USP Apparatus 7 – Reciprocating Holder

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Description of subject matter

A description of Apparatus 7 – reciprocating holder apparatus is found in USP General Chapter <724> Drug Release.

Its most notable utility is in the analysis of products with low amounts of active pharmaceutical ingredient (API) which become difficult to analyze in traditional dissolution apparatus with higher volumes.

The reciprocating disk apparatus, originally known as the Alza Apparatus, after Alza corporation who pioneered transdermal delivery systems (TDS) and other sustained release products. An apparatus of suitable design was unavailable during the 1980s to accommodate their sustained release products. They developed their own which was eventually incorporated into the USP in 1990 as Apparatus 5 – The Reciprocating Disk apparatus. A few years later, two new apparatus were adopted into the USP. The Reciprocating Disk Apparatus along with four new holders was re-introduced as the USP Apparatus 7 – Reciprocating Holder Apparatus around the year 2000.

Apparatus 7 is also ideal for extended-release oral dose products or any dosage form requiring a release profile demonstrated in various media pH and agitation representing in-vivo conditions present in the GI-tract. The apparatus can run unattended for periods up to six days while allowing the in-vitro drug release apparatus to control biorelevant conditions such as agitation rate and residence time in various media.

Technical Details

The reciprocating holder apparatus is ideal for automatic drug release testing for smaller, low dose delivery systems which may require different media and agitation rates to characterize the release of the API from the drug formulation or device. Although it was originally developed for testing small transdermal systems it has become much more flexible for testing other dosage forms such as osmotic pumps, drug eluting stents, bead formulations and pacemaker leads.

The reciprocating holders utilize a stroke length of 20 mm and can be programmed to reciprocate between 5 and 60 dips per minute (DPM). At the end of the designated time, samples may be taken automatically, then the holder will pick up and move to the next row containing fresh media. The traditional USP 7 utilizes 7 holders and provides six rows of media in 100 or 300 mL vessels for executing the test. The 7^{th} sample position may be used for containing standard or blank solutions for analysis with the samples. For lower dose products, a 12-sample, 12-row system with 50 mL vessels is available.

Features of the reciprocating holder apparatus include:

- Simulating biorelevant conditions for the skin and various tissues for TDS and implants as well as various media, agitation rates and residence time for bioavailability studies with solid oral dose forms.
- Saving valuable bench space with its footprint and ability to connect to automatic sample collection and filtration through 0.22 and 0.45 µm membrane filters with the Agilent 850-DS for the 7-sample system.
- Storage for up to 15 programmable methods to control time points, agitation rate, and movements between vessel rows including hold dip times and drain times.
- Various Compendial holders for transdermal systems; reciprocating disk, angled disk and reciprocating cylinder; and for various other dosage forms including osmotic pumps, the spring holder and pointed rod. Several other noncompendial holders have been designed for drug eluting stents and other implants.
- Vessel dimensions of 50, 100 and 300 mL provide numerous volumes for accommodating the various holders. A Compatibility Table is included that provides the compatibility between various holder sizes and vessel sizes.

Performing the test: Attach each dosage unit to the appropriate holder according to the validated method or monograph. Osmotic pumps are typically attached to the rod holder with a small drop of cyano-acrylic glue or methyl acrylate glue and allowed to dry. Osmotic pumps or nondisintegrating dosage forms may alternatively be placed in one of the 4 sizes of spring holders. Media for these systems must be 37 ± 0.5 °C.

For TDS dosage forms, the appropriate holder should be used according to the validated method or monograph. The TDS will be attached to one of the following; the reciprocating disk (5 sizes), the angled disk (2 sizes) or the PTFE Cylinder (single size). For each of these systems, the release surface of the TDS should be kept as smooth as possible and the entire release surface should be exposed. With the release surface mounted to face the media, O-rings are typically used to hold the systems in place, but they should not cover the release area of the patch, only the border. Otherwise, double-sided adhesive tape or suitable glue may be used to hold the system in place. If membranes such as Cuprophane are used as a barrier, care must be taken to avoid entrapping air bubbles.

After mounting the dosage forms to their specific holder, the holders must be attached to the drive shafts, the vessels filled with the proper media and volume and allowed to equilibrate to the proper temperature. When the test begins, the reciprocating holders descend slowly into the first row of the vessels. Then after a hold dip time which for apparatus 7 is usually less than 1second, the reciprocating motion starts. The dosage units must remain submerged during the test.

After the programmed time for this row expires, the reciprocating holders rise above the vessels to drain for a programmed time, and automatically move to the next row. Then the reciprocating process is repeated in the vessel containing the next media. Vessel evaporation covers should be installed with the proper tension so they freely move and retract as the drive unit moves from forward positions to the rear. In the event of evaporative loss from lengthy testing, vessel volume may be restored by

weighing vessels with media prior to the test. Water may then be added back to the vessels when removed from the apparatus to restore their original volume.

Apparatus Qualification: USP Apparatus 7 has no USP Performance Verification Test (PVT). However, the system does have operational parameters with specifications and tolerances. Although specifications and tolerances exist for the holders, there are no compendial dimensions stated in the USP <724> chapter for the vessels.

The current physical parameters and tolerances stated in USP <724> for USP Apparatus 7 are:

Physical Parameter	Specification and tolerance
Vessel Temperature	(TDS) 32 ± 0.5 °C, (Oral) 37 ± 0.5 °C
Dip rate (DPM)	Usually 30 cycles/min. No set tolerance for speed but Agilent recommends ± 5% of set speed
Stroke Distance	2.0 cm ± 0.1 cm
Time points	± 2% of specified time or 15 min, whichever is less

As an alternative to the PVT, some quality programs have adopted a similar transition to enhanced mechanical qualification. These additional steps should ensure the suitability of the apparatus under guidelines of analytical instrument qualification (AIQ). These steps should include certification of components, documentation of preventative maintenance, mechanical parameters verification and operational checks performed at time of use.

Operational checks at time of use should include:

- Reciprocating holders are free from residue, no dents, corrosion or scratches
- Vessels are clean and free from residue, scratches and cracks
- O-rings are clean, undamaged and free from residue
- Vessel temperature is maintained at 37.0 ± 0.5°C
- Evaporation covers (2) for the vessels tray are installed with the proper tension to retract and move freely during the test

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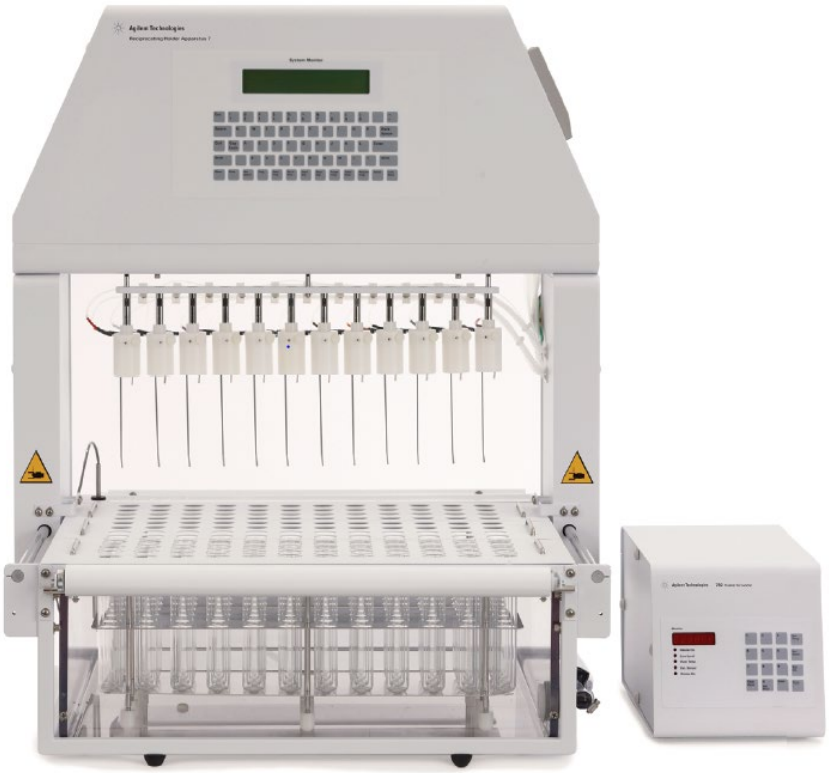
Calculations: The calculations for Apparatus 7, which utilizes separate rows during a test, differ slightly from traditional Apparatus 1 and Apparatus 2 methods. When multiple rows of media are used, add the amount of drug from previous rows to the amount of release in the current row. This is most easily done by calculating the mg of drug released in each row, adding them, and then comparing that to the total label claim of the drug. For example:

- mg dissolved row 1 = (sample absorbance row 1/standard absorbance) x (standard weight/standard volume) x vessel volume
- mg dissolved row 2 = mg dissolved row 1 + [(sample absorbance row 2/standard absorbance) x (standard weight/standard volume) x vessel volume]
- mg dissolved row 3 = mg dissolved row 1 + mg dissolved row 2 + [(sample absorbance row 3/standard absorbance) x (standard weight/standard volume) x vessel volume]
- Note: mg dissolved divided by the label claim will be the % dissolved for each time point



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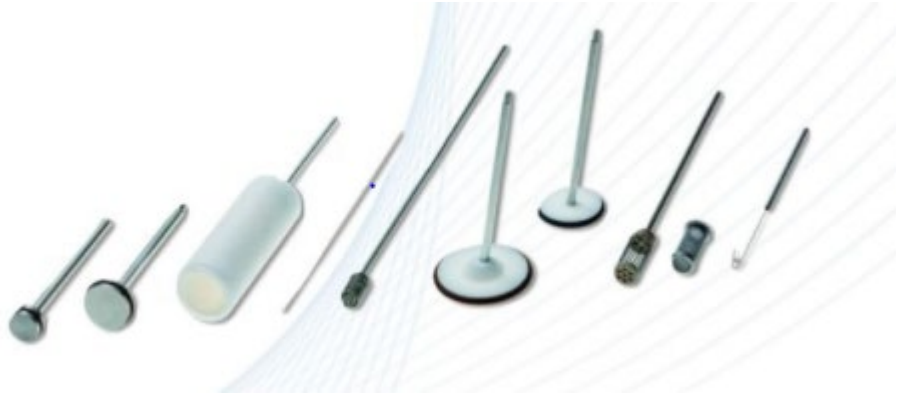
Apparatus 7 Specifications

Altitude	0-2000 m (0 – 6562')
Temperature	5 to 40 (°C)
Humidity (non-condensing)	Not more than 80% RH
Voltage requirements	115 V / 60 Hz 230 V / 50 Hz
Current requirements	115 V—2.0 Amp 230 V—2.0 Amp
Fuse requirements	115 V—2.0 Amp, 250 V, 5 mm x 20 mm FAST 230 V—2.0 Amp, 250 V, 5 mm x 20 mm FAST
Minimum dips per minute	5
Maximum dips per minute	60
Stroke length	2 ± 0.1 cm
Water bath temperature	Ambient + 5 to 55 °C
Number of rows	Standard 100 / 300 mL versions—6 rows of 7 tubes Modified 12 rows of 12 tubes 1L version—3 rows of 3 tubes Dual dipping rows available
USP holders	Reciprocating disk, angled disk, cylinder, acrylic rod and spring holder
Run time display format	hhh:mm programmable up to 999:59
Dip time interval display format	hhh:mm programmable up to 999:59
Drain time display format	mm:22 programmable up to 99:59

Hold time display format	mm:22 programmable up to 99:59
Printer	Impact
Dimensions	Height: 73.66 cm (29 in.) Width: 68.58 cm (27 In.) Depth: 69.85 cm (27.5 in.)
Equipment weight	43.1 kg (95 lbs), dry without vessels

Ordering Information

Product Description	Part Number
Apparatus 7, 7-row, 115V	25-2000
Apparatus 7, 7-row, 230V	25-2100
Apparatus 7, Alza, 12-row, 115V	25-2490
Apparatus 7, Alza, 12-row, 230V	25-2495
Apparatus 7, 12-row, 115V	25-2500
Apparatus 7, 12-row, 230V	25-2600



Agilent catalog numbers (or links to Digital Source Book)

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Accessory Ordering Information

Product Description	Part Number
Rod, acrylic-pointed kit, one position	27-3000
Holder, transdermal kit, one position	27-3001
Rod, acrylic-pointed, replacement assembly	27-3002
Reciprocating disk, Alza type, 1.6 cm sq.	27-8005
Reciprocating disk, Alza type, 2.5 cm sq.	27-8010
Reciprocating disk, Alza type, 5.0 cm sq.	27-8015
Reciprocating disk, Alza type, 7.0 cm sq.	27-8020
Reciprocating disk, Alza type, 10 cm sq.	27-8025
Angled disk holder, 1.98 in.	27-8035
Angled disk holder, 1.42 in.	27-8036
Basket shaft, mini, threaded, for use with PN 27-8620 and 27-8621	27-8600
Mini basket, 40-mesh, for use with PN27-8600	27-8620
Mini basket, 50-mesh, for use with PN27-8600	27-8621
Basket assembly, titanium	27-8622
Spring holder, Alza, 1.45 in. L x 0.58 in. inner dia. x 0.031 in. wire inner dia.	27-0100
Spring holder, Alza, 1.40 in. L x 0.31 in. inner dia. x 0.040 in. wire inner dia.	27-0101
Spring holder, Alza, 0.96 in. L x 0.33 in. inner dia. x 0.031 in. wire inner dia.	27-0102
Spring holder, Alza, 0.60 in. L x 0.25 in. inner dia. x 0.031 in. wire inner dia.	27-0103
Outer tube, 50 mL	27-5130
Outer tube, calibrated, 50 mL, class B	27-5135

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Compatibility of the reciprocating holders for various vessel volumes:

Compatibility Table

Part Number	Holder	Apparatus 3 – Outer Tube			
		50 mL	100 mL	300 mL (USP)	1000 mL
27-5000	Inner tube (300 mL)	-	-	◆	◆
27-5010	Inner tube (100 mL)	-	◆	◆	◆
12-2100	Basket, USP, 40-mesh, 381 µm	-	-	◆	◆
27-2400	Durafit basket adapter	-	NR	◆	◆
27-2401	Basket adapter with clip assembly	-	NR	◆	◆
		Apparatus 7 – Outer Tube			
		50 mL	100 mL	300 mL (USP)	1000 mL
27-5000	Inner tube (300 mL)	-	-	◆	◆
27-5010	Inner tube (100 mL)	-	◆	◆	◆
27-2400	Durafit basket adapter	-	NR	◆	◆
27-2401	Basket adapter with clip assembly	-	NR	◆	◆
27-8620	Basket, mini, 40-mesh	◆	NR	◆	◆
27-8621	Basket, mini, 50-mesh	◆	◆	◆	◆
27-8600	Basket shaft, mini	◆	◆	◆	◆
27-8622	Basket assembly, titanium	◆	◆	◆	◆
27-3000	Pointed acrylic rod	◆	◆	◆	◆
27-3002	Replacement acrylic rod kit	◆	◆	◆	◆
27-3001	Transdermal patch holder kit	-	-	◆	◆
27-8005	1.6 cm^2 reciprocating disk	◆	◆	◆	◆
27-8010	2.5 cm^2 reciprocating disk	-	-	◆	◆
27-8015	5.0 cm^2 reciprocating disk	-	-	◆	◆
27-8020	7.0 cm^2 reciprocating disk	-	-	◆	◆
27-8025	10.0 cm^2 reciprocating disk	NR	NR	◆	◆
27-6540	Replacement stent holder	◆	◆	◆	◆
27-6541	Stent holder, 8 mm (horizontal)	◆	◆	◆	◆
27-6542	Stent holder, 18 mm (vertical)	◆	◆	◆	◆
27-6543	Stent holder, 30 mm (vertical)	◆	◆	◆	◆
27-0101	Spring holder, 1.40 in. L x 0.31 in. inner dia. x 0.040 in. wire inner dia.	◆*	◆*	◆*	◆
27-0102	Spring holder, 0.96 in. L x 0.33 in. inner dia. x 0.031 in. wire inner dia.	◆*	◆*	◆*	◆
27-0103	Spring holder, 0.60 in. L x 0.25 in. inner dia. x 0.040 in. wire inner dia.	◆*	◆*	◆*	◆
27-0104	Spring holder, 1 in. L x 0.50 in. inner dia. x 0.031 in. wire inner dia.	◆	◆	◆	◆
27-8035	Angled disk, 1.98 in.	-	-	-	◆
27-8036	Angled disk, 1.42 in.	-	-	-	◆

USP Apparatus 7 Reciprocating Holder:
http://read.nxtbook.com/agilent/source_book/dissolution_systems_2017_2018/transdermal_delivery_systems.html

Literature/specification sheet
Data Sheet – Reciprocating Holder Apparatus 7
http://www.agilent.com/cs/library/datasheets/public/5990-7411EN_Apparatus%207.pdf

Specification Sheet – Reciprocating Holder Apparatus 7
http://www.agilent.com/cs/library/specifications/public/5990-7410EN_App7_12x12%20Station.pdf

Agilent BIO-DIS Apparatus 3/7 Operator's Manual
http://www.agilent.com/cs/library/usermanuals/public/App_3_App_7_Op_Man.pdf

Frequently Asked Questions
https://community.agilent.com/docs/DOC-7391

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