



**DissoPrep X8™/DissoPrep X15™**

Dissolution Media Preparation and Delivery Station

EFFICIENT · REPRODUCIBLE · SAFE

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### DEAERATION – THE PRINCIPLES

The effects of air bubbles and other dissolved gases in the media used to conduct dissolution tests can be significant. A Design of Experiment (DOE) study reported by USP in 2007 (Joseph Eaton et al. „Perturbation Study of Dissolution Apparatus Variables – A Design of Experiment Approach“. Dissolution Technologies February 2007 Volume 14 Issue 1) found that of the 9 variables and 36 two-factor variables studied, three variables stood out as being statistically significant as far as mean percent dissolved was concerned: level of deaeration, vessel type and rotation speed, with the level of deaeration contributing to 52.3% of the total reported effects. The major influence of gas or air in dissolution work seems to be physical. Air bubbles may collect on the dosage form, the basket containing the dosage form or the sampling probe or their filters used to draw off samples for analysis. Their presence in spectrophotometer flow cells or on fibre optic probes may lead to incorrect absorbance readings. They may also accumulate on the membranes employed in the vertical diffusion cells used in transdermal and percutaneous absorption tests.

### THE REGULATIONS

The Pharmacopoeias recognise that „dissolved gases in the dissolution medium may affect dissolution test results and recommends that gases be removed before the test is performed“. They advocate the following procedure as one method of deaeration: „Heat the medium, while stirring gently, to about 41 degrees C, immediately filter under vacuum using a filter having a porosity of 0.45 microns or less, with vigorous stirring and continue stirring under vacuum for about 5 minutes“. This „filtering, warming and stirring under vacuum“ approach is echoed by the FDA (Terry W. Moore. „A Fast, Efficient Procedure for Degassing Dissolution Medium“ Dissolution Technologies. May 1996). The Pharmacopoeias also state „Place the stated volume of the Dissolution Medium (+/- 1%) in the vessel of the specified apparatus given in the indi-

vidual monograph, assemble the apparatus, equilibrate the Dissolution Medium to 37 +/- 0.5 degrees C, and remove the thermometer“.

The temperature of the medium is critical to volumetric precision. The volume of the dissolution medium at the stated temperature of 25 degrees C is different for that at 37 degrees C, at which point the volume would be greater because the medium expands as the temperature rises. It is for this reason that USP suggests that a more accurate and temperature independent measure of the media volume is gravimetric i.e., by weight.

### USER REQUIREMENTS

In addition to conformity to the compendial and regulatory requirements, there are a number of user requirements which must be taken into account:

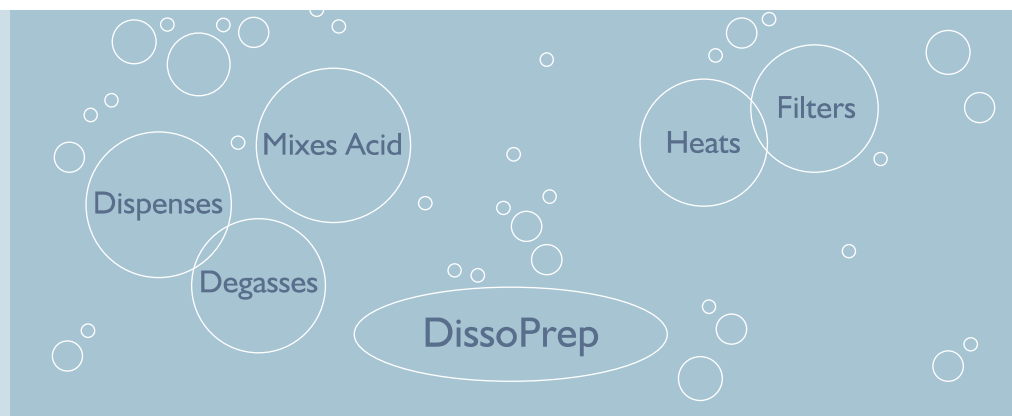
- Simple, safe and easy-to-use operation
- Proven time savings in comparison with manual methods
- Compact (space saving)
- Accurate and reproducible
- Capable of validation
- Documentation

The „DissoPrep“ Media Preparation Station combines degassing and dispensing to provide a fresh source of prewarmed, deaerated and dosed dissolution medium thus substantially reducing down times between dissolution tests. There is no necessity to premix the dissolution medium in advance. The „DissoPrep“ automatically adds the appropriate volume of acid, buffer or surfactant to the prewarmed medium prior to mixing and dispensing.

### PRINCIPLE OF OPERATION

The principle of operation is extremely simple. The „DissoPrep“ operates on the same „filtering, warming and stirring under vacuum“ approach as recommended by the Pharmacopoeias and FDA. On initiation, dissolution medium is withdrawn under vacuum from the media reservoir (not provided) through the heater which warms the medi-





um to the desired temperature and into the polypropylene mixing chamber. An easily exchangeable filter cartridge located in-line within the fill tube filters the medium prior to use. The life of the filter is constantly monitored in terms of total elapsed volume filtered and the user prompted to change the filter when required. The default setting is 5,000 litres.

The medium is preheated to the appropriate temperature (adjustable between 20 and 45 degrees C in 0.1 increments) en route to the mixing chamber by means of a special continuous-flow heater, before degassing takes place. This enhances the degassing process and saves considerable time in testing.

If the „Additive“ function has been selected, then the concentrated acid, buffer or surfactant is automatically added to the mixing chamber at this point. Dilution ratios of between 1:3 and 1:100 can be accommodated. An in-built magnetic stirrer ensures a homogenous mix within the mixing chamber (Accuracy: <0.5%, typically <0.2%). The efficiency of the degassing process is dependent on:

- the vacuum applied, in this case, <250 mbar (typically <100 mbar) pressure absolute
- the time the medium is exposed to the vacuum
- the temperature of the medium
- the stirring of the medium

All of these factors assist in the deaeration process. In the case of the „DissoPrep“, the interaction of heating, mixing and degassing generates a typical effective deaeration level of 3 to 4.5 ppm dissolved oxygen (measured after filling into the vessel).

The mixing chamber has a maximum total capacity of 11 litres (DPX8) or 16 litres (DPX15). This allows for 8 litres (DPX8) or 15 litres (DPX15) of fresh medium sufficient to fill all the vessels of one or two dissolution bathes, plus additional litres to accommodate the dead volume created by the tubes, etc., and also provide a flush sequence at the start of the dispense cycle.

Note: The importance of fresh medium cannot be overestimated. An investigation into the overnight re-aeration of unused previously de-aerated media found that the concentrations of dissolved oxygen almost doubled during the period concerned (Owen S. Degenhardt et al. „Comparison of the Effectiveness of Various Deaeration Techniques“. Dissolution Technologies. February 2004). The prewarmed and de-aerated medium is dispensed directly into the dissolution vessels by means of a hand-held dispense nozzle (Dispense rate: 2L/min and Accuracy <1%).

Tip: A single „DissoPrep“ could possibly service all of your Dissolution and Disintegration Testing needs.

### THE „DISSOPREP“

It typically takes 15 minutes from start to prepare 8 litres of medium and about 30 seconds per vessel to dispense. This means that a single „DissoPrep“ will handle several dissolution testers concurrently. Accuracy is paramount in any drug release study. One of the unique features of the „DissoPrep“ is that both fill and dispense volumes employed are determined gravimetrically, i.e. by weight using the in-built load cell provided for this purpose. Different media have different volumes dependent on their temperature and pressure conditions – only weight remains constant under such changing conditions. The use of a load cell means that all the processes involved can be documented and output to an external printer or PC. The „DissoPrep“ provides a full report detailing, weights, mixing ratios, vacuum and temperature after each „Dispense“ Cycle. Separate functions are available for Emptying, Autowashing and Calibration. A „Calibration“ protocol is also provided out from the „DissoPrep“. A „Calibration“ protocol is also provided out from the „DissoPrep“. Dissolution methods and protocols can be administered by a Remote Control Software compliant to 21 CFR Part 11 rules.

The „DissoPrep“ is extremely compact, it measures 30 x 59 x 66 cm (w x d x h) and weighs 26 kilos (DPX8) or 28 kilos (DPX15)



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### SPECIFICATIONS

UNIT	DissoPrep X8	DissoPrep X15
<b>DIMENSIONS</b>	B 30cm x H 65cm x T 60cm	B 30cm x H 65cm x T 60cm
<b>WEIGHT</b>	26kg net weight	28kg net weight
<b>VOLTAGE SUPPLY AND POWER RATING</b>	230V, 50/60Hz, 1.85kW, 115V, 50/60Hz, 1.85kW, 100V, 50/60Hz, 1.5kW	230V, 50/60Hz, 1.85kW, 115V, 50/60Hz, 1.85kW, 100V, 50/60Hz, 1.5kW
<b>PC INTERFACES</b>	PC Interface RS-232 (serial): COM1 and COM2; LAN Optional: PC Software (21 CFR Part 11 compliant)	PC Interface RS-232 (serial): COM1 and COM2; LAN Optional: PC Software (21 CFR Part 11 compliant)
<b>PRINTER INTERFACE</b>	Centronics (LPT parallel), USB PCL-5 and PCL-6, ASCII font	Centronics (LPT parallel), USB PCL-5 and PCL-6, ASCII font
<b>OUTPUT CHANNEL</b>	1 dispense output Optional: Remote Control Nozzle	1 dispense output Optional: Remote Control Nozzle
<b>INPUT FILTER</b>	PP Cartridge Filter 20µ	PP Cartridge Filter 20µ
<b>INPUT CHANNELS</b>	2 Inputs (water/premixed media line, additive line); Input pressure max. 0.1 bar	2 Inputs (water/premixed media line, additive line); Input pressure max. 0.1 bar
<b>MAX. ACID CONCENTRATION</b>	36% hydrochloric acid at the additive input line (~3N); 0.5% hydrochloric acid at the medium input/output line (~0,1N)	36% hydrochloric acid at the additive input line (~3N); 0.5% hydrochloric acid at the medium input/output line (~0,1N)
<b>DOSING PRINCIPLE</b>	Gravimetric	Gravimetric
<b>CALIBRATION</b>	Manual / Automated calibration capabilities with Protocol consolidation of the calibration instruments	Manual / Automated calibration capabilities with Protocol consolidation of the calibration instruments
<b>STORAGE VOLUME</b>	8,000g net, apportionable from 1 - 36 vessels, 11,000g gross	15,000g net, apportionable from 1 - 72 vessels, 16,000g gross
<b>PREFILL VOLUME</b>	1,500g (necessary for prefilling the tank)	1,800g (necessary for prefilling the tank)
<b>PREHEATING</b>	till 45 °C (setting in 0.1 °C digits)	till 45 °C (setting in 0.1 °C digits)
<b>TEMPERATURE</b>	< 1.5°C at 32°C to 37°C	< 1.5°C at 32°C to 37°C
<b>ACCURACY</b>	and > 5,000g, monitored	and > 5,000g, monitored
<b>MIXING UNIT</b>	Magnetic Stirrer, functionally monitored	Magnetic Stirrer, functionally monitored
<b>ADDITIVE MIXING</b>	1:3 - 1:100 (33% to 1%) (setting in 0.1g digits) Max. 1,000g Additive per vessel	1:3 - 1:100 (33% to 1%) (setting in 0.1g digits) Max. 1,000g Additive per vessel
<b>MIXING ACCURACY</b>	< 0.5% of ratio 1:3 - 1:100, typ. 0.2%, monitored	< 0.5% of ratio 1:3 - 1:100, typ. 0.2%, monitored
<b>DEGASSING</b>	Vacuum typ. < 100mbar pressure absolute, monitored < 5.5 ppm, typ. 3.5 - 4.5 ppm	vacuum typ. < 100mbar Vpressure absolute, monitored < 5.5 ppm, typ. 3.5 - 4.5 ppm
<b>THROUGHPUT</b>	24 - 32 l/h, 400 - 533 mL/min	26 - 35 l/h, 400 - 533 mL/min
<b>DOSING RATE</b>	2,000mL/min	2,000mL/min
<b>DOSING VOLUME</b>	100g - 8,000g (setting in 1g digits)	100g - 15,000g (setting in 1g digits)
<b>DOSING ACCURACY</b>	< 1% at 500 - 8,000g, typ. 2g, monitored	< 1% at 500 - 15,000g, typ. 3g, monitored
<b>AUTOWASH</b>	volume and number of cycles selectable 1 cycle, 1,500g, typ. 7 - 8 min	volume and number of cycles selectable 1 cycle, 1,500g, typ. 7 - 8 min