight loss of not more than 1% is acceptable for most tablets. If necessary, repeat the test twice more basing the result on the mean of the three tests.

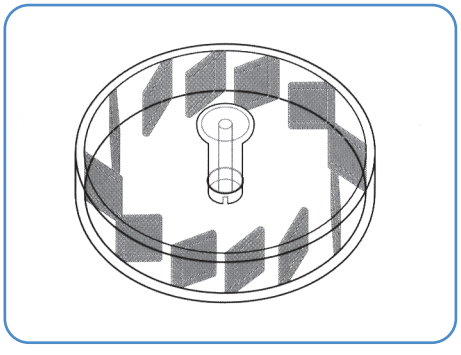
Dimensions (mm):
FR 1000 / FRV 1000 = 290 mm (W) x 360 mm (D) x 350 mm (H)
FR 2000 / FRV 2000 = 297 mm (W) x 360 mm (D) x 350 mm (H)

Cat. No.	Description
1401	Friability Tester FR 1000 (Fixed Speed - 1 Drum)
1402	Friability Tester FR 2000 (Fixed Speed - 2 Drums)
1403	Friability Tester FRV 1000 (Variable Speed - 1 Drum)
1404	Friability Tester FRV 2000 (Variable Speed - 2 Drums)
1405	Extra for Numbering & Certification (per Drum)
1406	IQ/OQ/PQ Documentation
1407	Abrasion Drum
1408	Friability Drum (Spare)
1409	Device for angling friability tester at 10 degrees

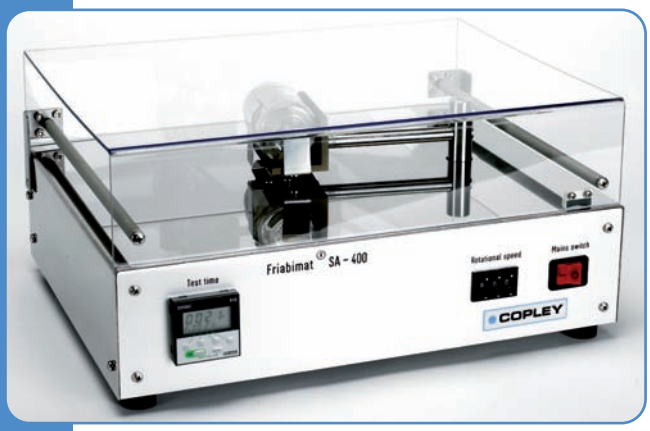
FRIABILITY TESTER FR 2000 WITH 1 FRIABILITY DRUM & 1 ABRASION DRUM



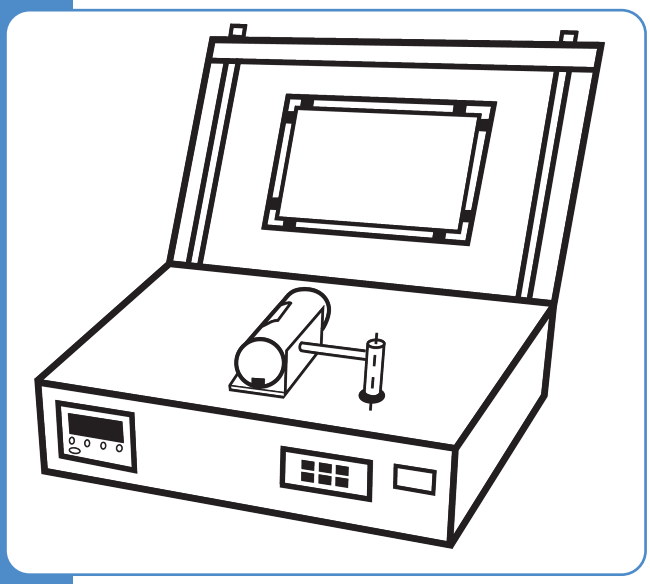
SCHEMATIC OF FRIABILITY DRUM



SCHEMATIC OF ABRASION DRUM



FRIABIMAT (WITH SAFETY LID CLOSED)



FRIABIMAT SCHEMATIC

FRIABIMAT

INTRODUCTION

In many cases, such as with **hard coated and uncoated tablets**, **granules and spheroids**, it is impossible to determine the friability of the dosage form using a conventional tablet friability tester (based on the Roche friability drum) even if the test time is extended simply because the resistance is such that no measurable attrition is obtained - the energy imparted by the friability tester is just not sufficient to generate quantifiable changes in surface mass.

The **Friabimat SA-400** is a new instrument specifically designed to address this particular problem by offering a method of friability measurement suitable for the hardest and most robust of solid dosage forms.

DESIGN AND CONSTRUCTION

The Friabimat was originally designed as a method to effectively determine the friability of hard pellets and granules prior to further processing, for example, drum coating under precisely defined, controlled and reproducible conditions.

The instrument is particularly useful in detecting variations in mechanical properties between different formulations and batches and is a convenient tool in both research and development and quality control applications.

Following review, the instrument has now been included in the 6th edition of the European Pharmacopoeia under **Chapter No. 2.9.41 Friability of Granules and Spheroids**.

This describes the Friabimat under **Method B Oscillating Apparatus 2.9.41.-2**.

The Friabimat's range of application has since been extended to include hard coated and uncoated tablets and other dosage forms which fall outside the scope of the standard friability tester.

For the purpose of the test, the sample to be tested is confined within a standard 105 mL glass bottle (measuring approx. 85 mm high x 49 mm i.d. with twist-off cap) which serves as the sample container.

During operation, this sample container is secured by means of a spring clip to the sample container holder horizontally mounted on the end of an oscillating arm having an arc of 37 degrees at a radius of 152 mm from the centre of oscillation.

The abrasive action is generated by the horizontal shaking movement of the oscillating arm which causes the samples to rub against and collide with each other and/or the internal surfaces of the sample container.

The intensity of the abrasive action and the duration of the test can be adjusted via the controls mounted on the front panel between 0 and 400 oscillations per minute and 0 and 9999 seconds respectively.

This enables the user to optimise the test conditions the test conditions applicable to each formulation and reproduce it at will.

Average test times are between 2 and 4 minutes. The combination of these short test run times together with the use of inexpensive, commercially available glass bottles as the sample container means that it is possible to carry out tests economically in batches as opposed to singularly on an infrequent basis.

The Friabimat measures 440 x 300 x 220 mm and weighs 13 kilos.

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FRIABIMAT

OPERATION

Adjust the number of oscillations to the desired frequency by adjusting the thumb wheel switches on the rotary speed adjuster mounted on the front panel to the appropriate setting (between 0 and 400 oscillations per minute).

Now set the test duration using the push button timer (between 0 and 9999 seconds).

Note: Shake for about 240 seconds at approx. 400 oscillations per minute for hard dose forms, or, for example, 120 seconds at 140 oscillations per minute for soft dose forms. Optimise these settings according to the dosage form concerned.

The Friabimat is now ready for operation.

Take a sample of the formulation to be tested and remove any fine particles present in the sample using a 355 micron sieve.

Weigh out approx. 10 grams (m_1) of the product into a sample container ensuring that the twist off cap is well secured. Now place the sample container into the spring clip fastening on the Friabimat provided to secure it and close the safety lid.

Start the test by pressing the appropriate key on the timer. The unit will switch off automatically on expiration of the preset time. The time remaining to the end of the test is displayed on the timer during operation.

Note: The Friabimat is fitted with a **safety interlock** which automatically pause operation if the safety cover is opened during a test. The test can be re-started once again by simply closing the lid.

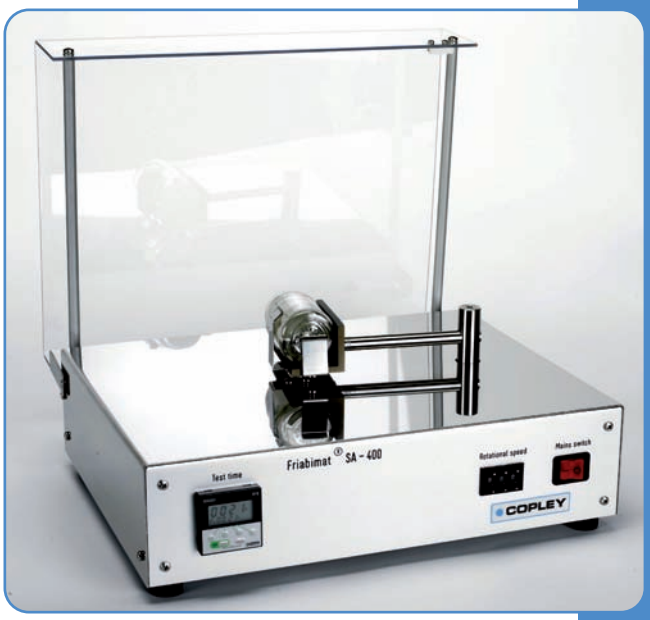
At the end of the test, sieve as at the start of the test and re-weigh (m_2). Perform three tests and calculate the mean value.

Express the results in terms of % weight loss using the formula (m_1-m_2) x 100 divided by m_1.

KEY FEATURES

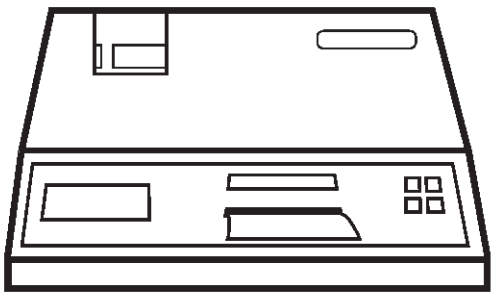
- Quantifiable friability of hard tablets, granules and pellets
- Bi-directional horizontal shaking action
- Programmable shaking rate (0-400 oscillations per minute)
- Programmable test times (0-9999 seconds)
- Stainless steel case for production environments
- Clear acrylic lid with magnetic interlock for safe operation
- Interchangeable glass sample containers for rapid throughput
- Oscillation frequency verification certificate (optional)

Cat. No.	Description
1450	Friabimat Model SA-400 including 1 Glass Container
1451	Oscillation Frequency Verification Chart
1452	Pack of 100 Spare Glass Containers

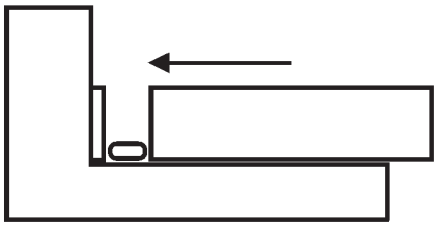


FRIABIMAT (WITH SAFETY LID OPEN)

OSCILLATING CONTAINER



TABLET HARDNESS TESTER TBF 1000



PRINCIPLE EMPLOYED IN BREAKING FORCE MEASUREMENT

INTRODUCTION

GENERAL

Modern day tablets come in a variety of forms: uncoated, coated, dispersible, effervescent, gastro-resistant, modified release, soluble, etc. Each type places different demands on the formulation concerned.

Manufacturing processes such as coating, printing and packaging and the rigours of handling and transportation place additional demands on the mechanical integrity of the finished product.

Together with friability testing, the testing of a tablet's **hardness** (or more correctly **breaking force***) plays a vital role in both product development and subsequent quality control.

In this test method, the tablet is placed between two platens (jaws), one of which is attached to a load cell and the other to a motor which provides the mechanical drive. During testing, the motorised jaw drives forward pressing the tablet against the fixed jaw until such time as the tablet fractures whereupon the motorised jaw retracts and the load required to fracture the tablet is measured.

High hardness values, for example, may increase disintegration times and decrease dissolution values. On the other hand, if hardness is too low then friability and hence % defective may well be too high.

By exploiting the correlation between hardness, disintegration, dissolution, friability, % defective and weight variation, the various parameters can be manipulated to produce a dosage form with optimal characteristics.

Significant advances have been made in the field of tablet hardness testing in recent years.

Copley Scientific offers a range of mechanical and electronic testers incorporating these advances and varying in sophistication from simple hand held testers for use on the production floor to fully automatic units incorporating print-out and data input/output facilities.

UNITS OF MEASUREMENT

The units of force normally employed to quantify breaking force are kiloponds or newtons.

Comparative values for these are as follows:

1 kilopond (kp) = 1 kilogram-force (kgf) = 9.80665 Newtons (N).

A kilopond is the force exerted by a mass of one kilogram in earth's gravity.

*** Note :**

The **United States Pharmacopoeia** describes the breaking force of a tablet as being the force required to cause it to fail (i.e., break) in a specific plane.

Traditionally, the **breaking force** of tablets has always been referred to as *hardness*. However, as USP points out, this term is really a misnomer since *hardness* refers to the resistance of a surface to penetration or indentation by a probe e.g., penetrometer.

The European Pharmacopoeia, on the other hand, uses the term **crushing strength**. Purists would, no doubt, argue that, in many cases, the tablet is not actually crushed, merely fractured, and that the term *strength* implies tensile strength as opposed to compressive load.

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MONSANTO TABLET HARDNESS TESTER

An inexpensive manual unit particularly useful for the press operator as it is extremely simple to use and can be slipped conveniently into the pocket. The instrument is designed to accept tablets up to 13 mm diameter and as small as is practical.

The tablet is placed between an anvil and a spring loaded pressure plunger. Pressure is then applied to the tablet via the plunger by means of a screw thread until the tablet fractures whereupon the force applied to break the tablet can be read from the graduated scale.

The scale is graduated between 0 and 20 kp and readings may be approximated to 0.25 kp. The units measures 210 mm long x 30 mm in diameter.

The hardness of the tablets will vary depending on their composition, the method of granulation and the pressure applied by the press. The use of this simple tool enables the operator to constantly monitor the product during the tabletting run.

Cat. No.	Description
7001	Monsanto Tablet Hardness Tester

Monsanto Tablet Hardness Tester

COPLEY TABLET HARDNESS TESTER TH3

A portable semi-automatic electronic tester with LCD display designed to accept tablets up to 30 mm in diameter - ideal for the tablet production area as a quick check as to compression force settings.

The tablet is placed on the test platform between the test jaw and the load cell plunger.

A multi-turn low-friction hand-wheel similar to the type used on machine tools is used to apply load to the tablet until it fractures. The resulting breaking force is displayed on the LCD display in either newtons (N), grams (g), pounds (lbs) or ounces (oz).

To test another tablet, simply press <Zero> to zero the load cell and proceed as above.

Two models are available, the TH3/200 having a range of 200 Newtons +/- 0.04N or the TH3/500 having a range of 500 Newtons +/- 0.1 N respectively.

The TH3 is provided with RS232, Mitutoyo and analogue data output facilities as standard. All displayed readings can be transmitted to peripheral devices, for example, a PC or printer, by pressing the <TXD> key. Alternatively, a PC can request data from the unit by sending a <?> character to the RS232.

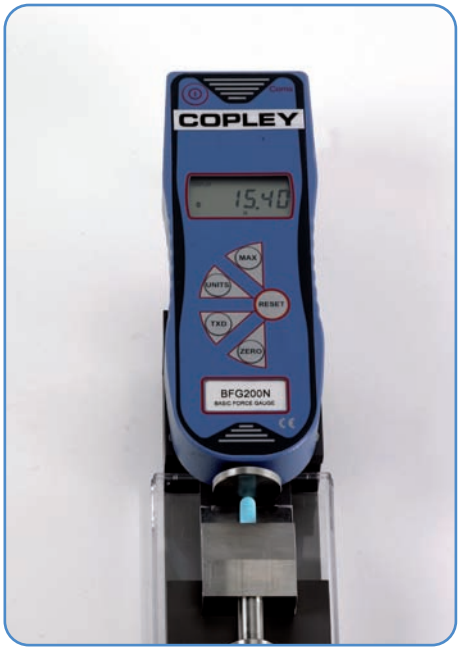
Provision is also made for a footswitch.

The unit measures 450 x 70 x 80 mm and weighs approx. 2 kilos and can be operated in either mains or battery modes. It includes a calibration certificate and mains adaptor/charger as standard.

The instrument performs an automatic self test (zero calibration routine) on switch on.

Cat. No.	Description
7801	Tablet Hardness Tester Model TH3/200
7802	Tablet Hardness Tester Model TH3/500
7803	Re-Calibration Certificate
7804	Calibration Verification Hanger & Weight

Tablet Hardness Tester Model TH3



Tablet Hardness Tester Model TH3

TABLET HARDNESS TESTER TBF 1000

Tab No.	Weight (mg)	Thick (mm)	Hard (kg)
1	379	3.25	5.19
2	379	3.25	5.31
3	380	3.24	5.54
4	380	3.24	5.47
5	379	3.26	5.02
6	378	3.25	4.98
7	381	3.25	5.28
8	380	3.26	5.05
9	379	3.23	4.92
10	380	3.25	5.30

BATCH STATISTICS

Batch No. 1
Batch Size: 10
Min: 4.92 kg
Max: 5.54 kg
Mean: 5.21 kg
Std. Dev: 0.21
Time: HH:MM DAY DD/MM/YY
Calibration No: 00004

TYPICAL PRINTOUT

COPLEY HARDNESS TESTER TBF 1000

The Copley Tablet Hardness Tester Model TBF 1000 combines the economy of a simple easy-to-use tester with the performance and accuracy of microprocessor controlled data collection.

It was designed in accordance with the specifications as laid down in **Ph.Eur. Chapter 2.9.8 *Resistance to crushing of tablets*** and **USP Chapter <1217> *Tablet Breaking Force***.

Foremost in the design specification were those features that you, the user, identified as being essential to the **'ideal'** hardness tester.

You told us, for example, that the unit must be as **compact** as possible such that it could be used in the confines of the tablet press booth.

Measuring only 283 mm wide x 235 mm deep x 160 mm high (including in-built printer and optional keyboard) and weighing 8.5 kilos, the TBF 1000 has the smallest footprint of any hardness tester on the market making it ideal for this purpose.

You told us that the unit should be **simple to operate** - the TBF 1000 employs just three touch sensitive keys located on the front panel to set up, perform a test and provide a print-out of the results, namely <*New Size*>, <*Test*> and <*Stats*> - nothing could be more simple.

At the same time, you asked for a number of **advanced and sophisticated features** - so, we provided them plus a small QWERTY keyboard located in the base of the instrument to access them.

The 4 line on-screen menu leads you through the measuring process. Attach a balance and/or thickness gauge and the TBF 1000 will collect **weight and thickness data** as well.

On completion of the test, the TBF 1000 automatically prints out the results and **statistical analysis** including time, date, min, max, mean and standard deviation together with the batch number and size.

Finally, you asked us whether it would be possible to **output data** to an external PC or printer - so, on the back of the unit, in addition to the interfaces for balance and thickness gauge, we have provided two further ports, one RS232 and one USB, to satisfy this request.

PRINCIPLES OF OPERATION

The principle of measurement is based on proven electronic load cell technology used in conjunction with a mechanical drive and electronic signal processing.

In practice, the tablet is placed on a platform between two precision-ground platens (jaws), one of which is attached to the load cell and the other to a motor which provides the mechanical drive.

During testing, the motorised jaw drives forward pressing the tablet against the fixed jaw until such time as the tablet fractures whereupon the motorised jaw retracts and the change in the resistance of the strain gauge employed on the load cell (the breaking force) is measured.

The pressure to the tablet can be applied in two ways. Most modern testers including the TBF 1000 work on the principle of **constant speed** (that is to say, the rate of jaw movement). Other units, mainly earlier models, monitor the rate at which the compressive force is applied i.e., **constant loading**.

Irrespective of which method is employed, it is essential that the uniformity and rate of loading be constant in order to assure comparability of results.

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COPLEY HARDNESS TESTER TBF 1000

In general, the lower the speed or load, the more consistent the results. The **US Pharmacopoeia**, for example, suggests a constant platen movement of less than 3 mm per second.

Needless to say, the TBF 1000 offers a choice of speeds between 0.06 and 0.5 mm per second with a default setting at 0.1 mm per second, all of which exceed the pharmacopoeial requirement by a considerable margin.

The standard TBF 1000 has a measuring range of **0 - 520 Newtons (+/- 0.1N)**. Other ranges, for example 50N and 1000N are available on request - please consult our technical staff for further details.

The unit will accept tablets up to **36 mm in diameter**.

Results can be expressed in either **kilograms-force (kgf)**, **kiloponds (kp)**, **newtons (N)** or **pounds (lbs)**.

The TBF 1000 has a **throughput** of approx. 5-8 tablets per minute dependent on the hardness and diameter of the tablets under test.

OPERATION

1. Setting up for a new tablet

Press the <*New Size*> key - the motorised jaw will retract allowing the operator to insert the new tablet between the jaws before advancing once again to press the tablet lightly against the fixed jaw.

This contact is detected by the load cell electronics which in turn instructs the motorised jaw to retract to the *Test* position approximately 5 mm wider than that of the diameter of the tablet. The **diameter** of the new tablet together is printed out on the in-built printer.

The unit is now ready to carry out a test.

2. Carrying out a test

Place a tablet on the test platform, lower the guard and press <*Test*> twice. The moving jaw will fast forward (2 mm per second) until it reaches a position approx. 0.2 mm from the tablet and then change to the test speed (default 0.1 mm per second).

The increase in load once the moving jaw reaches the tablet is displayed on the LCD display together with the **tablet count**, the time and date.

Tablet fracture is detected automatically - once detected, the result is printed out on the printer and the moving jaw retracts back to the *Test* position ready for the next sample.

Testing of the next sample can be initiated in two ways depending on the set-up mode (a) by pressing the <*Test*> key or (b) by lowering the guard.

The tablet testing position is arranged for horizontal loading and incorporates a removable tray in order to dispose of any **tablet debris**.

3. End of Batch - Statistical Analysis

Ph.Eur. and **USP** recommend that 10 and at least 6 samples are tested respectively.

At the end of the test, to initiate the print-out and re-zero the tablet count, press <*Stats*>. A further batch of tablets can now be tested.

TABLET DEBRIS COLLECTION TRAY

TBF 1000 (WITH KEYBOARD OPTION)

REAR PANEL

CALIBRATION

COPLEY HARDNESS TESTER TBF 1000

ADVANCED FEATURES

The TBF 1000 has been specifically designed such that all basic day-to-day operations can be performed using the four touch sensitive keys located on the front panel. Other obvious features like the **safety guard** system which prohibits operation unless closed, the tablet **debris collection tray**, the integral 30 column **printer** and **keyboard drawer** are, of course, included as standard.

This outward simplicity disguises the many special sophisticated and advanced features available to the user via the **setup menu** which may be accessed through the optional **keyboard**. This feature is **passcode protected** to prevent unauthorised changes to operational settings.

In the original design brief for the TBF 1000, considerable emphasis was placed on providing the user with the ability to configure the unit to their own specific needs.

This emphasis is reflected in the setup menu. In addition to basic settings such as time and date, units (kgf, kp, N or lb), test speed (4, 6, 10, 16 or 30 mm/min), PC interface (RS232 or USB) and LCD backlight functions, the user can also configure the way in which the unit actually operates: the print format, the way in which the unit interfaces with other peripherals and the calibration of the instrument.

Operational settings include the ability to change the way in which batches are counted and incremented, whether a test is instigated via the <*Test*> key or simply closing the safety guard and the fracture detect percentage, a particularly useful feature for soft crumbly or extra hard tablets.

During a test, the load cell constantly monitors the increasing force applied to the tablet. The breaking point of the tablet is said to have been reached when the force falls to a set % (the fracture detect percentage) of the maximum (peak) load reached during that particular test. The default setting for this percentage is 70% - it can however be adjusted if circumstances dictate between 30 and 90%.

Print format settings include options available to enable or disable start-up messages, the print-out of individual tablet results and diameter print-out, together with the provision to enter product names and operator identities (requires optional keyboard).

Peripheral and **calibration** settings allow the user to connect the hardness tester to a balance and/or a micrometer for measuring thickness and to calibrate the instrument, respectively.

SYSTEM SUITABILITY

The TBF 1000 incorporates an automatic load check routine that runs automatically every time the unit is switched on.

This routine imposes a simulated load of known proportions. The simulated load and the difference between this and the value stored at the last full calibration are displayed on the LCD.

A difference of > 0.1 kg, for example, would suggest a potential problem and the need for recalibration (see below).

CALIBRATION

All tablet hardness testers should be calibrated on a periodic basis, for example, monthly or quarterly.

Calibration on the TBF 1000 can be carried out 'in-house' and takes only a few minutes using the calibration rig provided for this purpose. It is based on a 'static' calibration technique using calibrated weights traceable to national standards.

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COPLEY HARDNESS TESTER TBF 1000

The user is guided through the passcode protected calibration process by a series of prompts from the in-built software accessible from the setup menu.

A full report is printed out at the end of the calibration process.

An individual calibration number is generated on each occasion the unit is calibrated and reiterated on subsequent test printouts - this ensures that any test printout is traceable to a specific calibration certificate.

IQ/OQ/PQ QUALIFICATION DOCUMENTATION

Analytical Instrument Qualification is no doubt an essential element of your quality control procedures. The following documentation is available in helping you to meet these obligations:

- **Certificate of Compliance to USP/Ph.Eur.:** Included with each unit. Written statement that the product, by design, complies with the current pharmacopoeial specifications.

- **IQ/OQ/PQ Qualification Documentation:** (option) Comprehensive documentation to guide the user through the installation, operating and performance checks of the equipment, in its operating environment, using specified test protocols. It provides a comprehensive record of the suitability of the equipment to perform its specified task, to be completed and archived.

WEIGHT AND THICKNESS MEASUREMENT

The versatility of the TBF 1000 does not end with the measurement of hardness - simply add a balance and/or a Mitutoyo micrometer for measuring thickness and you have a complete system for measuring the **hardness**, **weight** and **thickness** of tablets and similar objects with the same capabilities as many of the more sophisticated systems that are commercially available.

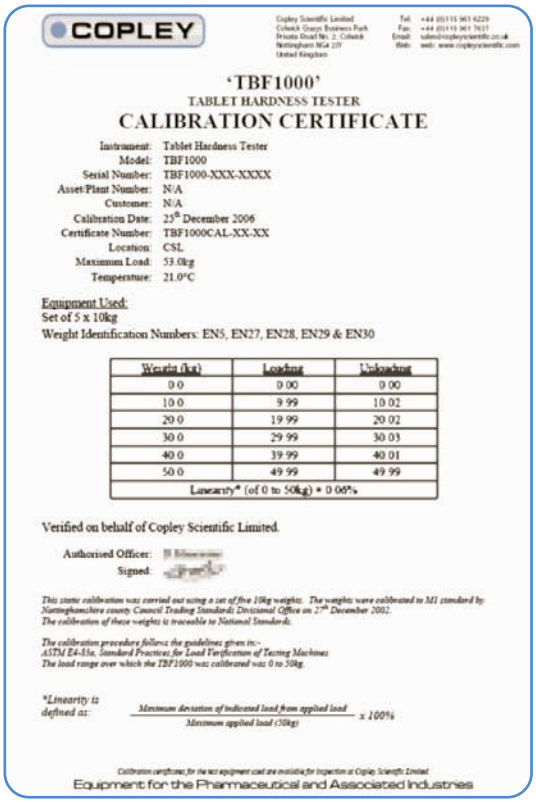
A list of compatible balances (by make and model) may be found in the setup menu - please consult our technical staff for further details.

Weight and thickness measurements are conducted in a similar manner to that of hardness (see section on **OPERATION** on Page 30).

If, for example, both weight and thickness are enabled, then at the start of the test the LCD display will show *Weight* - the operator should then place the tablet on the balance, wait for the weight to stabilise and then press <*Test*>. The weight of the tablet will now be displayed and the LCD will show *Thickness* to request a thickness measurement. Remove the tablet from the balance pan, place it in the micrometer and press <*Test*>. Repeat the exercise for hardness.

At the end of the individual tests, the results relating to all three parameters are printed out on the printer.

Cat. No.	Description
2501	Tablet Hardness Tester Model TBF 1000
2502	Compact Keyboard (optional)
2503	Calibration Rig
2504	Set of Weights for above (4 x 10 kg, 2 x 5 kg)
2505	IQ/OQ/PQ Documentation Pack
2506	Pack of 10 Paper Rolls
2507	Sartorius Balance Model CP324S
2508	Mitutoyo Thickness Measuring Gauge



COPLEY

'TBF1000'
TABLET HARDNESS TESTER
CALIBRATION CERTIFICATE

Instrument: Tablet Hardness Tester
Model: TBF1000
Serial Number: TBF1000-XXX-XXXX
Asset/Plant Number: N/A
Customer: N/A
Calibration Date: 25th December 2006
Certificate Number: TBF1000CAL-XX-XX
Location: CSL
Maximum Load: 53.0kg
Temperature: 21.0°C

Equipment Used:
Set of 5 x 10kg
Weight Identification Numbers: EN5, EN27, EN28, EN29 & EN30

Weight (kg)	Loading	Unloading
0 0	0 00	0 00
10 0	9 99	10 02
20 0	19 99	20 02
30 0	29 99	30 03
40 0	39 99	40 01
50 0	49 99	49 99
Linearity* (of 0 to 50kg) = 0 06%		

Verified on behalf of Copley Scientific Limited.

Authorised Officer:
Signed:

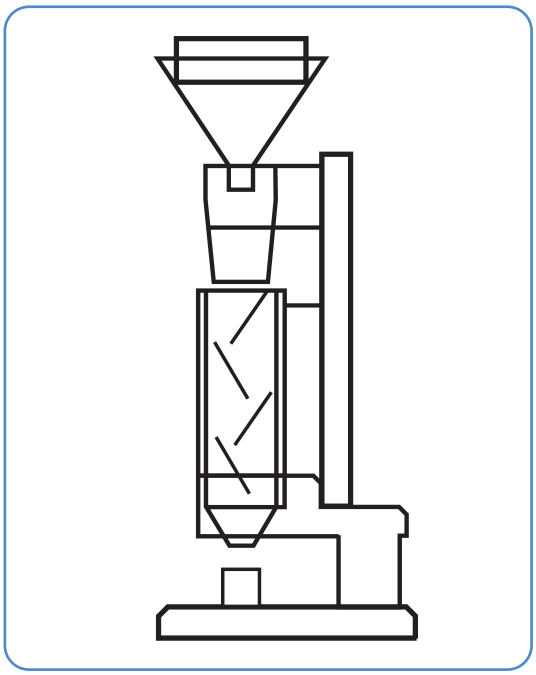
Linearity is defined as: $\frac{\text{Maximum deviation of indicated load from applied load}}{\text{Maximum applied load (50kg)}} \times 100\%$

Equipment for the Pharmaceutical and Associated Industries

CALIBRATION CERTIFICATE

WEIGHT & THICKNESS MEASUREMENT

Scott Volumeter USP <616>



Schematic of Scott Volumeter

BULK DENSITY TESTER

THE SCOTT VOLUMETER

The bulk density of powders can be extremely difficult to measure since the slightest disturbance may result in a change in the results.

This is the result of the relationship between the particles that constitute the powder bulk. This same relationship effects the ability of the powder to flow.

The bulk density of a powder may be described as the density of the powder 'as poured' into a measuring vessel.

Tapped density, on the other hand, is the density attained after 'tamping down': this is normally measured using an instrument that lifts and then drops a measuring cylinder containing the powder through a fixed distance (see the Tapped Density Tester described on the next page).

A comparison of the bulk and tapped densities of powders can give an indication of the type of interaction present between the various particles making up the powder mass and hence provide an index of powder flowability (see ***Compressibility Index*** and ***Hausner Ratio*** described on the next page).

The **Bulk Density Tester (Scott Volumeter) is described in USP Chapter <616> Method 2** and is designed for measuring the **bulk density of fine powders** and similar products.

CONSTRUCTION

The apparatus comprises:

- A stainless steel top funnel having an integral SS 18-mesh screen
- A baffle box containing four glass baffle plates over which the powder slides and bounces as it passes
- A stainless steel bottom funnel to direct the powder into the receiving cup
- A cylindrical receiving cup having a capacity of 25 +/- 0.05 mL
- A stand available in either metal or wood to support the apparatus and to ensure that the cup when placed in position is exactly 19 mm from the bottom of the funnel

MODE OF OPERATION

1) Weigh the empty receiving cup and place it in position

2) Slowly pour the powder through the upper funnel until it overflows the receiving cup. (Note: Use a minimum of 35 cubic cm)

3) Level the top of the receiving cup with a spatula such that it is completely full being careful not to compress or shake the powder

4) Re-weigh the receiving cup and its contents

5) Calculate the bulk density in terms of grams per mL by dividing the weight of the powder by the volume of the cup

Cat. No.	Description
6301	Scott Volumeter (USP <616> Method 2) in Metal
6302	Scott Volumeter (USP <616> Method 2) in Wood

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TAPPED DENSITY TESTERS SERIES JV

The Tapped Density Testers Series JV have been designed to measure the tapped density of powders, granules and similar products in accordance with **USP Chapter <616> Method 2** and **EP Chapter 2.9.15**.

This technique is particularly useful in powder flowability studies and also in determining the amount of settlement during transit to optimise pack sizes e.g. washing powders.

Tapped density is achieved by mechanically tapping a measuring cylinder (i.e. raising the cylinder and allowing it to drop a specified distance under its own weight) containing the sample under test.

Two versions of the tester (JV 1000 and JV 2000) are available dependent on the number of test stations required (1 or 2). Both versions utilise 250 mL measuring cylinders as standard, however 100 mL cylinders together with appropriate platforms are also available if required.

Both of the instruments concerned are equipped with membrane keypads for setting the number of strokes or time and an LCD screen to set the appropriate parameters and monitor the progress of the test.

MODE OF OPERATION

The mode of operation is identical on both models.

Weigh out a predetermined amount of the sample, say 100 g +/- 0.1%, place it in the graduated cylinder provided and note the unsettled volume. Secure the graduated cylinder to the test platform of the tester using the bayonet fitting provided for this purpose.

Unless otherwise specified, set the number of taps via the membrane keypad on the front of the instrument to 500 and operate the device making a note of the resulting tapped volume. Repeat this operation for a further 750 taps noting the volume once again. Continue repeating the test in increments of 1250 taps until the difference in tapped volume is less than 2%. Note the final reading.

The **tapped density in grams per mL** can now be calculated by dividing the sample weight by the final tapped volume.

Measures of the ability of the powder to flow and its compressibility can now be given in the form of the **Hausner ratio** (Tapped Density/Bulk Density) and the **Compressibility Index** ((Tapped Density - Bulk Density/Tapped Density) x 100).

In a free flowing powder, inter-particulate interaction is less significant and unsettled and tapped densities will be closer in value. In poorly flowing powders, the inverse is to be expected. It follows that the closer the Hausner ratio is to 1, the better the flow. Powders with poor flow generally have a ratio of greater than 1.25.

A special **acoustic cabinet** is available on request. The tapped density testers measure 280 mm (W) x 250 mm (D) x 670 mm (H).

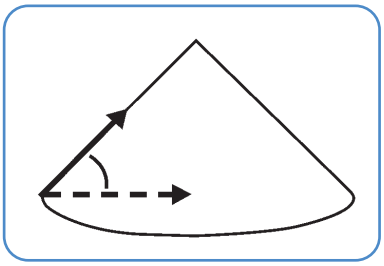
Cat. No.	Description
1601	Tapped Density Tester JV 1000 (1 Cylinder)
1602	Tapped Density Tester JV 2000 (2 Cylinders)
1603	IQ/OQ/PQ Documentation
1604	250 mL Measuring Cylinder for above (spare)
1605	100 mL Measuring Cylinder for above (option)
1605A	Special Platform for use with 100 ml Cylinder (option)
1606	Acoustic Cabinet

JV 1000 (One Cylinder Version)

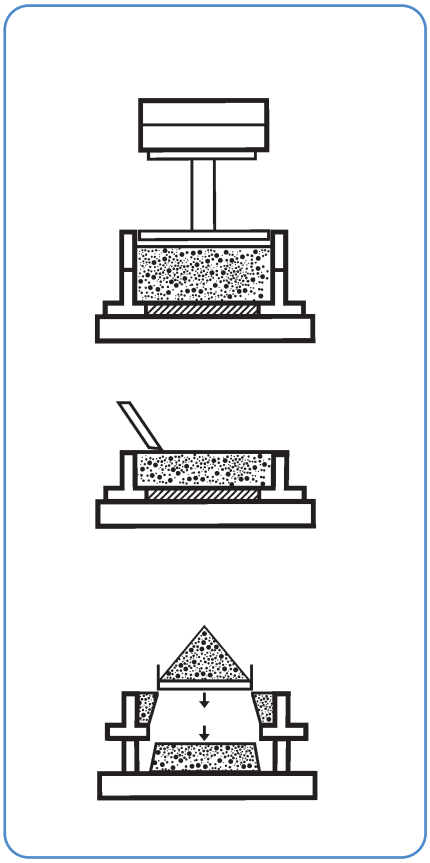
JV 2000 (Two Cylinder Version)

SCALE OF FLOWABILITY

Compressibility Index (%)	Flow Character	Hausner Ratio
< 10	Excellent	1.00 - 1.11
11-15	Good	1.12 - 1.18
16-20	Fair	1.19 - 1.25
21-25	Passable	1.26 - 1.34
26-31	Poor	1.35 - 1.45
32-37	Very poor	1.46 - 1.59
> 38	Very, very poor	> 1.60



Angle of Repose



Shear Cell (See Page 37)

BEP with Cylinder Attachment

FLOWABILITY TESTER MODEL BEP

INTRODUCTION

The Flowability Tester BEP has been specifically designed to address the specifications in and comments raised by the **European Pharmacopoeia Chapter 2.9.36** and the **US Pharmacopoeia Chapter <1174>** on **Powder Flow**.

The widespread use of powders in the pharmaceutical industry has led to a proliferation of test methods for measuring powder flow. As the pharmacopoeias point out, to be useful, any such method must be simple, practical, sensitive, reproducible and yield meaningful results.

The **harmonised** Ph.Eur. Chapter 2.9.36 and USP Chapter <1174> on powder flow have been introduced in order to standardise the methodology concerned.

The result is a list of four methods:

1. Compressibility Index and Hausner Ratio
3. Flow through an Orifice
3. Angle of Repose
4. Shear Cell

The **Compressibility Index** and **Hausner Ratio** (see 1. above) are functions of the bulk and tapped densities of a powder and are described in detail on the previous two pages.

All of the other three tests can be performed using the Flowability Tester BEP equipped with suitable attachments (see below).

The Flowability Tester Model BEP was originally designed to measure the flowability of powders and granules based on the **flow through an orifice** principle.

More recently, the versatility of the instrument has been extended to include **angle of repose** and **shear cell** measurements.

CYLINDER ATTACHMENT (FLOW THROUGH AN ORIFICE)

Measuring the time it takes for a powder to flow through an orifice of known size is a useful method of quantifying powder flow. As the title suggests, this technique is only suitable for materials capable of flow - not for cohesive materials.

At the same time, it is important to recognise that the ability of the powder to flow through the orifice can be affected by factors other than the characteristics of the powder itself.

Such factors include the shape and material employed in the construction of the powder container, the diameter and height of the powder bed and the shape and diameter of the orifice concerned.

The Pharmacopoeia suggest that the use of a circular cylinder as the powder container encourages powder over powder flow as opposed to powder over container wall minimising any effect brought about by differences in the material used to produce the powder container.

Furthermore, providing that (a) the height of the powder bed (the 'head') is much greater that that of the orifice, (b) the diameter of the opening is greater than 6 times the diameter of the particles and (c) the diameter of the cylinder is greater than 2 times the diameter of the opening then any differences in results brought about by either powder bed or orifice can be considered negligible.

The **cylinder attachment** has been designed to take all of these factors into account.

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FLOWABILITY TESTER MODEL BEP

The cylinder attachment comprises a stainless steel **cylinder** having a capacity of 200 ml combined with a **flat-faced bottom plate** incorporating various orifice diameters.

A series of stainless steel discs are supplied as part of the attachment each containing a precision drilled hole in the centre covering the following sizes: 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30 and 32 mm.

Each disc can be easily attached to form a bottom for the cylinder. A shutter covers the hole during the filling operation. This can be smoothly removed without vibration to allow the powder to flow through the selected hole.

Operation is extremely simple.

Select a disc having the appropriate orifice size for the powder concerned and secure it to the bottom of the cylinder using the collar provided for this purpose. Adjust the shutter so that the hole in the bottom of the funnel nozzle is covered.

Introduce the test sample (100 grams unless inappropriate) into the flow funnel. Now open the shutter and measure the time required for the entire sample to flow out of the funnel using a suitable stopwatch.

Carry out three measurements: express the flow rate results in terms of mass per time i.e., grams per second.

Alternatively, the cylinder attachment can be used to determine the **intrinsic flowability** of the powder concerned in the form of a flowability index in the same manner as the Flotest Tester described on Page 38.

FUNNEL ATTACHMENT (FLOW THROUGH AN ORIFICE)

In certain instances where, for example, the purpose of the test is to simulate flow in a hopper or other production situation, it may be preferable to use a funnel in the form of a truncated cone.

The **funnel attachment** is based on the stainless steel flow funnel and nozzle described in the **European Pharmacopoeia Chapter 2.9.16** for **Flowability**.

The funnel attachment is supplied with three nozzles corresponding to aperture sizes of 10, 15 and 25 mm respectively. Both funnels and nozzles are manufactured from pharmaceutical grade 316 stainless steel. The nozzles can be quickly interchanged using the connecting nut provided for this purpose.

The opening at the bottom of the funnel is secured with an adjustable shutter which is closed during the filling operation and the test carried out in a similar manner to the cylinder attachment described above.

BALANCE / TIMER ATTACHMENT

By adding a balance and a timer linked to a microswitch located on the shutter mechanism, it is now possible to conduct time vs mass tests using either **cylinder** or **funnel** methods without the need for an external stopwatch.

The balance/timer option allows the use of the unit in 4 modes:

- Determination of the flow time of a predetermined sample weight
- Determination of the flow time of a predetermined sample volume
- Determination of the weight of sample in a predetermined time
- Plot of time against sample weight (weight/time)

BEP WITH FUNNEL ATTACHMENT

BEP WITH CYLINDER & BALANCE/TIMER

BEP WITH FUNNEL & BALANCE/TIMER

BEP WITH ANGLE OF REPOSE OPTION

FLOWABILITY TESTER BEP

ANGLE OF REPOSE ATTACHMENT

The **angle of repose** is the angle (relative to the horizontal base) of the conical pile produced when a granular material is poured onto a horizontal surface. It is related to the density, surface area and coefficient of friction of the material concerned.

The angle of repose attachment comprises a 100 mm dimeter circular test platform together with a **digital height gauge**, having a range of 0-300 mm and an accuracy of 0.03 mm. The test platform has a protruding outer lip in order to retain a layer of powder, upon which the cone is formed. Surplus powder is collected in a tray below the test platform.

For this particular test, the funnel is normally equipped with a special 10 mm i.d. nozzle mounted 75 mm above the test platform. A stirrer is provided to assist in the flow of more difficult products.

The tangent of the angle of repose (in degrees) can be determined by reading off the height of the powder cone in mm from the digital display of the height gauge and dividing it by 50.

FLOW PROPERTIES & ANGLE OF REPOSE

Flow Property	Angle of Repose
Excellent	25 - 30
Good	31 - 35
Fair - aid not needed	36 - 40
Passable - may hang up	41 - 45
Poor - must agitate, vibrate	46 - 55
Very poor	56 - 65
Very, very poor	> 66

BEP WITH SHEAR CELL OPTION

SHEAR CELL ATTACHMENT

Shear cell methodology is widely used in the pharmaceutical industry to determine the flow properties of fine grained powders and bulk solids and how they will behave in bins, hoppers, feeders and other handling equipment.

The ability of a material to flow through such devices is dependent on the bulk density of the material and its shear strength.

The **shear cell** employed with the BEP comprises a cylindrical chamber (manufactured from clear acrylic) measuring 140 mm i.d. and 32.5 mm high and capable of holding 500 ml of the sample. In the floor of the chamber, there is a 100 mm hole which can be sealed during the consolidation process using an acrylic disc provided for this purpose.

The test is based on measuring the force required to shear a circular disc through a prepared sample of bulk material. It comprises two stages (a) sample consolidation (bulk density measurement) and (b) failure inducement (shear strength).

The sample is first subjected to a consolidated load such that the bulk density of the material can be determined - ideally, this should be similar to the loads experienced by the material in practice. Alternatively, a standard reference can be employed e.g., 10 kilos.

The acrylic disc sealing the bottom of the test cell is now removed and load steadily applied to the test sample by pouring sand through the BEP funnel into a container resting on top of the sample until such time as the sample fails (shears).

Report the results in terms of bulk density, shear strength and if appropriate, estimate of device outlet required.

Cat. No.	Description
1650	Flowability Tester Model BEP
1651	Cylinder Attachment (Flow through an Orifice)
1652	Funnel Attachment (Flow through an Orifice)
1653	Balance/Timer Attachment
1654	Angle of Repose Attachment
1655	Shear Cell Attachment

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FLOTEST TESTER

The Flotest Tester, like the BEP, is an instrument for measuring the ability of powders to **flow through an orifice** thus providing a simple and repeatable technique for the determination of powder flow characteristics.

As such, it takes into account most of the physical characteristics affecting flowability such as particle size, shape, fines, unit surface, actual and bulk density, porosity, settling and electro-static charge without a direct quantitative measurement of any of these parameters.

Unlike the BEP, however, which employs a truncated cone as a 'funnel', the Flotest uses a **cylinder** as the container combined with a flat-faced bottom plate incorporating various orifice diameters.

Furthermore, the Flotest determination of intrinsic flowability is based upon **the ability of a powder to fall freely through a hole in a plate** to characterise the powder as opposed to mass per time as in the BEP. For convenience, the **flowability index** is given as the diameter (in mm) of the smallest hole the powder falls through freely on three successive attempts.

The unit has been successfully used to establish dry powder characteristics prior to setting up filling equipment such as capsule fillers, tablet presses and dry packaging machines, thus avoiding high coefficients of variation. The flowability index may also be used in purchasing specifications to ensure consistent flow characteristics of materials received and general quality control procedures.

CONSTRUCTION

The tester comprises a stainless steel cylinder with an approximate capacity of 200 mL.

Supplied with the instrument are a series of stainless steel discs each containing a precision drilled hole in the centre covering the following sizes: 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30 and 32 mm.

Each disc can be easily attached to form a bottom for the cylinder. A shutter covers the hole during the filling operation. This can be smoothly removed without vibration to allow the powder to flow through the selected hole.

MODE OF OPERATION

For new formulations, it is recommended to start with the 16 mm disc. Once the disc is in position and with the shutter in the closed position, a 50 gram sample is introduced into the test cylinder using the funnel provided for this purpose.

After waiting for approx. 30 seconds to allow for any possible formulation of flocculi, the lever operated shutter is opened. The test is positive if the powder flows through the hole leaving a residue in the cylinder in the form of an upside-down truncated cone.

A powder that flocculates in bulk will on the other hand fall abruptly forming a cylindrical cavity. In this instance, as is the case if the powder refuses to flow through the hole, the test is adjudged to be negative.

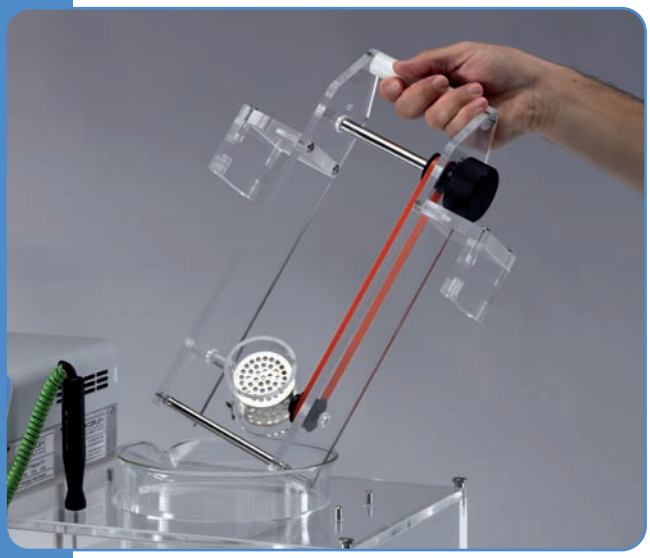
In the case of a positive result, the test must be repeated with smaller and smaller disc holes until the result is negative. For negative results increase the size of the disc hole until the test is positive.

Cat. No.	Description
1620	Flotest Tester

FLOTEST (SHUTTER CLOSED)

FLOTEST (SHUTTER OPEN)

SUPPOSITORY DISINTEGRATION TESTER



REMOVING THE TEST STATION

SOFTENING TIME ATTACHMENT

SUPPOSITORY TESTER MODEL SDT 1000

The Suppository Tester SDT 1000 has been designed in accordance with the specifications as laid down in the European Pharmacopoeia **Test 2.9.2 for the disintegration of suppositories, pessaries and vaginal tablets** and with suitable attachments **2.9.22.-2 Apparatus 2 for measuring the softening time of lipophilic suppositories**.

The **disintegration test station** is made up of a 60 mm long acrylic cylinder having an internal diameter of 52 mm into which is inserted the sample holder containing the sample under test. The sample holder comprises of two stainless metal discs 50 mm in diameter and containing 39 x 4 mm holes held 30 mm apart by three spring clips.

Consistent heating of the media is achieved by immersing the test station into a 4 L glass vessel contained within a plexiglass water bath. The temperature of the media is controlled at 37 degrees C by an immersion thermostat and measured in the water bath using a PT100 probe connected to a digital display.

During operation, the black knob is rotated through half a turn at 10 minute intervals which automatically inverts the sample holder through 180 degrees using a water resistant pulley system. The whole test station can be quickly removed from the beaker for cleaning.

Agitation of the test media is achieved through an electro-magnetic stirrer which, located on a sliding drawer, sits beneath the water bath directly below the centre of the test station.

The drawer can be withdrawn to allow the setting of the stirrer speed and then retracted during the test. The stirrer speed can be varied between 80 and 2000 rpm at 10 rpm intervals. The stirrer can be removed and used for other purposes if required.

MODE OF OPERATION

Preheat the test media to 36-37 degrees C using the combination of the immersion thermostat provided and a slow speed stirrer (optional).

Place a **suppository** or **pessary** in the sample holder, place the latter in the perspex cylinder and secure. Run the test for the time prescribed in the appropriate monograph inverting the apparatus every ten minutes using the black knob provided for this purpose. Repeat the test for two more suppositories or pessaries - all samples should disintegrate within the stated time.

The tester can also be used for testing **vaginal tablets**. In this case, only the sample holder is employed. The test station used for suppositories and pessaries should therefore be removed. Place the sample holder on the base of the beaker and adjust the level of the test media (preheated to 36-37 degrees C) such that it just covers the perforations on the upper plate. Place a tablet on the latter and cover with a suitable glass plate (not provided) to maintain appropriate conditions of humidity. Repeat the test for two more tablets - all samples should disintegrate within the stated time.

A special attachment designed to be used in place of the disintegration test station and 4L beaker containing 3 glass rods (C1) is available for measuring the **softening time of lipophilic suppositories** (2.9.22.-2).

The unit measures 510 mm (W) x 280 mm (D) x 500 mm (H).

Cat. No.	Description
1704	Suppository Disintegration Tester SDT 1000
1705	Electro-Magnetic Stirrer for above
1706	Softening Time Attachment (Ph.Eur. 2.9.22.-2)

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TERGOTOMETER DETERGENT TESTER

The **Tergotometer** is a versatile laboratory scale multiple washing machine which simulates the action of a domestic washing machine. Typical applications include:

- Evaluation of the effectiveness of soap, detergents, etc.
- Washability and colour fastness of fabrics and other materials.
- Optimisation of temperature, speed and water hardness parameters applicable to different detergents.
- Routine screening for dirt removal, brightening, softening, foaming, scale build-up, etc.

The unit has eight test stations each comprising a 1000 mL test vessel located in a clear view acrylic water bath. The temperature of the water bath is controlled by an external digital heater/circulator which is adjustable between ambient and 70 degrees C. A refrigeration unit can be provided as an optional extra if temperatures are required below ambient (down to 0 degrees). In this case, the number of test stations is reduced to 7.

Agitation (50 - 200 rpm) is provided by a series of **eight stirrers** located in each vessel which produce a scaled down version of larger machines. Provision is made for controlling and monitoring the speed and temperature during the test. Plain 316 stainless steel paddles are available as an option, or paddles which allow pieces of fabric to be attached to them are available on request.

A **special modification** to allow for **reverse rotation** of the paddle to the following specification is available on request: stirrer rotation 10 revolutions (360 degrees) clockwise followed by 1 second pause followed by 10 revolutions anti-clockwise *ad infinitum* throughout the test.

OPERATION

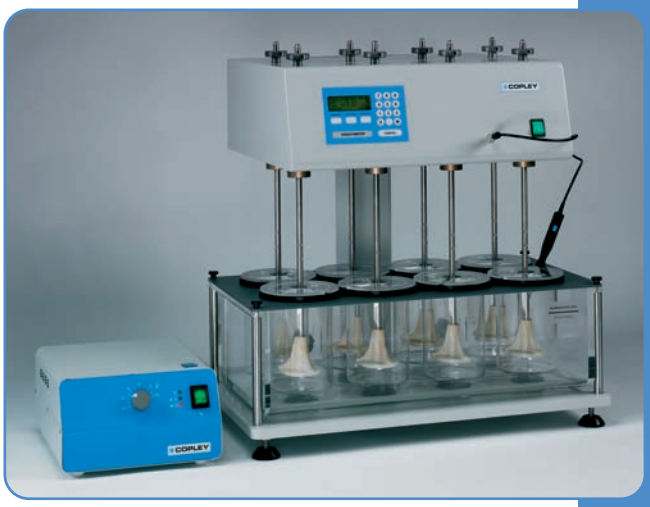
The detergency value of any washing material is normally determined by washing standardised soiled fabrics and measuring the amount of soil removed by determination of the reflectance before and after the washing process.

Operation is simple. Adjust the water bath to the desired temperature, add 1000 mL of water to each test vessel and allow to equilibriate until the desired temperature has been attained. Add the pre-weighed volume of soap or detergent to each test vessel and operate the paddles at the prerequisite speed until homogenisation is complete.

Add the test sample to each test station and operate at the speed required for the time specified. At the end of this phase, remove the samples and empty and refill the vessels with clean water. Wring the samples out and return them to the vessels for rinsing at the temperature and for the time specified in the protocol. Repeat the washing and rinsing operations as required.

Any number of variables can be tested in this manner: not only the temperature, agitation speed and period of test but also composition of the wash solution, degree of water hardness, pH, bleach, etc.

Cat. No.	Description
6401	Tergotometer (Ambient to 70 degrees C)
6402	Refrigeration Unit (Ambient to 0 degrees C)
6403	Modification to allow for reverse rotation of the Stirrers
6404	Set of 8 Stainless Steel Paddles (option)



TERGOTOMETER

STANDARD STIRRERS

TERGOTOMETER WITH REFRIGERATION

DIGITAL CALIPER 500

MINI PROCESSOR FOR SPC 264

DIGITAL CALIPER FOR MEASURING TABLETS

DIGITAL CALIPER MODEL 500

An inexpensive hand-held electronic caliper, the Model 500 is particularly useful for the press operator as it is extremely easy to use and completely dust resistant.

The instrument is designed to accept tablets and similar samples up to a **maximum of 150 mm (6")** and to an accuracy of 0.01 mm (0.0005").

The unit features a clear high-contrast direct reading 1 cm high LC display (no more time consuming interpretation of a dial gauge) and comes complete with 2 x SR44 Batteries.

The unit can be switched off when not in use.

The caliper is manufactured from fully hardened stainless steel and features automatic wear compensation and positive locking clamp as standard.

The convenient one-handed operation could not be simpler.

Holding the gauge in the right hand, use the thumb to move the display head of the caliper to the right in order to open the jaw of the gauge, insert the tablet with the left hand between the jaws.

Then by moving the display head to the left to close the jaws, read off the measured value from the digital display.

Provision is made to measure in either metric or imperial at a single push button with a **resolution of 0.01 mm** or 0.0005". The gauge can be zero set at any point thus enabling the display to show a +/- variance.

The gauge can be used in **four modes**, that is to say, to measure either outside, inside, depth or step measurements.

The unit comes complete in a handy plastic storage case to prevent inadvertent damage. A 6-pin socket is provided as standard such that the unit can be connected to a data processor for statistical process control (Model 264).

MINI PROCESSOR MODEL 264

The **Digimatic Mini Processor Model 264** is a powerful and compact data processor which provides a wide variety of calculations for generating X-R control charts, histograms and data displacement charts.

The Model 264 employs the Digimatic electronic communications format in conjunction with STATPAK, a powerful multi-level SPC software package available for networking to provide unsurpassed flexibility and ease of use.

Parameters available for statistical process control include measurement data, maximum, minimum, range, mean, standard deviation, number of defectives, fraction defective, process capability indices, histogram, displacement chart, number of sub-groups, sample size, mean of sub-group, range of sub-group, mean of x, upper and lower limits, mean of R and upper and lower limits of R.

Cat. No.	Description
4901	Digital Caliper 500
4902	Mini Processor for SPC 264

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TABLET THICKNESS TESTER

The 547 and 700 Tablet Thickness Testers are both inexpensive hand-held dial thickness gauges particularly useful for the press operative as they are extremely simple to use and can be slipped conveniently into the pocket.

TABLET THICKNESS TESTER 700

The least expensive of the two units, the **Tablet Thickness Tester Model 700** is designed to accept tablets up to **12 mm** (0.5") thick to an accuracy of **0.01 mm** (0.0005").

Operation is simplicity itself.

Press 'on' button to switch the unit on and to zero the gauge, select the appropriate unit of measurement (mm or inches), depress the red button to open the jaw, insert sample, release the red button and read off the result on the clear LCD display.

This unit is truly hand held measuring only 94 mm long x 45 mm wide.

TABLET THICKNESS TESTER 700

TABLET THICKNESS TESTER 547

The **Tablet Thickness Tester Model 547** is a rather more sophisticated unit designed to accept tablets and similar samples up to **10 mm** (0.4") thick to an accuracy of **0.01 mm** (0.0005").

The unit features a clear high-contrast direct reading 1 cm high LC Display (no more time consuming interpretation of a dial gauge) and comes complete with two x SR 44 Batteries.

The unit can be switched off when not in use. All faces coming into contact with the product are of high grade tool steel, hardened, ground and lapped for final accuracy. The gauge has a throat of 30 mm (1.2").

The convenient one-handed operation could not be simpler.

Holding the gauge in the right hand, depress the thumb-lever with the right thumb in order to open the jaw of the gauge, insert the tablet with the left hand between the jaws and then releasing the thumb-lever to close the jaws, read off the measured value from the digital display.

Provision is made to measure in either metric or imperial at a single push of a button with a resolution of 0.01 mm or 0.0005".

The gauge can be used in two modes, that is to say, either in 'direct measurement' mode whereupon the actual thickness value is displayed or in 'comparator' mode whereby a +/- variance from a preset norm is indicated on the display. The unit comes complete in a handy plastic storage case to prevent inadvertent damage.

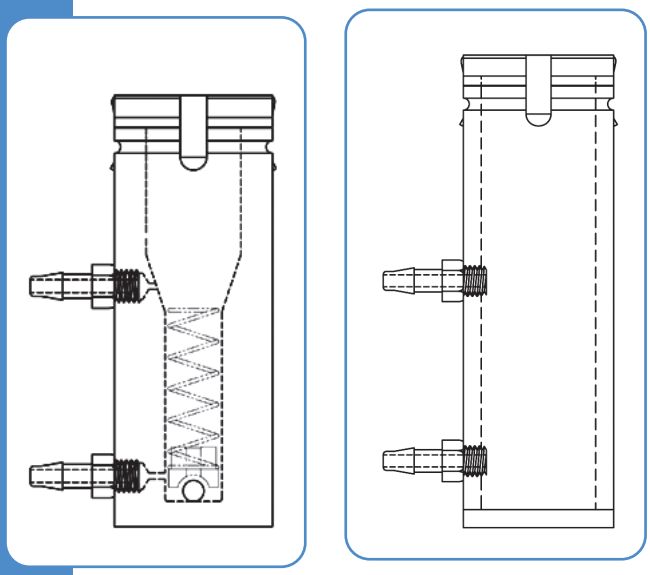
Model 547 is also provided with a 6-pin socket as standard such that it can be connected to the **Digimatic Mini Processor Model 264.**

The Mini Processor Model 264 is a powerful yet compact data processor providing a wide variety of data, statistics and graphics in a single unit.

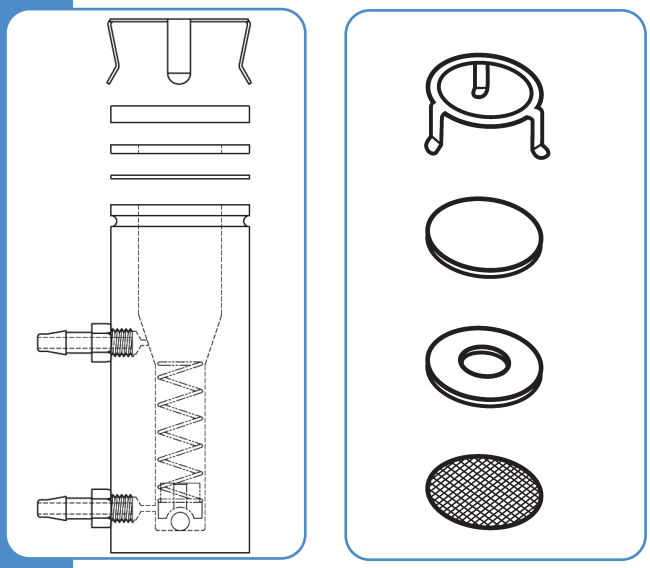
A full description of this unit together with an illustration of the 264 may be found on the previous page.

TABLET THICKNESS TESTER 547

Cat. No.	Description
4903	Tablet Thickness Tester 700
4904	Tablet Thickness Tester 547
4905	Mini Processor for SPC 64



6 & 20 mL Vertical Diffusion Cells



Exploded Cell & Sample Holder

Vertical Diffusion Cell

VERTICAL DIFFUSION (FRANZ) CELL

INTRODUCTION

At the present time, there are no compendial methods relating to the *in vitro* release testing of topical semi-solid dosage forms such as **creams, ointments and gels** described in the pharmacopoeia.

However, there does appear to be a growing body of opinion in support of the **vertical diffusion cell** system (sometimes called the **'Franz Cell'** after the name of its originator, Dr.T.J.Franz) to fulfill this role.

The vertical diffusion cell is, for example, already the system of choice for the FDA's "Guidance for Industry on Scale Up and Post Approval Changes for Semisolid (SUPAC-SS) Dosage Forms", the OECD "Guidelines for the Testing of Chemicals - Skin Absorption: *in vitro* Method" and the FIP/AAPS "Guidelines to Dissolution/in Vitro Release Testing of Novel/Special Dosage Forms" relating to topical semi-solid dosage forms and is currently under study by the USP Advisory Panel on the "USP Performance Test for Topical and Transdermal Dosage Forms" as to its suitability for this purpose.

DESIGN

The design of the vertical diffusion cell is illustrated in the schematic to the left. It is occluded to avoid air bubbles that may affect the test.

Two sizes of cell are available. The **standard cell** has a surface diameter of 15 mm and a receptor media volume of approx. 6 mL. A **larger cell** is available with a 20 mm orifice and a volume of 20 mL.

Both cells are fitted with ports to facilitate sample withdrawal and media replacement. The cell contents are continuously stirred during operation by means of a magnetic stirring bar in association with a helicoil stirring element to ensure homogeneous distribution of temperature and adequate mixing of the contents.

The **sample holder** comprises a three part sandwich made up of:

a) clear view sample support disc
b) PTFE sample chamber ring and
c) 25 mm diameter PVDF membrane (representing the skin)

The three part sandwich is held together by means of a three pronged spring clip which also serves to clip the assembled sample holder to the cell.

SAMPLE PREPARATION

Sample preparation is quick, easy and precise. Insert the clear view support disc and PTFE sample chamber ring into the three pronged spring clip and place the inverted assembly on to the worktop. Now, fill the sample chamber with the sample cream or ointment to be tested (approx. 250 mg or 425 mg according to cell) removing any excess with the aid of a spatula. Finally, place the artificial membrane (or excised skin if you prefer) over the top of the sample with the membrane or visceral side of the dermis (the underneath of the skin sample) uppermost such that when the holder is inverted and placed on the cell this side is bathed with receptor media. Note: the membrane should be thoroughly wetted with a suitable wetting agent prior to use. **The sample sandwich is now complete**.

Now, fill the **Franz Cell** with receptor media e.g., isotonic saline solution at pH 7.4 suitably de-gassed to remove air bubbles and pre-warm using suitable means to 32 degrees C to reflect normal skin temperature (37 degrees C for vaginal preparations). Note: It is helpful to marginally overfill the cell with media to ensure contact between media and membrane once the cell and sample holder are assembled.

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VERTICAL DIFFUSION (FRANZ) CELL

RUNNING A TEST

Once the desired temperature has been reached, **start the test** by securing the prepared sample holder to the cell and activating the stirrer (it is important to stir the cell contents during testing to ensure homogeneity of its contents). Precautions should be taken to remove any air bubbles from the cell which may affect the test.

SAMPLING

Take samples as appropriate.

The vertical diffusion cell is equipped with two ports for sampling and media replacement respectively.

It is essential, whilst sampling, to ensure that the volume of receptor media and hence contact between media and maintenance is maintained. One of the most effective ways of achieving this is to use a syringe in conjunction with a check valve inserted in the replacement media line. The purpose of this valve is to allow replacement media to be introduced into the cell whilst prohibiting media flowing back once the syringe is removed.

The action of introducing the replacement media displaces an equal volume of aliquot concurrently pushing it out of the sampling port for collection.

STIRRING AND HEATING

The **HDT 10** is a **heated magnetic stirrer specifically designed** to accommodate **ten diffusion cells**. It comprises a heated aluminium block accepting two rows of 5 cells. A powerful magnetic stirrer is mounted beneath each test station.

The heating block approach to heating the diffusion cells eradicates the difficulties in use and spaghetti of tubing associated with its water jacketted cell predecessors.

Temperature and stirrer speed are set, controlled and displayed from a single control panel on the front of the unit.

The HDT 10 will accommodate either end-point, discrete manual or fully automatic sampling techniques. Please ask our technical staff for further details.

The HDT 10 is incredibly compact measuring only 243 x 160 x 135 mm (L x W x H) - a footprint less than an A4 sheet of paper.

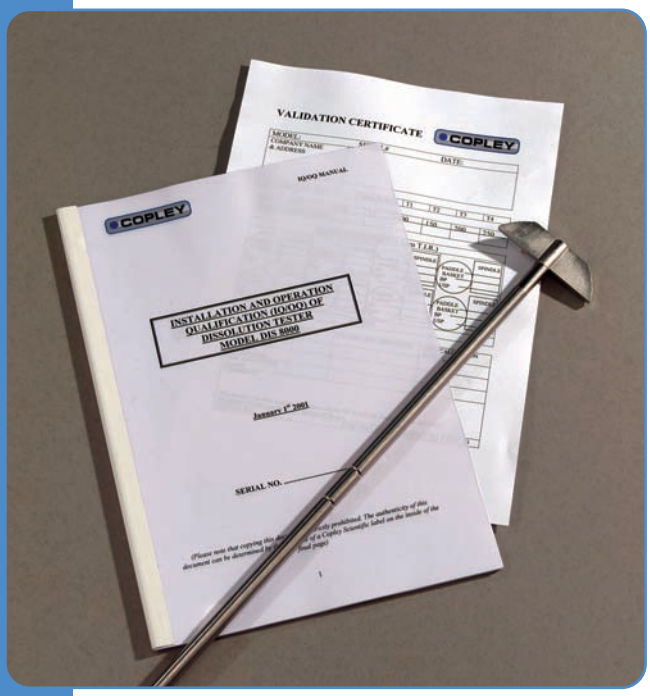
A second and less expensive unit is available to accommodate a **single diffusion cell**. The **HDT 1** is a conventional heated magnetic stirrer with single stirring point and equipped with a special beaker and jholder designed to accept a single vertical diffusion cell.

Cat. No.	Description
7265	Vertical Diffusion Cell 15 mm x 6 mL (in Acrylic)
7269	Vertical Diffusion Cell 20 mm x 20 mL (in Acrylic)
7278	Vertical Diffusion Cell 15 mm x 6 mL (in Glass)
7279	Vertical Diffusion Cell 20 mm x 20 mL (in Glass)
7270	Pack of 100 PVDF Membranes 25 mm o.d.
7271	10 Cell Magnetic Stirrer HDT 10 (excluding cells)
7276	Single Cell Magnetic Stirrer HDT 1 (excluding cells)

VERTICAL DIFFUSION CELL

SINGLE CELL MAGNETIC STIRRER HDT 1

10 CELL MAGNETIC STIRRER HDT 10



IQ/OQ/PQ Documentation

QUALIFYING ANALYTICAL INSTRUMENTS

SOURCES OF ERROR

The pharmaceutical industry employs a wide variety of analytical instrumentation to help ensure the efficacy and safety of their products.

Unfortunately, in many cases, the validity of the results produced by this instrumentation can be influenced by factors other than the product itself.

The source of these potential errors are two fold:

- Human (inappropriate method development or execution)
- Instrumental (errors in instrument and/or ancillary equipment)

If these sources of error can be eliminated then it is fair to assume that any anomalies in results are reliable and are a direct result of the formulation itself.

<1058> ANALYTICAL INSTRUMENT QUALIFICATION

The Good Manufacturing Practices (GMP) regulations require that

(a) the **test methods** used to monitor pharmaceuticals must meet proper standards of accuracy and reliability and
(b) that companies should establish procedures to ensure the fitness for use of **instruments** that generate data supporting product testing.

However, the GMP regulations do not provide definitive guidance as to how these goals are to be achieved.

The United States Pharmacopoeia (USP) has sought to address this problem by the introduction of a series of chapters as follows:

- <1225> Validation of Compendial Procedures
- <1226> Verification of Compendial Procedures
- <1058> Analytical Instrument Qualification (draft)

Attention is drawn at this point to the terms 'validation' and 'qualification' above. Hitherto, these terms have been used on an interchangeable basis creating a degree of ambiguity in the scientific community.

For this reason, USP have suggested that:
(a) the term **'qualification'** be applied to instrumentation and
(b) the term **'validation'** to processes and software

Hence, the term **'analytical instrument qualification'** (AIQ) is used for the process of ensuring that an instrument and the term **'analytical method validation'** for ensuring that the analytical and software procedures employed is suitable for its intended application.

The **USP Chapter <1058>** ***Analytical Instrument Qualification*** describes in detail the four phase approach to Qualification based on design (DQ), installation (IQ), operational (OQ) and performance (PQ) qualification.

Copley Scientific recognises the regulatory importance of these new initiatives. For this reason, for a wide selection of our products, you can request full supporting documentation in the form of full **IQ/OQ/PQ manuals** (Installation, Operation and Performance Qualification) to guide you through the qualification process.

It is important to note that the purpose of analytical instrument qualification and analytical method validation is to ensure the quality of analysis ***before*** conducting the tests whereas system suitability tests and quality control checks ensure the quality of analytical results ***immediately before*** or ***during*** sample analysis.

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SERVICING/TRAINING

SERVICING

Copley Scientific offers a comprehensive range of both in-house and on-site service contract options tailored to individual customers' needs and designed to provide quality maintenance and calibration procedures at really competitive prices.

Contracts can be prepared for **individual instruments** or complete **calibration management** systems.

The creation of a typical service contract follows a structured format: 'discussion' to establish a User Requirement Specification (URS), 'quotation' to establish costs, 'implementation' to implement the contract and 'review' to ensure compliance with the initial specification.

Our skilled team of engineers and technicians are trained to a high standard on the complete range of Copley Scientific and other related products and are well versed in all aspects of calibration and qualification (IQ/OQ/PQ) procedures from actual performance to document control and storage.

All documentation supplied conforms to GxP standards as required by the international regulatory authorities.

Similarly, the instrumentation used by our service engineers for critical calibration of equipment is certified to a traceable standard. Such instruments are calibrated by, or traceable to, an accredited UKAS calibration company in the UK or equivalent international standards.

Such calibration companies encompass all the relevant requirements of EN and ISO. Certificates for the instruments used to calibrate the customer's equipment are available for viewing on request.

We will be pleased to discuss your individual requirements and quote accordingly.

TRAINING

As a world leader in the provision of equipment for testing pharmaceutical dosage forms Copley Scientific offers a range of tailored training packages for both analysts and laboratory managers of pharmaceutical companies developing such products.

Training courses vary depending on existing levels of knowledge and can be performed at Copley Scientific's training facility in Nottingham, UK, or at the customer's facility (in most cases).

Typical training programs include: -

- Presentation on dosage form types, test equipment, regulatory requirements, monographs and methodology and new industry developments
- Provision for the supply of technical papers and documents where appropriate
- Audit of current system set-up and procedures used (on-site training courses only)
- Training of users in operation of the equipment supplied
- Troubleshooting, Questions and Answers

Please feel free to contact us to discuss your own requirements. We will be pleased to provide you with a quotation for a training program designed to meet your particular needs.

Training Session

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