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Research Article

**VALIDATION OF COMPENDIAL EQUIPMENT OF
DISSOLUTION TEST APPARATUS-I.P**¹Sushma Desai, ²Lakshmi Kalyani.B, ³B. Chandrasekhara Rao, ⁴Shiva Kumar¹⁻³Chilkur Balaji College of Pharmacy, Hyderabad.⁴Principal & Professor, Department of Pharmaceutical Sciences, Gitam School of Pharmacy, Hyderabad

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Abstract:

Dissolution test apparatus stands one of key requirements of pharmacy academia & research lab in understanding the bioavailability and bioequivalence of prepared and available drug formulations as an estimate for further studies in continuing research. Hence validating this compendia equipment for quality assuring as preapproval inspections is need of the hour for timely appropriateness in using the equipment on regular basis. In this experimental work is detailed with the design, installation, operational and performance & maintenance qualification procedures as provided by the equipment vendor. This process has to be performed from time to time for expedite effectiveness and compliance.

Keywords: design qualification, installation qualification, operational qualification, performance qualification, maintenance qualification, validation.

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INTRODUCTION:

Validating instrument is a continuous process of establishing the assurance in aspects of quality & continuity of the results and the data so obtained is documented on regular basis of inspection. There are facilities, process, HVAC, computer system, analytical, equipment and cleaning types of validation.

Dissolution apparatus number and the equipment type in it is given in table.No.1[1,2].

DISSOLUTION APPARATUS**Table no.1 COMPENDIAL EQUIPMENT**

APPARATUS No.	USP	IP
1	Rotating basket	Paddle assembly
2	Paddle assembly	Rotating basket
3	Reciprocating cylinder	
4	Flow through cell	
5	Paddle over disk	
6	Cylinder	
7	Reciprocating holder	

After document authentication and protocol approval qualification of the equipment process is done.

Qualification of this instrument is given in step-wise manner by the vendor and completion of these steps justifies its operation and performance to carry out with assurance[3]. The qualification steps are as follows

- ❖ **Design qualification:** this step includes system purpose as apparatus 1 & 2 are for solid pharmaceuticals and other rules, featuring instrument in physical dimensions, precision heat and RPM control, operational specification, conformance statement, system and process description, system validation conclusions and using physical operational and performance qualification given in table no.2.
- ❖ **Installation qualification:** this step includes customer details and reconciliation against purchase order, identity of the unit, firmware and individual operation manual, site qualification, qualifying cable and tubing connections, installation procedures with any additional comments and IQ completion details like Installation date, company, engineer, customer representatives, position and department need to be furnished as give in table no.3-10.
- ❖ **Operational qualification:** this step includes level check, shaft & vessel ID(number or serial number), baskets height check, center & wobble check, RPM & vibration check, temperature check, system control check followed by documentation of calibration, OQ, training & certificate record as given in table no. 11-27.
- ❖ **Performance qualification:** this step includes USP tablet calibrator test and documentation of PQ completion details as date, company, engineer, customer representatives, position and department & record with additional comments.
- ❖ **Maintenance qualification:** this step includes furnishing documentation of service & operator record and training policy.

EXPERIMENTAL WORK**Table no.2 Main system contents:**

INSTRUMENT	ORDERED Quantity	RECEIVED Quantity	OBSERVATION
LABINDIA dissolution test apparatus (DS 8000) with power cord Supply voltage:....Vac, $\pm 10\%$,Hz	220 v	220 v	yes
DS 8000 controller unit with 25pin & 15pin D type interface cable	–	–	yes
Operator's instruction manual with validation certificate	–	–	Yes
Paddle blades-USP apparatus 2(6nos)	6	6	Yes
Shafts for apparatus fitting(6NOS)	6	6	Yes
Baskets with holder(6nos) - optional	6	6	Yes
Glass or poly-carbonate bowls (clear)(8nos)	8	8	Yes
Circulation pump (1 no.)	1	1	Yes
Bath assembly. Top cover with bowl centering corners & screws (16nos)	16	16	Yes
Allen key 1mm.(1no0	1	1	Yes
Fuses 10A & 2A. (2nos each)	2	2	Yes
Bowl RTD-ext. temp. sensor (1no)	1	1	Yes
Depth gauge balls -25mm(8nos)	25mm	25mm	Yes
Cannula withsyring (10ml)	–	–	Yes
O-ring for stirrer shaft (6nos)	6	6	Yes
Mini paddle for replenishing bowl(2nos)	2	2	Yes
Drain pipe (PVC)	1	–	Yes

INSTALLATION QUALIFICATION:**INSTRUMENT IDENTIFICATION & VERIFICATION****Accessories for automated sample collection****Table no.3 Sample collector: a) main contents – standard supplies**

INSTRUMENT	ORDERED Quantity	RECEIVED Quantity	OBSERVATION
LABINDIA sample collection for dissolution test apparatus (DS8000) with power cord Supply voltage:Vac, $\pm 10\%$,... Hz.	220 v	220 v	yes
Puse 1A/FB (2nos)	2	2	yes
Sampling assembling (1no)	1	1	Yes
Tefion tubing with numbering(6nos)	6	6	Yes
Dispense tips (6nos)	6	6	Yes
Sampling vials (amber colour 72nos)	–	–	Yes
Sampling tray 12×6	–	–	Yes
Waste tray	–	–	Yes
Interface cable assembly	–	–	Yes

INSTALLATION QUALIFICATION**• PRE- INSTALLATION REQUISITES & VERIFICATION:-**

Check the installation place for fulfillment for manufacturer's recommendation

(Utilities such as power requirement, water and environmental conditions such as humidity, temperature, light and dust etc., please refer pre-installation requisites attached with this document).

Table no.4: PRE- INSTALLATION REQUISITES & VERIFICATION

ITEM	CONDITION	OBSERVATION
Instruments & accessories appearance checks	No damages to instrument & accessories	Yes
Installation table space leveling & vibration	As per requirements. (leveled & free from vibration – ref- USP/BP/IP)	Yes
Power requirements connections sockets Supply voltage* Supply frequency* Earthing Earth to neutral potential	Servo Stabilized & Free From transients 15A-1no. & 5A-1NO./3NOS. 110/220Vac or 115/230VAC,±10% 50/60Hz,±10% Proper Not more than 3V.	Yes
Environmental conditions: Sunlight Air draft Room temperature Humidity Dust Flammable, toxic & corrosive vapors Water discharge facility	Away from direct sunlight No direct over head fan or air conditioner 15° C ~ 32° C 20% ~ 80% Free from dust Free from vapors Drain tap connectivity	Yes
Instrument electrical connectivity check	Instrument power cable & control cable connectivity with peripherals	Yes

INSTALLATION QUALIFICATION**STANDARD ACCESSORIES PHYSICAL DIMENSIONS CHECK:-****A) PADDLE****Table no.5:Paddle Specifications**

DIM.	DIM.	DIM.	DIM.	DIM.	DIM.	REMARKS
	A	B	C	D	E	
USP Limits	9.40-10.1mm before coating	42.0 mm	74.0-75.0mm	19.0±0.5 mm	4.0±1.0 mm	
Paddle no.	MEASURED VALUE					
1	10mm	42mm	42mm	27mm	5mm	
2	10mm	42mm	42mm	27mm	5mm	
3	10mm	42mm	42mm	27mm	5mm	
4	10mm	42mm	42mm	27mm	5mm	
5	10mm	42mm	42mm	27mm	5mm	
6	10mm	42mm	42mm	27mm	5mm	
7	10mm	42mm	42mm	27mm	5mm	
8	10mm	42mm	42mm	27mm	5mm	

NOTE: - tolerances are ±1.0mm unless otherwise stated.

X&Y dimensions are not to vary more than±0.5mm when part is rotated on center line axis

B).BASKET**Table No.6 Basket Specifications**

DIM.	DIM. A	DIM. B	DIM. C	DIM. D	DIM. E	DIM. F	DIM. G	DIM. H	DIM. I	REMARKS
USP Limits	9.40-10.1 mm	20.2±0.1 mm	27.0 ±1.0 mm	37.0 ±3.0 mm	20.2 ±1.0 Mm	25.0 ±3.0 mm	22.2 ±1.0 mm	5.1 ±0.5 mm	2.0 ±0.5 mm	
Basket	Measured value									
1	10mm	20mm	25mm	41mm	20mm	25mm	22.2mm	7mm	4mm	
2	10mm	20mm	25mm	41mm	20mm	25mm	22.2mm	7mm	4mm	
3	10mm	20mm	25mm	41mm	20mm	25mm	22.2mm	7mm	4mm	
4	10mm	20mm	25mm	41mm	20mm	25mm	22.2mm	7mm	4mm	
5	10mm	20mm	25mm	41mm	20mm	25mm	22.2mm	7mm	4mm	
6	10mm	20mm	25mm	41mm	20mm	25mm	22.2mm	7mm	4mm	
7	10mm	20mm	25mm	41mm	20mm	25mm	22.2mm	7mm	4mm	
8	10mm	20mm	25mm	41mm	20mm	25mm	22.2mm	7mm	4mm	

C). BOWL/JAR (dissolution vessel)**Table no. 7 C). BOWL/JAR**

BOWL/JAR 1 LITER	HEIGHT A	DIAMETER B
	USP Specification 160-210mm	USP Specification 98-106mm
1	200mm	110mm
2	200mm	110mm
3	200mm	110mm
4	200mm	110mm
5	200mm	110mm
6	200mm	110mm
7	200mm	110mm
8	200mm	110mm

Table no.8 INSTALLATION QUALIFICATION VERIFICATION:-

MODEL NO. : DS 8000	
SR NO. OF INSTRUMENT:	DT12420511

• INSTRUMENT IDENTIFICATION & VERIFICATION		
NO.	DESCRIPTION	OBSERVATION
A)	Shipment contents as per purchase order.	Yes

• PRE- REQUISITIES INSPECTION		
NO.	DESCRIPTION	OBSERVATION
1	Instrument & accessories checked for Damages	Yes
2	Table space & leveling	Yes
3	Power supply availability	Yes
4	Environmental requirements	Yes
5	Instrument electrical connectivity	yes

Table no.9 STADARD ACCESSORIES & PHYSICAL DIMENSION INSPECTION

STADARD ACCESSORIES & PHYSICAL DIMENSION INSPECTION		
NO.	DESCRIPTION	OBSERVATION
A)	Paddle Blades And Shafts	yes
B)	Baskets	yes
C)	Bowl / Jar	yes

Table no.10 OTHER USP REQUIREMENT INSPECTION

OTHER USP REQUIREMENT INSPECTION		
NO.	DESCRIPTION	OBSERVATION
A)	WOBBLE & SHAFT CENTERING CHECK	Yes
B)	DEPTH HEIGHT SETTING	yes

OPERATIONAL QUALIFICATION

Operational qualification (OQ) is the process of demonstrating that an instrument will function according to its operational specification in the selected environment.

- **CUSTOMER ORIENTATION & TRAINING:-**
- Orientation For the end users /will be performed as per the operator's instruction manual.

Table no.11: Orientation For the end users /will be performed as per the operator's instruction manual

Orientation topic	status	Verified
1).Instrument setup/connectivity with the accessories, peripherals and etc.	Explained/shown	yes
2).Instrument front panel- display& key functions,	Explained/shown	Yes
3).Instrument back panel-connection	Explained/shown	Yes
4).Instrument menu & its functions, <ul style="list-style-type: none"> • Program-add/edit, copy& delete. • Run-run& view • Print-run, prog. Para & validation report generation • Function-clock, wake up, pump, sampler clean, config. & validation. • Data evaluation(optional) 	Explained/shown	yes
5)Instrument & accessory maintenance	Explained/shown	yes

• **OPERATIONAL CHECKING & VERIFICATION**

Fill the tank with D.M. water till the level indicated on tank.

Assemble the pump, cassette and tygon tubing. Load the sample collection tray with dry empty vials/bottles. Ensure interconnectivity between the main systems, pump and sample collector.

• **POWER ON CHECK FOR DISSOLUTION TESTER &SAMPLING ACCESSORY**

Table no.12 POWER ON CHECK FOR DISSOLUTION TESTER &SAMPLING ACCESSORY

REQUIREMENT CONDITIONS	OBSERVATION
Initialization & system diagnostics – check the LCD display Status after power on. (refer manual)	yes
Sampling accessory Up/Down Movement check	Yes
Display status for Bowl & Bath temperature sensor/s (6bowls – if temperature reader installed)	yes
Press the RESET key and check the system resets and initializes	Yes
check Tablet dispenser operation, if installed.	Yes
Press all the keys on the front panel & check for the buzzer beeps and check the related functions. (refer manual)	yes

• **POWER ON CHECK FOR SAMPLE COLLECTOR & PUMP**

Table no.13 POWER ON CHECK FOR SAMPLE COLLECTOR & PUMP

REQUIREMENT CONDITION	OBSERVATION
Initialization & system diagnostics-check the display status after power on.	Yes
Sample collector arm moves forward and MANUAL & READY LED glows.	Yes
Check operation of sampling arm movement by front panel keys	Yes
Pump when turned ON-Display reads pump RPM or flow rate as per selection after initialization	yes

C) STIRRER HOOD LIFT MOVEMENT CHECK**Table no.14 STIRRER HOOD LIFT MOVEMENT CHECK**

REQUIREMENT CONDITIONS	OBSERVATION
Take the stirrer Hood UP , by pressing the UP key from the keyboard <ul style="list-style-type: none"> • Check for the LCD display message • Check for the smooth movement 	yes
Stopping the lift movement in between by pressing the DOWN key	Yes
Take the stirrer Hood DOWN, by pressing the DOWN key from the keyboard. <ul style="list-style-type: none"> • Check for the LCD display message • Check for the smooth movement. 	yes
Stopping the lift movement in between by pressing the UP key	Yes

D) BATH WATER WITH CIRCULATION PUMP CHECK**Table no.15 BATH WATER WITH CIRCULATION PUMP CHECK**

Bath circulation pump operation & safety inter lock with water level sensing. <ul style="list-style-type: none"> • Circulation pump remains continuously ON during system power is available. • It should be inoperative OFF (this is the inhibit check) when the water level drops below the sensor. 	yes
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OPERATIONAL CHECKING & VERIFICATION**• RPM CHECK:****Table no.16 RPMCHECK:**

MEASUREMENT	RPM			PASSED	FAILED
	SET ±4%	ACTUAL			
		PADDLE	BASKET		
1	25±0.4	25	25	Yes	
2	50±0.4	50	50	yes	

Table no.17 OPERATIONAL CHECKING & VERIFICATION

MEASUREMENT	BATH TEMPERATURE			PASSED	FAILED
	SET	ACTUAL			
		DISPLAYED TEMPERATURE	EXTERNAL THERMOMETER		
1	37	37.5°C	37.9°C	Yes	
2	37	37.5°C	37.9°C	Yes	
3	37	37.5°C	37.9°C	yes	

- Verify the temperature with the standard calibrated thermometer, set $\pm 0.5^\circ\text{C}$.

G) BOWL MEDIA TEMPERATURE CHECK

- Fill the bath with D.M. water & bowl/vessels with the DM water & place them in the bath.
- RUN the program with bath set temperature 37.5°C. Let it stabilizes for at least 30 minutes.
- Wait till the temperature reaches the set value & stabilizes in the bowls.
- Verify the temperature with the standard calibrated thermometer
- Check the temperature in individual bowls/jars. (37.0°C, $\pm 0.5^\circ\text{C}$)

Table no.18 BOWL MEDIA TEMPERATURE CHECK

MEASUREMENT T BOWL/JAR	TEMPERATURE		PASSED	FAILED	
	NOMINAL	ACTUAL			
		DISPLAYED TEMPERATURE			EXTERNAL THERMOMETER
1	37.0,±0.5°C	37.5°C	37.9°C	Yes	
2		37.5°C	37.9°C	Yes	
3		37.5°C	37.9°C	Yes	
4		37.5°C	37.9°C	Yes	
5		37.5°C	37.9°C	Yes	
6		37.5°C	37.9°C	Yes	
7		37.5°C	37.9°C	Yes	
8		37.5°C	37.9°C	Yes	

Table no.19 RUN TEST

REQUIREMENT CONDITIONS	OBSERVATION
Select the program no. with the required test parameter. Enter the RUN parameter- ID. No. and start RUN. Display reads the bowl temperature measured by ext. sensor, RUN and bath temperature.	Yes
Check for the display- bowl temperature 37.0, ±0.5°C. Ready condition.	Yes
Check 6bowl & ext. temperature reading by dot “.” Key.	Yes
Press the RUN/HOLD key to stop the paddle stirrer and repress the same key to start the dissolution run. Display reads the process parameters.	Yes
Sample collector initializes and sampling arm moves to first position.	Yes
Check that sampling assembly is lowered down in prior to actual interval time ends and pump is started at interval time. Check the interval time with the standard calibrated stop watch.	Yes
Check that samples collected in the first row of the sample collector and check the increment of interval no. after the set interval time is over and next intervals time is displayed	Yes
Check the reversal of pump for replenishing at the end of sampling	Yes
Check the sample collector arm is advanced to next row	Yes
Check for the end of the dissolution run after the last interval time is over.	Yes

J) OPERATIONAL CHECKING & VERIFICATION:**Table no.20 ERROR INDICATION CHECK**

REQUIREMENT CONDITIONS	OBSERVATION
Check for invalid entry by entering out of the range set parameters values	Yes
Check for water level sensor by lowering the sensor arm. Warning beeper turns on and display reads - *w on 2 nd line RHS	Yes
Check for high temperature, set the program temperature less than the actual bath by 1.0°C- display reads – “wait cooling”.	yes
Temperature sensor check- remove the ext. bowl temperature sensor’s connector- display reads – “open”.	Yes

RESULTS AND DISCUSSION:

Calibration curve of paracetamol pure drug was determined at 243 λ max using 6.8 pH phosphate buffer measured and % drug release was calculated[4].

RPM Check**Table no.21 at 25 RPM (TRIAL I):-**

TIME	ABSORBANCE	CONCENTRATION	OPTIMUM	ADR	CDR	% OF DRUG RELEASE
5	0.2759	2.60	20	4696	46.91	9.39
10	0.4530	5.88	20	106	106.7	21.2
15	0.5210	9.14	20	128.6	129.1	28.7
20	0.6425	9.39	20	169.1	190.2	33.85
25	0.7121	10.68	20	192.3	193.5	38.4
30	0.7803	11.95	20	215.1	215.5	43.02

Table no.22 at 25 RPM (TRIAL II):-

TIME	ABSORBANCE	CONCENTRATION	OPTIMUM	ADR	CDR	% OF DRUG RELEASE
5	0.3521	4.02	20	72.36	72.36	14.47
10	0.3721	4.39	20	79.03	79.8	15.90
15	0.4284	5.43	20	97.8	98.1	19.5
30	0.6102	8.8	20	158.4	158.7	31.68
45	0.7213	10.85	20	195.4	195.7	39
60	0.7910	12.14	20	216.6	219.2	43.7

Table no.23 at 25 RPM (TRIAL III):-

TIME	ABSORBANCE	CONCENTRATION	OPTIMUM	ADR	CDR	% OF DRUG RELEASE
5	0.3713	4.37	20	78.7	78.7	15.7
10	0.5093	6.94	20	124.9	125.1	24.9
15	0.563	9.93	20	142.8	143.2	28.5
30	0.692	10.32	20	185.7	185.9	37.1
45	0.757	11.53	20	207.6	208.3	41.5
60	0.781	11.96	20	215.3	215.9	43.06

% DRUG RELEASE mean at 25 RPM operated for 1 hour = trial I + trial II +trial III/3= 43.02+43.7+43.06/3=43.26

Table no.24 at 50 RPM (TRIAL I):-

TIME	ABSORBANCE	CONCENTRATION	OPTIMUM	ADR	CDR	% OF DRUG RELEASE
5	0.165	0.572	100	51.5	51.5	10.3
10	0.201	1.229	100	110.6	110.9	22.1
15	0.240	1.951	100	175.6	176.3	35.1
20	0.285	2.784	100	250.6	252.1	50.1
25	0.363	4.228	100	380.6	383.4	76.1
30	0.402	4.951	100	445.6	446.9	89.1

Table no.25 at 50 RPM (TRIAL II):-

TIME	ABSORBANCE	CONCENTRATION	OPTIMUM	ADR	% OF DRUG RELEASE
5	0.381	20	1	18	36
10	0.499	26.6	1	24	48
15	0.539	30	1	27	54
20	0.638	34.7	1	31	62
25	0.715	38.8	1	35	70
30	0.826	45	1	40	81

Table no.26 at 50 RPM (TRIAL III):-

TIME	ABSORBANCE	CONCENTRATION	OPTIMUM	ADR	%OF DRUG RELEASE
5	0.315	8.55	1	7.7	38.5
10	0.379	10.48	1	9.44	47.2
15	0.44	12.32	1	11.4	55.7
20	0.53	15.15	1	13.64	68.2
25	0.60	17.24	1	15.52	77.6
30	0.655	18.23	1	16.82	84.3

% DRUG RELEASE mean at 50 RPM operated for ½ hour = trial I + trial II +trial III/3= 89.1+81+84.3/3=84.8

Table no. 27 OPERATIONAL QUALIFICATION & VERIFICATION

MODEL NO. OF INSTRUMENT:	LABINDIA DS 8000 SC/TR
SR. NO. OF INSTRUMENT:	DT12420511

NO.	DESCRIPTION	OBSERVATION
1.	OPERATIONAL CHECKING & VERIFICATION <ul style="list-style-type: none"> power on check for dissolution tester & sampling accessory power on check for sample collector & pump stirrer hood lift movement check bath water circulation pump check RPM check Water bath temperature check Bowl media temperature check Tubing (dead) volume & pump flow rate check Sampling & replenishing volume check RUN test Error indication check 	Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes yes

With the observations from the conducted design, installation, operational qualifications the dissolution apparatus was found to be as within the specified results as mentioned in the vendor's guide.

CONCLUSION:

Dissolution test apparatus being a crucial test in –vitro evaluation parameter has been validated as compendial equipment's specified in vendors order and the results are in compliant with the qualifications of operational, installation, performance, and design qualification. With this validated process the dissolution apparatus is considered to be acceptable for use and assuring to perform dissolution testing of the specified drug formulations.

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