



DPX8-AIS

DISSOPREP X8 ADDITIONAL INFORMATION SHEET

ID 20100927 REV 5

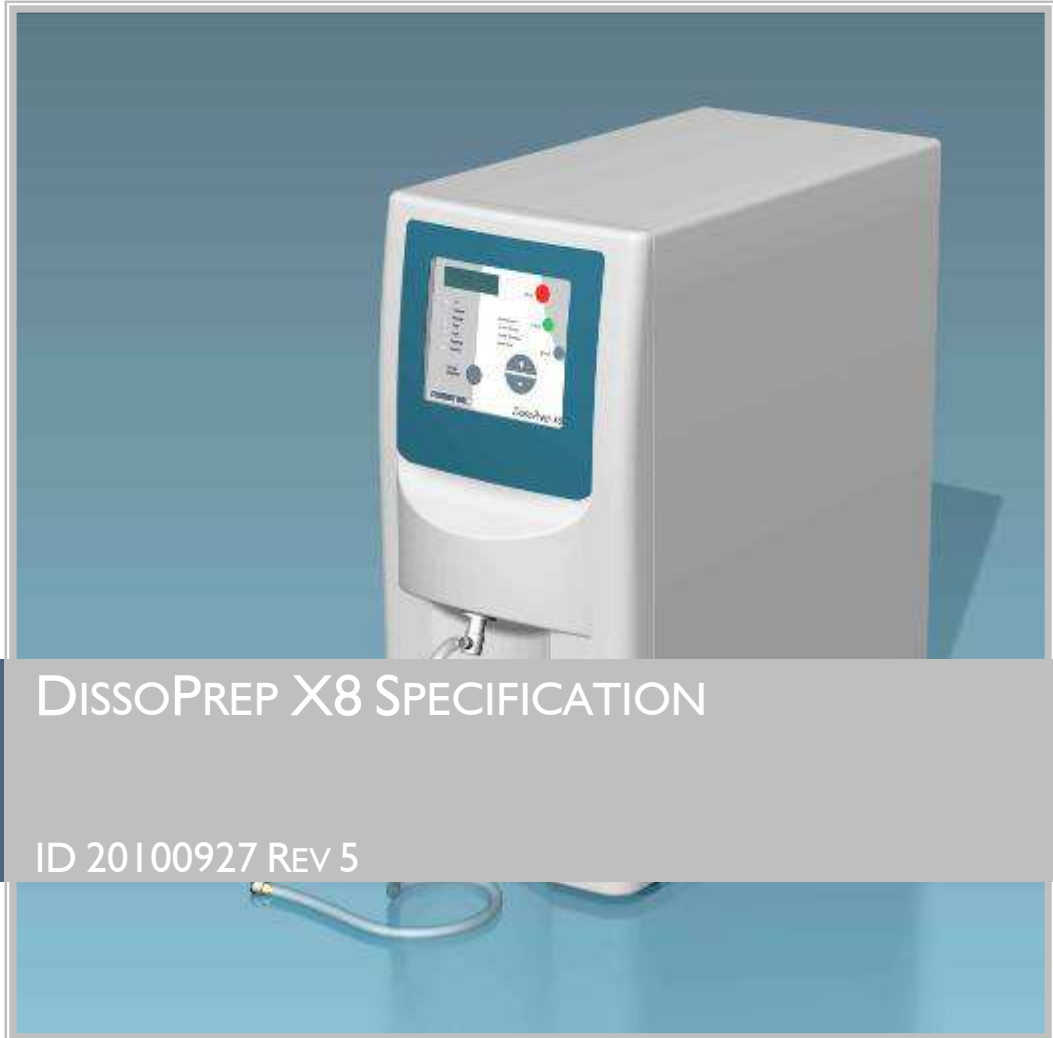
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DISSOPREP X8 SPECIFICATION

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Dimensions	B 30cm x H 65cm x T 60cm
Weight	26kg net weight
Voltage Supply and Power Rating	230V, 50/60Hz, 1.85kW, 115V, 50/60Hz, 1.85kW, 100V, 50/60Hz, 1.5kW
PC Interfaces	PC Interface RS-232 (seriell): COM1 and COM2; Optional: PC Software (21 CFR Part 11 Compliant);
Printer Interface	Centronics (LPT parallel), ASCII font
Calibration	Manual / Automated calibration capabilities with protocol consolidation of the calibration instruments
Storage Volume	8000mL netto, apportionable from 1 to 36 vessels, 11000mL brutto
Prefill Volume	1500mL (necessary for prefilling the tank)
Throughput	24 - 32 l/h
Degassing	Vacuum typ. < 100mbar pressure absolute, monitored
Dosing Principal	Gravimetric
Dosing Volume	100g – 8000g (setting in 1g digits)
Dosing Accuracy	< 1% at 500 – 8000g, typ. 2g, monitored
Preheating	20 - 45 °C (setting in 0.1 °C digits)
Temperature Accuracy	< 1,5°C at 32°C to 37°C and > 5000g, monitored
Mixing Unit	Magnetic Stirrer, functionally monitored
Additive Mixing	1:3 to 1:100 (33% to 1%) (setting in 0.1g digits) Max. 1000 g Additive per vessel
Mixing Accuracy	< 0.5% of ratio 1:3 to 1:100, typ. 0.2%, monitored
Max. Acid Concentration	36% hydrochloric acid at the additive input line; 0.5% hydrochloric acid at the medium input/output line
Input Channels	2 Inputs (water/premixed media line, additive line); Input pressure max. 0.1 bar)
Input Filter	PP Cartridge Filter 20µ
Output Channel	1 Output (standard outlet line); Optional: Remote Control Nozzle

E N D of DissoPrep X8 Specification



BASIC INFORMATION

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I Intro

“DISSOLVED GASES AFFECT DISSOLUTION TEST RESULTS NEGATIVELY”

(USP 23/NF 18; United States Pharmacopeia Convention: Rockville, MD, 1994; p. 1792)

DissoPrep X8 avoids falsified dissolution test results by dissolved gases and deviated volume dosages!

Thereby DissoPrep X8 fulfills regulatory requirements of USP (United States Pharmacopeia), EP (European Pharmacopeia), FDA, (Division of Drug Analysis) and GLP (Good Laboratory Praxis)/GMP (Good Manufacturing Praxis).

2 Regulatory Demands

2.1 USP and EP Regulations

2.1.1 Volume Determination under Standard Conditions of the USP



“Place the stated volume of the dissolution medium with an accuracy of 1% in the vessels and equilibrate it to $37 \pm 0.5^\circ\text{C}$...” (USP).

The "Stated Volumes" must be the volume at „Standard Conditions" not the volume at 37°C . Measuring warm media in a volumetric flask or other device calibrated at 20°C will give an incorrect result. It is also wrong to use the specific weight (density) for gravimetric volume measuring of the media at e.g. 37°C . Weigh the "Quantity of Mass" of the "Stated Volume". Pay attention to the specific weight at "Standard Conditions".



*Standard Conditions are normally 20°C and 1 bar.
d.h. 1000mL H₂O weigh 998,3g.*



Standard Conditions according to the USP: 25°C . / 1 bar.
d.h. 1000ml H₂O weigh 997,1g;
d.h. 900ml H₂O = 897,4g etc.



Additive must be used like medium water. Take care of the respective producer specifications.



The volume may be related in no case to the test temperature, e.g. 37°C .



The DissoPrep X8 entries must be made in g.

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2.1.2 Degassing of the Dissolution Medium after the USP



„The USP recognizes that dissolved gases in the dissolution medium may affect dissolution test results and **recommends that gases be removed before the test is performed.**” (USP)

In the literature there have not been any clear reports on the consequences of various degassing methods until recently (Ref: Dissolution Technologies, February 2004, “Comparison of the Effectiveness of Various Dearation Techniques”). The USP method is only a recommendation. Other degassing methods with comparable results are also allowed. Usually, internal company experiences are not published. Therefore a summary shall be given of the several years practical experience.

- The DissoPrep X8 degasses using an automated and reproducible method.
- The degassing method of the DissoPrep X8 corresponds essentially to the USP recommendation with regard to the parameters “Filtering, Warming and Stirring under Vacuum”.
- In the comparison with other degassing methods the degassing efficiency of the DissoPrep X8 absolutely corresponds to the degassing method of the USP or FDA recommendation and the method of the helium degassing, particularly if the measuring is done in the vessel at the start of the dissolution test.

2.2 FDA Recommendations

The FDA (Division of Drug Analysis) targeted the degassing more than ever as an area of concern and raised the awareness of the issue for a huge number of users.

FDA member Terry W. Moore published in the professional journal “Dissolution Technologies / MAY 1996” a recommendation for degassing of dissolution medium with illustration of a principle (see Illustration “FDA Degassing Procedure”). The recommended method refers to parameters of the USP recommendation “filtering, warming, stirring, vacuum and process time”. Stirring is realized by feeding air bubbles in the process carboy.

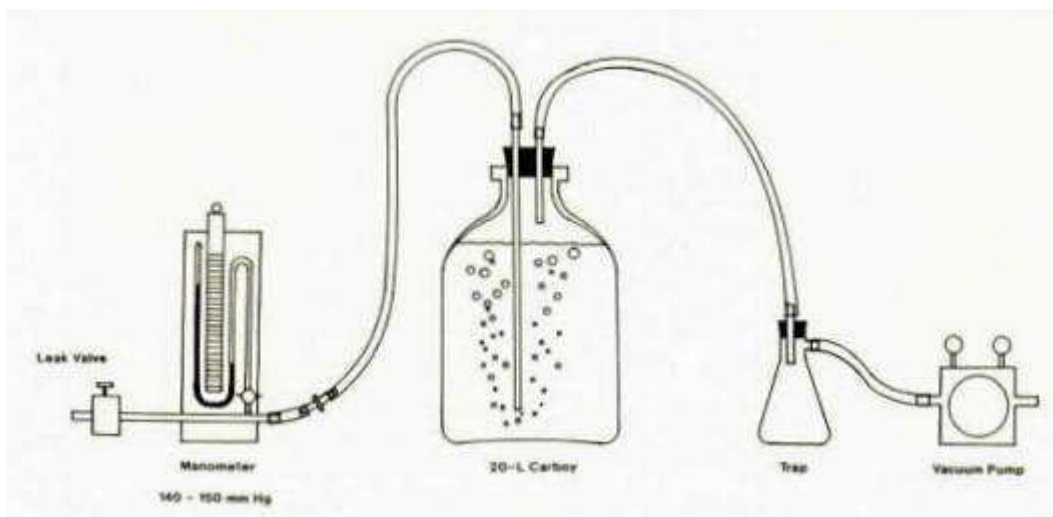


Illustration I: FDA Degassing Procedure

2.3 GLP/GMP Recommendations

The GLP/GMP rules demand a prescribed handling method SOP for the production of the medium and the **documentation of all working steps actually taken place (traceability).**

3 User Demands

3.1 Functionality in handling

The handling must be simple and convenient. Efficiency is increased only in connection with the ***full acceptance of the unit by the laboratory staff.***

3.2 Time and space saving

Media filtering, heating, mixing and degassing must be performed without user intervention in a reasonable time.

The throughput by avoidance of unnecessary manual steps and unnecessary waiting for the heating of the medium before beginning of test should be increased. Precise media dispensing directly into the sample vessels, saves time and unnecessary media handling.

In many laboratories the space for instruments is often not sufficiently or scarcely limited.

Therefore a unit must be compact.

3.3 Reproducibility - Process and Dosage Validation

All internal dosage events are controlled using a precision pondering cell. Introduction of the liquids, mixing of water and concentrated additive, and dispensing accurate volumes into each vessel is precisely controlled and documented each step of the way. For validation documentation an external printer or PC can be easily interfaced to the DissoPrep X8.

3.4 USP, EP, FDA, GLP/GMP conformity

There is a quantity of most different requirements from regulations and standards. The fulfillment of these requirements produces a considerable operational and administrative work.

The performance and simplification of procedures is a serious concern.

Tests show that at physical ambient conditions with <95% saturation and 37°C the failure rate is significantly higher when using non de-aerated media than when using de-aerated media. That includes also the volume precision, which must be better than 1%.

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4 Features of the DissoPrep X8

The Media Delivery Station DissoPrep X8 (media degasser and media dispenser) filters and heats media, mixes and degasses both components medium and concentrate under stirring and vacuum. The mixture of medium and concentrate is precisely dispensed into the vessels in singles portions. All dosing processes are internally controlled by a Precision Load Cell and the result of the individual dosing is documented.

4.1 Filtering

An easily exchangeable filter cartridge is located inline within the fill tube. The capacity of the filter is checked automatically by monitoring the total elapsed volume filtered. Upon exceeding the filter capacity the DissoPrep X8 prompts the user to change the filter.

4.2 Additive Mixing

For the precise addition of concentrated hydrochloric acid (max. 36%) or buffer a second liquid inline channel is available. The composition calculation is carried out gravimetrically via a precision pondering cell.

4.3 Heating

A special continuous-flow water heater warms the media to a desired temperature before degassing takes place. This promotes an enhanced degassing and saves considerable time when heating in the dissolution tester.

4.4 Mixing

An *electronic stirrer mixes the components* medium and concentrate in the storage tank of the DissoPrep X8 and ensures a homogenous concentrate concentration. The stirrer is monitored.

For the *precise addition of concentrated hydrochloric acid (max. 36%, buffer or surfactant (SLS))* a second inlet channel (Inlet Tube for concentrate = Additive Tube) is available.

The composition calculation is carried out gravimetrically via a Precision Load Cell.

The precision of the composition is *better than 0.3%*.

4.5 Degassing

The medium is exposed to a constant vacuum of better than 95 mbar absolute pressure, below continues stirring and during sucking up to the dosage. The interaction of heating, mixing and degassing provides an *effective de-aeration of the medium e.g. for water with typically 3-5ppm O₂ (after filling into the vessel).*

The achieved de-aeration level (e.g. of 3-5ppm O₂ for water) is not nominally specified as the dissolved oxygen measurement is not robust and not asked from the USP. Furthermore no traceable standards for the calibration of oxygen meters exist. The physical effect parameters "saturation, temperature and vacuum" can be measured however reliably.

The dissolved air in the media contains more or less carbonic acid. Also carbonic acid is effectively removed when degassing and thus the pH value is stabilized.

The following consideration proves the effective degassing of the DissoPrep X8 according to the USP:

All affect parameters of the USP recommendation "filtering, heating, stirring, vacuum and process time" are used. The both essential parameters "temperature and vacuum" provide each exclusively the same result, but the combination enhances the process velocity.

In case of water temperature of 20°C and an atmospheric pressure (air pressure) of 1 bar, there are 9.08ppm oxygen and in addition further air components solved. With a warming to 37°C a value of 6.72ppm oxygen is reached theoretically. With the much lower than 300mbar pressure absolute the DissoPrep X8 reaches approximately the same degassing effect as when heating up on 70°C (at a temperature of 70°C water has a steam pressure of 300mbar).

4.6 Preparation and Dispensing

The preparation of 8 liters of media is complete within 15 minutes and can be done while a test is running, in order to save additional time. A target volume between 100 and 8000 ml can be selected. High precision dispensing of +/-0.5% in each vessel directly into the dissolution tester by means of a dispensing tube requires approx. 25 seconds/900 ml.

4.7 Documentation

All internal dosage processes are accurately controlled and monitored by a Precision Load Cell.

After each DISPENSE cycle the DissoPrep X8 provides a **DISPENSE Protocol** containing the values of each single dispensed volume, the mixing ratio, the temperature and the vacuum are internally stored and documented in protocols and can externally be shown on PC and/or printed on a printer. Any malfunction of operation processes is logged in an Error Trail File. For operation, validation and maintenance of the DissoPrep X8 comprehensive documentation is available.

See attached Dispense Protocol next Page.

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MEDIA DISPENSE PROTOCOL

No: 2

DissoPrep X8 RIGGTEK GmbH Germany

Serial Number : R30030356

Firmware Version: 7.108

General Data:

Nominal filter capacity [l]: 5000

Remaining filter capacity [l]: 4948

Volume throughput up to now : 52

Method: 1

900, 9.0, 6, 38.0

RATIO 1:100

Result of the dosages [g]:

	MEDIUM	ADDTV	RATIO	DEV%
Fill Nominal:	5400	54.0	0.010	
Fill Actual :	5919	59.2	0.010	+0.0

	MEDIUM	DEV%	ADDTV	DEV%
Vessel No. 6:	899	-0.1	9.0	+0.0
Vessel No. 5:	901	+0.1	9.0	+0.0
Vessel No. 4:	900	+0.1	9.0	+0.0
Vessel No. 3:	900	-0.0	9.0	+0.0
Vessel No. 2:	900	+0.0	9.0	+0.0
Vessel No. 1:	900	-0.0	9.0	+0.0

Temperature (average): 38.1 C

MAX.VACUUM at 89 mbar absolute pressure *

Date, Time:

.....

Name:

.....

Signature:

.....

* The information of the maximal vacuum is made after the serial number 2408XXXX

4.8 Time and space saving

DissoPrep X8 prepares up to **8L of dissolution medium** automated. The preparation lasts less than 15 minutes (12 minutes with prepared medium). The **fast and precise dosage** via a tube into the individual vessels saves time-consuming handling steps and handling steps, which require attention. The **preheated medium shortens long preheating times in the dissolution tester**.

The “Continuous-flow Principle” prevents bacteria growth when using the DissoPrep X8 regularly and provides fresh medium. The flush program is efficient and fast. There are practically no memory effects when changing the medium. The medium change hardly wastes medium, since the residues are very small in the DissoPrep X8.

The dimensions of the DissoPrep X8 are W 30cm x H 66cm x D 59cm. The weight of the unit is 27kg. The voltage supply is 230V 50/60Hz 16A or 115V 50/60Hz 15A or 100V 50/60Hz 15A. The rated power is 2300W maximal.

USP, EP, FDA, GLP/GMP conformity

DissoPrep X8 fulfils all requirements of the medium preparation **according to the demanded rules of the USP** (United States Pharmacopoeia) and **EP, as well as according to the recommendations of the FDA** (Division of Drug Analysis) and of the **GLP/GMP**.

5 Features in the Laboratory

5.1 Safety in the Laboratory

By automating the process, particularly the acid preparation and media dispensing, **the risks to laboratory personnel are held to a minimum**.

5.2 Time saving

The saving of time is considerable.

Once provided procedures (SOP) are started by push of a button. The DissoPrep X8 mixes ready for use medium from water and concentrate. The dispensing is fast and precise, faster and more precise than manually.

The preheating of the media could **save up to 45 minutes**, which a conventional dissolution tester with water bath would need for the heating.

5.3 Reproducibility of the results

Reproducibility of the results independently of the diversity of personnel is a result of the automation of the media preparation.

The demands of the USP/EP/GLP are easily fulfilled.

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5.4 Simplification of administrative documentation

With the optional available Remote Control Software DPX8_RC all protocols (Validation Certificates after a calibration and Protocols after each processed media batch) which are generated with the DissoPrep X8 can be filed in a PC network ***"21CFR Part 11 compliant"***.

The DissoPrep X8 files the protocols in an internal stack memory, so that a temporary separation from the network does cause no loss of data. The protocols can be seen and printed out at any time. Any method changes and protocol inquiries, as well as print orders at the DissoPrep X8 are documented in an AUDIT Trail with the stamp of the respective user.

Such documentation completes all test reports without omissions.

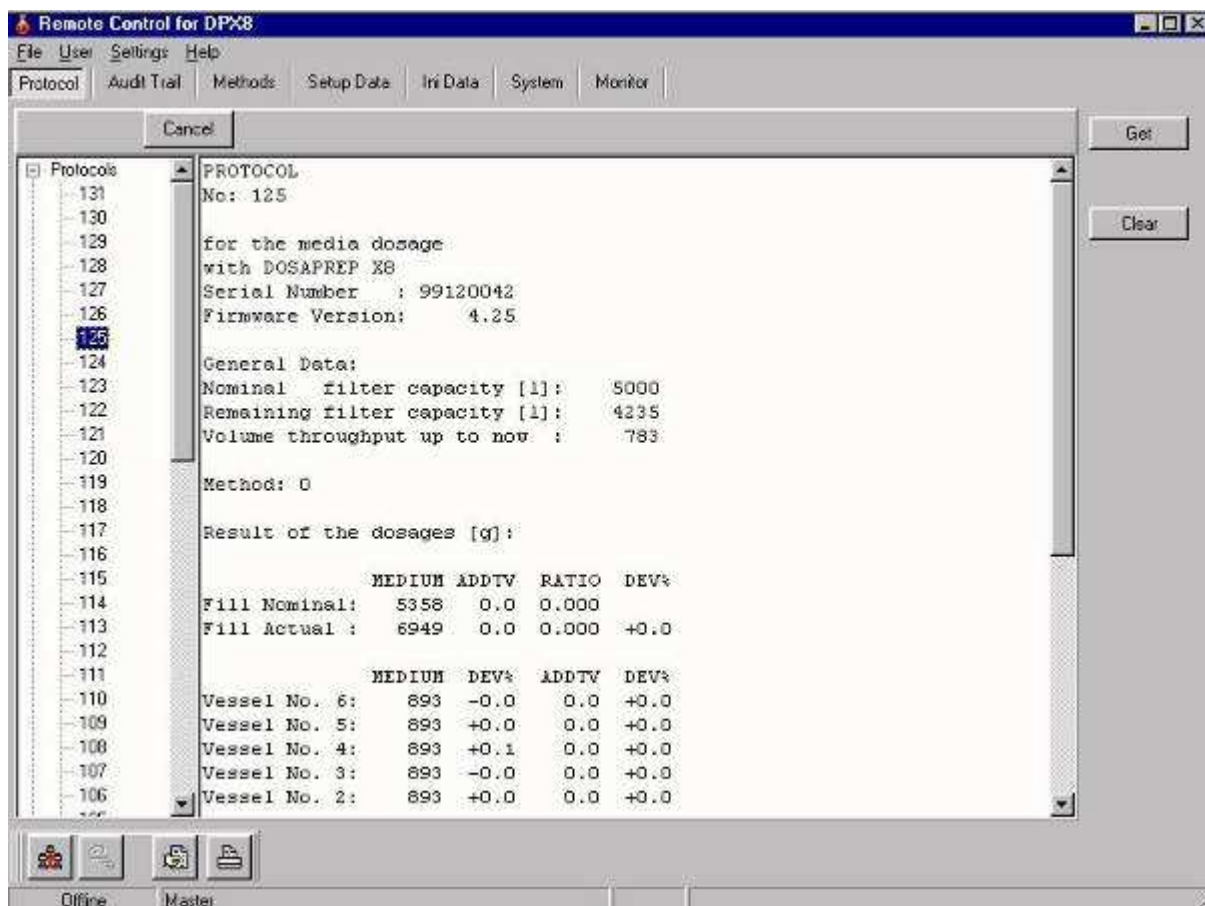


Illustration 2: RC Software for the DissoPrep X8

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6 Definition of Calibration, Adjustment, Verification & Basics of Validation

6.1 Introduction

The qualification of the Dissolution Test Systems is necessary to comply with the rules of the USP , the GLP/GMP and ISO 9000 /EN 45000.

The qualification procedures are separated into 4 sections, the Design Qualification (DQ), the Installation Qualification (IQ), the Operational Qualification (OQ) and the Performance Qualification (PQ). The OQ normally includes a calibration with adjustment, while the PQ includes a calibration without an adjustment (see later "In-Tolerance Adjustment Policy").

In this respect there are used terms and wordings, which are leading quite often to confusions. The definition of calibration is vague and debatable. When ANSI/NCSSL/Z540 was written a full day was dedicated to the discussion over the definition of calibration versus verification.

6.2 Definitions

6.2.1 Calibration

From "calibre" (= "to size");

Calibration is the setting or the correction of a measuring device or base level, usually by adjusting to match with or conform to a dependably known and unvarying measure.

Also: Traditionally the act of checking and adjusting (by comparison with a standard) the accuracy of a measuring instrument.

Also: Definition according the VIM only includes the measurements or comparison (no adjustments) to standards of known value.

Also: The output of an electronic instrument or production equipment under test is compared with a reference instrument. The deviations are documented in a protocol.

6.2.2 Adjustment

Adjustment is setting or correcting an instrument's measure output.

Such adjustment in many instances is seen as a form of repair.

6.2.3 Verification

Verification is a calibration according the definition of the VIM (no adjustments) through a by law accredited authority (Gauging Office; Germany: Eichamt, „Eichen“).

The result of such verification is documented in a "Verification Certificate" or so called "Calibration Certificate" with additional traceable certificates of the "Accredited Authority".

6.2.4 Validation

Validation is an activity or procedure with a summary report that uses the results of the calibration and/or of the adjustment and/or of the verification, and some decision rule(s) to decide if the tolerance(s) or specification(s) is (are) met.

6.2.5 Validation Test

The Validation Test is part of a Validation.

The Validation Test is the calibration according the definition of the VIM (no adjustments) through the operator or a contractor.

6.2.6 Performance Test

Performance Test is the identical meaning of "Validation Test".

To make the difference of the definitions Validation versus Validation Test more accented, one should use the wording Performance Test.

6.2.7 Intolerance Adjustment Policy

The Intolerance Adjustment Policy describes the decision procedure for an adjustment.

In many cases there is defined an intolerance limit of 70% of the full specification, e.g. if parameters are adjustable.

6.2.8 Confidence Level

Confidence Level is a more sophisticated term of quality formulation derived from "Intolerance Adjustment Policy", "Intolerance Probability" and „Measurement Uncertainty".

6.3 Basics of "Laboratory Practice of Validation"

The supplier of dissolution equipment provides a Validation Logbook (normally not free of charge). The operator or a contractor (normally the supplier) can validate the equipment according this Validation Logbook by means of certified measuring tools.

The Validation Logbook contains specifications and the function principle with conclusions for the validation and the procedures for the IQ, OQ and PQ.

The Installation Qualification (IQ) includes settings and adjustments according the Operation Manual. It may include "calibration with adjustment" activities.

The Operation Qualification (OQ) will be performed after installation or reinstallation and after repair or any change of hardware or firmware responsible for the specified parameters. The OQ may include "calibration with adjustment" activities in the first step, followed by a "Performance Test" in any case.

The Performance Qualification (PQ) will be performed in predetermined intervals to check the functionality with its specified parameters. The PQ does not include "calibration with adjustment" activities. In case the results of the PQ are out of specification or do not meet the requirements of an "Intolerance Adjustment Policy", a repair of the equipment will follow and consequently "calibration with adjustment" activities. The purpose of the PQ is to check that the instrument was working "in specification" or "in tolerance" over the last operation interval. In case the instrument fails the specification, all measurements or production activities performed with it are not valid and products checked are not proofed.

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6.4 Result

In case the instrument fails a Performance Test according the specification or Intolerance Adjustment Policy there must follow a repair and a calibration with adjustment.

The common denominator of all definitions in the practice of Dissolution Laboratories is as follows:

CALIBRATION is the traditional checking of the accuracy of a measuring instrument or production equipment including "setting" or "adjustment" by comparison with a standard.

If the operator of an instrument wants to perform a colloquial "calibration", it must not be the strong wording of that definition above, but must be understood generally as to follow the standard operation procedure of a VALIDATION (SOP of Validation).

7 Validation of the DissoPrep X8

7.1 Validation

For Validation (Qualification) the DissoPrep X8 an extensive Validation Logbook is available. Thus the correct execution of Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ) is guaranteed. The unit can be used within short time after delivery.

7.2 Calibration

The DissoPrep X8 can be calibrated through a software guided procedure.

An external printer or PC can be interfaced to the unit. The results of a performed calibration will be printed automated at the connected printer or printed via the RC Software DPX8_RC.

See attached Performance Protocol next Page..

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AUTOMATIC QUANTITY CALIBRATION PROTOCOL
No: 5

DissoPrep X8 RIGGTEK GmbH Germany

Serial Number : R30030356
Firmware Version: 7.108

General Data:

Nominal filter capacity [l]: 5000
Remaining filter capacity [l]: 4981
Volume throughput up to now : 19

VMethod: 3
900, 0.0, 6, 37.0
Cal Mass/Vol 900

RESULT of the QUANTITY measurings [g]

	INTERN	EXTERN	DEV%
Vessel No. 6:	905	902	+0.3
Vessel No. 5:	905	903	+0.2
Vessel No. 4:	904	903	+0.1
Vessel No. 3:	905	904	+0.1
Vessel No. 2:	904	904	+0.0
Vessel No. 1:	905	905	+0.0

Result (average):
 904.7 903.5 +0.1
Max. deviation: 3
Std deviation: 0.5 1.0

EXTERNAL QUANTITY MEASURINGS:

Name : XB 10200D
Software : N01-0200 P17
Serienr : 2436-283

Operator:
.....

7.3 Maintenance

No special maintenance work is necessary. But once a year the service personnel should check the functionality of the vacuum pump, the diaphragm valves and the magnetic stirrer. ***The fault diagnosis is supported by the internally stored AUDIT Trail, which traces all error messages during the operation.***

E N D of BASIC INFORMATION



DISSOLUTION MEDIA DEGASSER AND DISPENSER - FEATURE ANALYSIS

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<i>RIGGTEK DissoPrep X8 (former DosaPrep X8)</i>	<i>SOTAX MPS</i>	<i>HANSON Media-Mate Plus</i>
USP- Relevant Demands		
Precise gravimetric dispensing better than +/- 5g (typically 2g) therefore temperature independent volume dosage referred to 20°C or 25°C according USP, 1 to 36 vessels selectable, quantity selectable in 1g increments.	Volumetric dispensing by a pump, < 1% accuracy specified but not reliable.	Volumetric measuring by individual mechanical levelling of max. 7 metering flasks, 1% accuracy not reliable. Volume setting in 50 mL increments by mechanical adjustment.
Degassing while sucking through a filter cartridge and stirring the continuous flow heater's warmed media under vacuum (typically less than 100 mbar) during defined time period; residual oxygen guaranteed less than 5.5ppm, typical 3 to 4.5ppm after filling into the vessel (independent from waiting until dispense), vacuum monitoring on protocol refers to degassing efficiency.	Degassing under vacuum (200mbar) and flow through a heater.	Degassing while sucking warm media through a filter cartridge into the metering flasks; poor degassing efficiency; residual oxygen content 95% (5% under saturation).
Timings		
Warming of the media with heater power of 1,85kW /1,5kW; warming of the dosage batch for 6 vessels last less than 8 min.	Warming of the media with heater power of 2kW /1,5kW; warming of the 20 liters tank lasts approx. 35 min.	Warming of the media with heater power of 1,85kW /1,5kW lasts over 75 min for the 40 liters storage tank.
Filling, warming, degassing 10 to 15min for an 8 liters batch (depending from acid mixing and degassing time setting).	n/a	Filling of metering vessels and degassing approx. 1,5 min for a 7 liters batch (timing independent of no. of vessels).
Filling of a 1L vessel approx. 30sec, for 6 vessels 3min net; dispense hose has to be fed manually from vessel to vessel.	Filling/dispense flow rate is 1.500mL/min, dispense hose has to be fed manually from vessel to vessel.	Unattended filling of 6 or 7 vessels in approx. 1,5min (timing independent of number of vessels).
Total throughput per hour approx. 24 to 32 liters (depending of the selected acid mixing method and degassing time).	Total throughput per hour approx. 26 liters (depending of the selected acid mixing method).	Total throughput per hour approx. 21 liters.
Handling		
Compact desktop model, weight 26kg (empty, 35 kg filled); may be operated mobile on a LabCart.	Mobile cart model, weight approx. 80kg (empty, 100kg filled).	Mobile cart model, weight approx. 67kg (empty, 107kg filled).
Sucks in media and concentrate via hoses from any storage.	Sucks in media via hose from any storage.	Media refill manually by buckets (heavy and not save).
Flow through principle keeps the tank (made of PP) sterile; no bacteria growth risk; flushing of the tank is software supported (auto-wash function).	Media storage principle; flush routine for media change is software supported.	Media storage principle leads to germination; manual clean of the storage tank necessary and very circumstantial.

RIGGTEK DissoPrep x8 (former DosaPrep x8)	SOTAX MPS	HANSON Media-Mate Plus
Special Features		
Simple calibration process is software supported; automatic validation report via printer interface. Auto Calibration and Auto Performance Test with external balance, temperature and barometer devices as option.	Simple calibration process is firmware supported; automatic validation report via internal or external printer. Self-calibration option with additional balance.	Physical adjustment and calibration of each media channel very time consuming; no validation reports on printer.
Dosing volume from 100 to 8000mL per vessel in 1mL increments over keypad selectable; proportionate mixing of concentrates in 0,1mL increments.	Dosing volume per vessel in 1mL increments over keypad selectable.	Dosing volume from 250 to 1000mL per vessel in 50mL increments through individual pointer handles on each measure vessel (not accurate).
Can mix highly precise water with concentrated acid or buffer or surfactant and documents the mixing result on an external printer.	In-situ preparation of media from concentrates with deaerated water with on-line mixing device (option).	No mixing capability.
The value of each dispensed volume and temperature and disposed vacuum is documented on an external printer.	Key data is shown on the display and can be transferred via serial port on a printer.	No printouts of the results.
50 methods can be stored in memory and edited on a PC (as an option).	n/a	No methods storage.
Dispense and calibration protocols are stored in an internal stack memory; protocol administration on a PC (as an option).	Last dispense and calibration protocols are stored.	No protocols.
Extensive self diagnosis and error trail memory for better maintenance.	Extensive self diagnosis and error message on the display.	No self diagnosis means.
The system prompts the user to change the filter when the capacity is exceeded.	Filter change is prompted when the capacity is exceeded.	No filter check.
Easy programming and intuitive operation including calibration by stepping through display sequences.	Easy to use, clean, program and validate.	Not at all simple but erroneous operation needs training; calibration is very time consuming.
Closed system with exhaust connection to feed away the acid evaporation.	Closed system, easy to observe (glass tank) and clean.	Open system with acidic evaporation.
In case of media change no waste of residual media in the tank.	In case of media change many liters (up to 20) waste of residual media in the storage tank.	In case of media change at least 8 liters (up to 40) waste of residual media in the storage tank.

E N D of Feature Analysis



PROFITABILITY ANALYSIS OF DISSOPREP X8

ID 20100927 REV 5



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I Introduction

The media preparation should be taken under the regulations of various organizations (including the USP, EP, FDA, GLP / GMP, ISO 9000, DAB, WHO). However, it happened too often without the necessary care, especially for degassing, volumetric measurement and documentation work. Too much time makes a careful approach.

The DissoPrep X8 completed all work by filtering of the heating, mixing, venting and dosage to the logging. The medium processing power including dosage in this case is up to 32 liters per hour. In an hour can thus 4 x 7 Vessels are filled each with 900 ml.

Another compelling advantage of DissoPrep X8 is its ease of validation and documentation of all test results on report printouts. This is inter alia documented how much ml of medium in each vessel were filled real consideration and documentation of the tolerances.

The price of DissoPrep X8 amortize after about 90 tests by full cost for an hour of minimum EUR 180.

The regulations for the media preparation and dispensing should be in the USP (and EP) guidelines summarized. The DissoPrep X8 met today, what is required in the future: filtering, heating, mixing, degassing under vacuum and stirring, metering and logging.

2 DPX 8 Work simplification

- Filtering, Heating and Degassing of Media
- Mixing of Media from Additive and DI Water by given Method
- Precise Dispensing of Media into the Vessels
- Complete logging of mixing, individual doses and validation
optional with software for logging- and method management on PC

3 DPX 8 Timesaving

- Filtering, Heating, Mixing, Degassing under vacuum and Stirring, Dispensing, Documentation as specified by the USP, EP, FDA, GLP / GMP, ISO 9000, DAB, WHO are done fully automatically by the DissoPrep X8 in 15 minutes..
- For this whole process you will have a timesaving of at least 75 minutes in comparison to a test by Hand.
- If you warm the media with a conventional water bath based dissolution tester you will have an timesaving of about 45 minutes because of the preheated media of the DissoPrep X8.

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4 Profitability Calculation

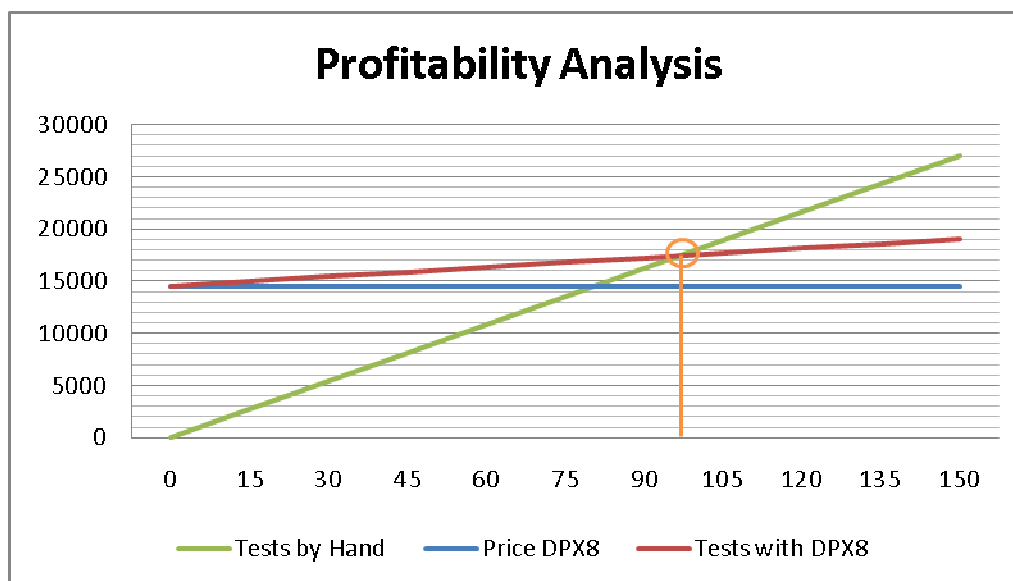
If you calculate with:

- 180€ full costs of a manual test (135€ labor costs for at least 1,5h manual work + 15€ consumables to prepare the media + 30€ raw material for the media),
- 30€ costs of a test with the DissoPrep X8 (30€ raw material for the media) and
- an investment of 14.544,05€ for a DPX8,

then **the ROI will already be reached after 90 tests!**

See the following calculation:

Amount of Tests	Costs per Manual Test	Costs for Test by Hand	Price DPX	Variable Costs per DPX8 Test	Variable Costs for Tests with DPX8	Total Costs Tests with DPX8
0	180,00 €	0,00 €	14.554,05 €	30,00 €	0,00 €	14.554,05 €
15	180,00 €	2.700,00 €	14.554,05 €	30,00 €	450,00 €	15.004,05 €
30	180,00 €	5.400,00 €	14.554,05 €	30,00 €	900,00 €	15.454,05 €
45	180,00 €	8.100,00 €	14.554,05 €	30,00 €	1.350,00 €	15.904,05 €
60	180,00 €	10.800,00 €	14.554,05 €	30,00 €	1.800,00 €	16.354,05 €
75	180,00 €	13.500,00 €	14.554,05 €	30,00 €	2.250,00 €	16.804,05 €
90	180,00 €	16.200,00 €	14.554,05 €	30,00 €	2.700,00 €	17.254,05 €
105	180,00 €	18.900,00 €	14.554,05 €	30,00 €	3.150,00 €	17.704,05 €
120	180,00 €	21.600,00 €	14.554,05 €	30,00 €	3.600,00 €	18.154,05 €
135	180,00 €	24.300,00 €	14.554,05 €	30,00 €	4.050,00 €	18.604,05 €
150	180,00 €	27.000,00 €	14.554,05 €	30,00 €	4.500,00 €	19.054,05 €



E N D of Profitability Analysis



DISSOLUTION MEDIA DEGASSING EFFICIENCY INVESTIGATION WITH DISSOPREP X8

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1 Introduction

There are many questions around degassing efficiency of the DissoPrep X8 dissolution media delivery station compared to the recommendation of the USP¹. USP proposes a reference method² for degassing of the dissolution media, mainly with parameters like “degassing while stirring heated media under vacuum”. The vacuum is not defined, also not the storage condition. Other validated deaeration / degassing techniques are permitted^{3, 4, 5}.

2 Experimental

We have investigated in several degassing tests while the parameters temperature and vacuum (absolute pressure defined) are the main variables. Stirring is performed through a magnetic bar in the storage tank which is digitally driven and software monitored in its function. Duration of degassing is dependant of the reproducible filling time of the storage tank and the additional degassing time which can be selected.

3 Results and Discussion

The results are listed in the table below. There are 7 tests, but the 7th is an arbitrary test out of the routine which proves the common uncertainty of the oxygen measurement. Therefore, the USP describes only the reference method but not the result of the degassing. Some of the persons in the dissolution lab have reported that the USP method results with approx. 1 to 2 ppm residual oxygen in the media. But this result is measured in the container of degassing and not in the dissolution test vessel. The DissoPrep X8 delivers media with the measured results of degassing directly into the test vessel, preventing re-aeration while handling the media from bulk storage to the test vessel.

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Degassing Efficiency Investigation with DissoPrep X8

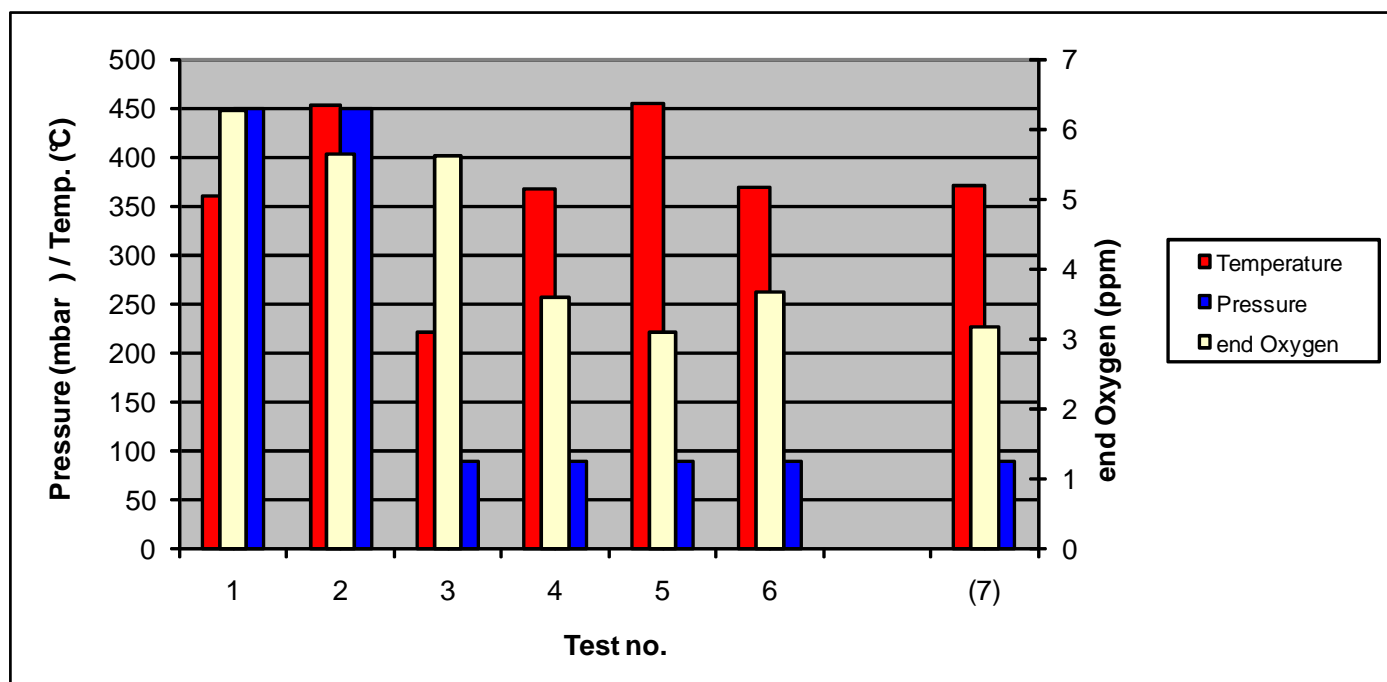
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Dipl.- Ing. Hansjuergen Riggemann

Oxymeter from WTW OXI 330
 DissoPrep X8 with Firmware 7.108

Method Parameter	Test No.	1	2	3	4	5	6		(7)
Temperature	°C	36	45,2	22,1	36,7	45,5	36,9		37,1
Temperature eff.	°C/10	360	452	221	367	455	369		371
min. Pressure (vacuum)	mbar	450	450	90	90	90	90		90
Volume	mL	1x 5000	1x 5000	1x 5000	1x 5000	1x 5000	6x 1000		6x 1000
add. Degas Time	sec	120	120	120	120	240	120		120
start Oxygen	ppm O ₂	8,54	8,47	8,36	8,24	8,55	8,1		8,55
end Oxygen	ppm O₂	6,26	5,64	5,62	3,59	3,09	3,66		3,18
DPX8 routine application (time saving method without add. Degas Time)					YES		YES		YES



The degassing is mainly effected by temperature or pressure or both in combination. The edge conditions are there

- boiling hot water or
- water under absolute vacuum.

In both cases no air can be dissolved in the liquid. Our test no. 2 was performed with relative high temperature of 45,2 °C and poor vacuum of 450 mbar while test no. 3 was performed under low temperature and high vacuum. Both methods resulted in almost the same degassing efficiency of 5,6 ppm oxygen.

The combination of higher temperature and higher vacuum of the tests no. 4 and 5 resulted in reasonable good degassing efficiency of 3,6 and 3,0 ppm oxygen in the test vessel. In routine application of the DissoPrep X8 the best time saving method (like test no. 4, 6, 7) delivers the most effective degassing result of less than 3,7 ppm oxygen.

4 Conclusion

The USP reference method and other degassing methods, e.g. with helium, do not provide in routine lower degassing results in the dissolution test vessels as the DissoPrep X8 does it .

The residual oxygen in the media is

- according the USP method 1-2 ppm in the container of degassing – not after dosing in the test vessels
- with DissoPrep X8 in routine application methods without additional Degas Time less than 3,7 ppm after dosing in the test vessels.

Besides DissoPrep X8 prepares dissolution media in

- an automated and therefore reproducible procedure,
- metering it directly into the dissolution test vessels,
- warming the media and
- provides a protocol documentation of the dispensing results.

5 References

¹ United States Pharmacopeia <http://www.usp.org>

² One method of deaeration is as follows: Heat the medium, while stirring gently, to about 41°C, immediately filter under vacuum using a filter having a porosity of 0.45 µm or less, with vigorous stirring, and continue stirring under vacuum for about 5 minutes. Other validated deaeration techniques for removal of dissolved gases may be used.

³ Terry W. Moore, <A fast efficient procedure for degassing dissolution medium>, Dissolution Technologies May/1996

⁴ Jennifer B. Dressman et al, <Dissolved oxygen as a measure of de- and reaeration of aqueous media for dissolution testing>, Dissolution Technologies August/1998

^{5,6} Owen S. Degenhardt et al, <Comparison of the effectiveness of various deaeration techniques>, Dissolution Technologies August/2004

E N D of Dissolution Media Degassing Efficiency



VOLUME TO MASS CONVERSION

ID 20100927 REV 5

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I Introduction

Repeatedly users are wondering how to convert “Stated Volume” into one mass or weight equivalent when working with the DissoPrep X8 Unit.

The United States Pharmacopeia (USP) prescribes “Place the stated volume of the dissolution medium with an accuracy of 1% in the vessels... and equilibrate it to 37°C +/- 0.5°C...”.

2 Definition of Volume & Mass

- „Volume”
“Volume” is the size (content) of a 3-dimensional space, occupied by an object (specimen) at certain temperature and pressure. The measure must be defined under the used environment conditions. The “normalized volume” includes defined environment conditions, so called “normalized condition”. The normalized volume is reproducible.
- „Mass”
“Mass” is the size (quantity) of an object (specimen) measured with its gravity. Mass is a measure independent from temperature, pressure and gravity. Nevertheless the common instrument to measure the mass, a balance, is dependable from the environment gravity (gravitational field). The mass is reproducible in any case.

3 Laboratory Practice of Volume & Mass Measurements

Liquids and gases are measured by volumetric usually, e.g. measuring cylinders, metering, volumetric flasks or pipettes.

Solid materials are measured gravimetrically by a balance. Liquids should be measured gravimetrically. Gases can be measured gravimetrically. The gravimetric measurement is indeed the most precise measurement as the instruments (electronic balances) are known as very reliable.

4 Dissolution Media Proportioning according USP

The USP wording under “I Introduction” can be interpreted as follows. The “stated volume” has to be filled coldly into the vessels at “normalized conditions” and then heated up to 37°C.

Most accurate and precise proportioning is performed when the “quantity of the mass” of a “stated volume” is weighed under “normalized conditions”. The density of the “normalized conditions” is inherently included. The mass of the “normalized volume” with its known density at “normalized conditions” can be calculated first also before proportioning the “stated volume” through weighing.

5 Setting of Weight Equivalents

Following are two theoretical and two realistic examples of setting weight equivalents.

- In each vessel are 1000mL media, which is water including 40mL buffer.
The weight of the media is measured experimental at 25°C (USP standard conditions) with 1003g.
Enter "Volume Vessel = 1003".
The weight of 40mL buffer is measured with 44g.
Enter "Volume Additive = 44".
- You want to mix 1000ml media of water and additive with a dilution ratio of 1:10.
Density of water = 0,997 kg/L (density at related USP conditions at 25°C).
Density of additive = 1,2 kg/L (density at 20 to 25°C).
Volume Ratio = 10:1 (equivalent to dilution ratio 1:10, means the "dilution" with the additive is 1/10 of the whole volume).

Calculate with the dilution ratio your volumetric mixture (900 mL water + 100 mL additive = 1000 mL media) and calculate the weight of the media for one vessel with the density:

$$0,9L * 0,997kg/L + 0,1L * 1,2kg/L = 897,4 g + 120 g = 1.017 g.$$

If there is no volume contraction, the weight of the mixture is 1.017g.

Enter "Volume Vessel = 1017".

Enter "Volume Additive = 120".

- You want to mix 1000ml media of 0,1 N HCL diluted from 1 N HCL.
1 N HCL has a density of 1,02 kg/L.
Density of water is 0,997 kg/L (USP related at 25°C).
Dilution ratio is 1:10, because of dilution from 1 N HCL.

Calculate with the dilution ratio your volumetric mixture (900 mL water + 100 mL additive = 1000 mL media) and calculate the weight of the media for one vessel with the density:

$$0,9L * 0,997kg/L + 0,1L * 1,02kg/L = 897,4 g + 102 g = 999 g.$$

Enter "Volume Vessel = 999".

Enter "Volume Additive = 102".

- You want to mix 1000ml media of 0,1 N HCL diluted from 5 N HCL.
5 N HCL has a density of 1,08 kg/L.
Density of water is 0,997kg/L (USP related at 25°C).
Diltuion ratio is 1:50, because of dilution from 5 N HCL.

Calculate with the dilution ratio your volumetric mixture (980 mL water + 20 mL additive = 1000 mL media) and calculate the weight of the media for one vessel with the density:

$$0,98L * 0,997kg/L + 0,02L * 1,08 kg/L = 977 g + 21,6 g = 998,6 g.$$

Enter "Volume Vessel = 999".

Enter "Volume Additive = 21,6".

6 Dilution Factor Limitations

According to the specification the dilution ratio has to be from 1:3 to 1:100 and is not allowed to be more than 1000g per vessel.

Following are two examples of dilution factor limitations.

- If you want to have 1000g media for each vessel, the maximum dilution ratio of 1:3 means a maximum of 333g additive
Enter "Volume Vessel = 1000" and "Volume Additive = 333,3".
- If you want to have 1000g media for each vessel, the minimum dilution ratio of 1:100 means, that you need at minimum 10g of additive.
Enter "Volume Vessel = 1000" and "Volume Additive = 10,0".

7 Conclusion

"Normalized Conditions" are usually referred to 20°C and 1 bar atmospheric pressure. In this case **1000 mL water weighs 998,3 g**.

The USP describes a reference temperature of 25°C. In this case **1000 ml water weighs 997,1 g**.

All other compositions of media must be measured accordingly.

8 Final Conclusion

If 900 mL water is filled in one vessel according USP description, the amount of the quantity is 897,4 g.

Measuring warm media in a volumetric flask or device, which is calibrated at 20°C, is just as wrong as using gravimetric measure and calculating the density of the media at

E N D of Volume to Mass Conversion



CALIBRATION MODE STATEMENT OF THE LOAD CELL (“BALANCE”)

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1 Introduction

Repeatedly the question of some users is arising how to calibrate the internal Load Cell of the DissoPrep X8 according the rules for laboratory balances. In GLP laboratories are strict rules for all balances so that the laboratory personnel want to include the Load Cell of the DissoPrep X8 itself in calibration procedures.

2 Definitions

2.1 "Balance"

A balance is an instrument dedicated for weighing the mass of a sample.

In GLP laboratories these balances are high precision instruments.

2.2 "Load Cell"

Load cells may be used as a component of balances.

The Load Cell is a component for transforming the physical parameter of force into an electrical signal. It can measure force, torque, tension, compression, etc.

2.3 "Pondering Cell" or "Weigh Cell"

Is more or less identically with "Load Cell" but more sophisticated for usage in scales or balances?

3 Function of the Load Cell

The internal Load Cell is used to measure the dynamic mass of the internal storage tank and to control the ongoing dynamic operation of the solenoid valves.

The DissoPrep X8 is an instrument ("black box") with dispensing capabilities (and some features more). The adjustment or calibration (see also the article from the author "Definition Calibration, Adjustment and Verification") of the dispensing amounts is an external job. The principle of the prescribed calibration of the DissoPrep X8 covers the full working range of the Load Cell and includes the dynamic functions like the flow rates and switching times of the solenoid valves. What the calibration delivers at the end is a multi-point calibration curve with offset. (Remark: no laboratory balance has a calibration curve with offset in any respect).

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4 Result

Why should the internal Load Cell component of the DissoPrep X8 be calibrated like a laboratory balance instrument?

Even the precision weigh cell as component of a balance is not calibrated directly itself (it includes the amplification electronic and read out device).

DissoPrep X8 and a balance, both are instruments. DissoPrep X8 does not contain a balance in the wording of a "laboratory balance". Therefore the adjustment and calibration of the DissoPrep X8 underlies its own individual rule where a Load Cell is used to control the dynamic dispense flow and to measure the "varying" dispensing results. (Remark: For the calibration of a laboratory balance there are used certified "static" test weights.)

It is recommended to use the content of the original "DissoPrep X8 Validation Logbook" or certified versions thereof.

5 Final Conclusion

DissoPrep X8 is not a balance and does not underlay the same procedures for calibrating balances.

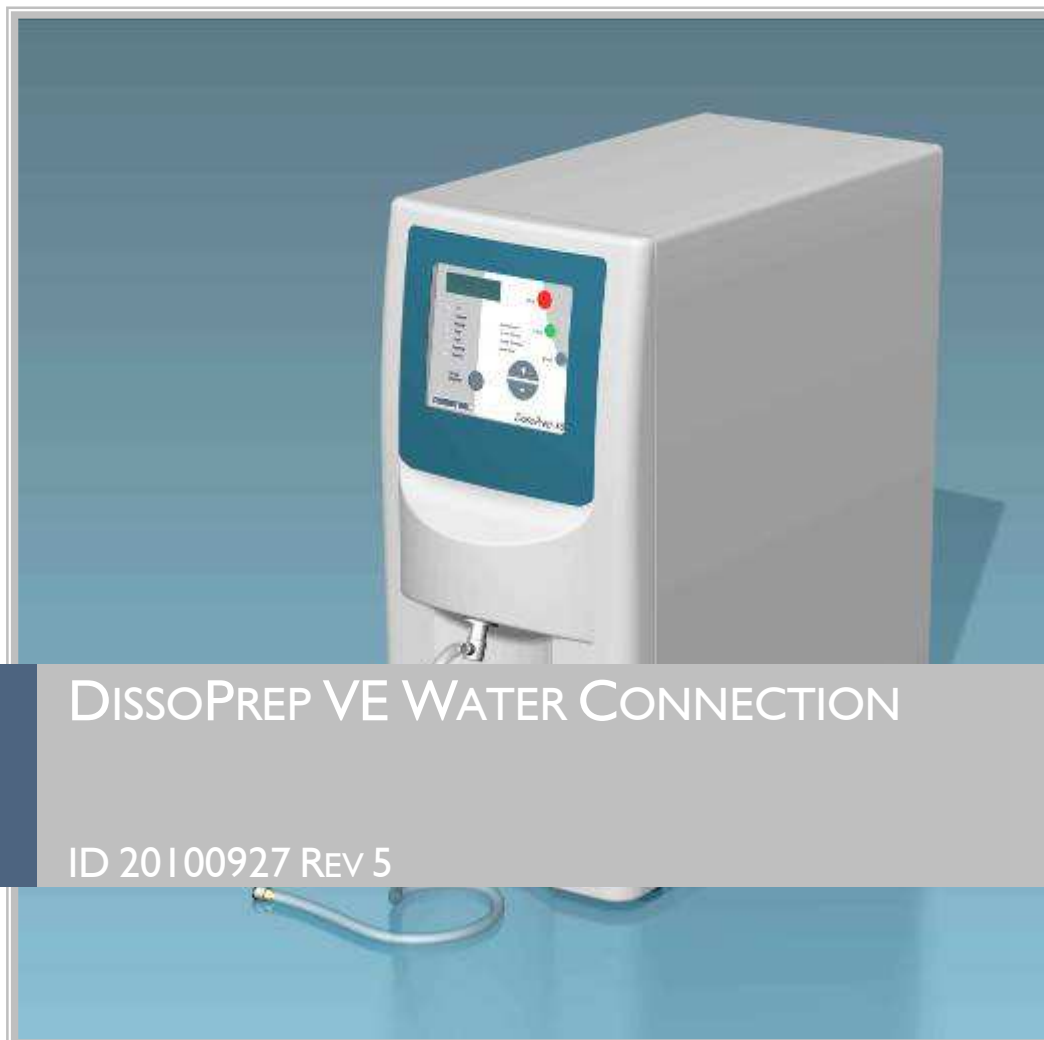
DissoPrep X8 needs its individual calibration procedure to adjust the dynamic dispensing operation.

DissoPrep X8 may underlay the same rules for calibrating as any instrument in GLP environment in terms of time periods, e.g. a daily plausibility test (one logged test sample of one arbitrary vessel amount), 3- or 6- or 12-monthly repeatedly calibration or in terms of routine maintenance (closing a service contract), etc.

6 Further Recommendation

For the calibration of DissoPrep X8 the responsible qualification managers should use at least the printouts of the protocols or even much better using the "21 CFR Part 11 compliant" documentation capability of the "Remote Control Software for DissoPrep X8".

E N D of Calibration Mode Statement of the Load Cell ("Balance")

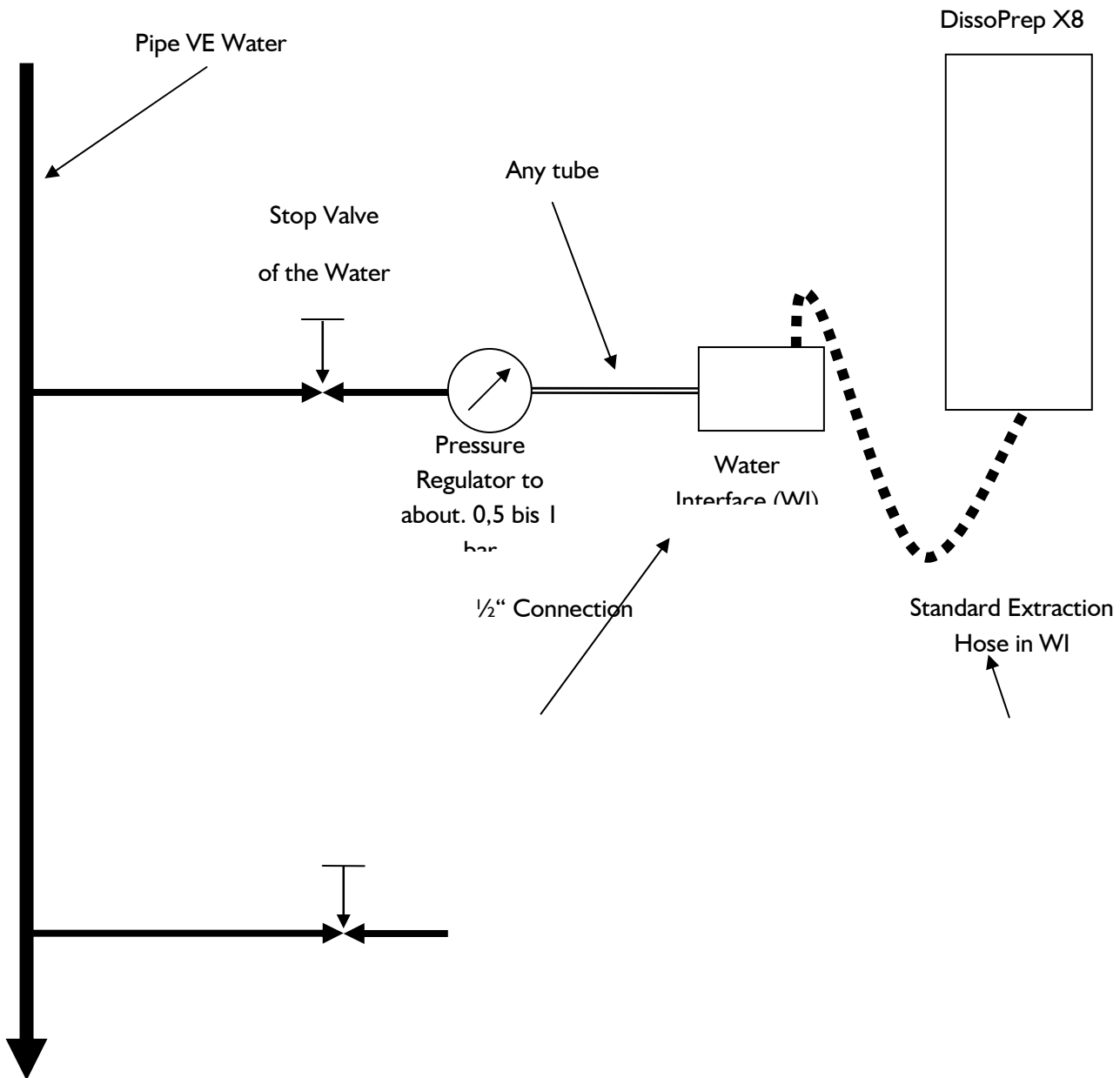


DISSOPREP VE WATER CONNECTION

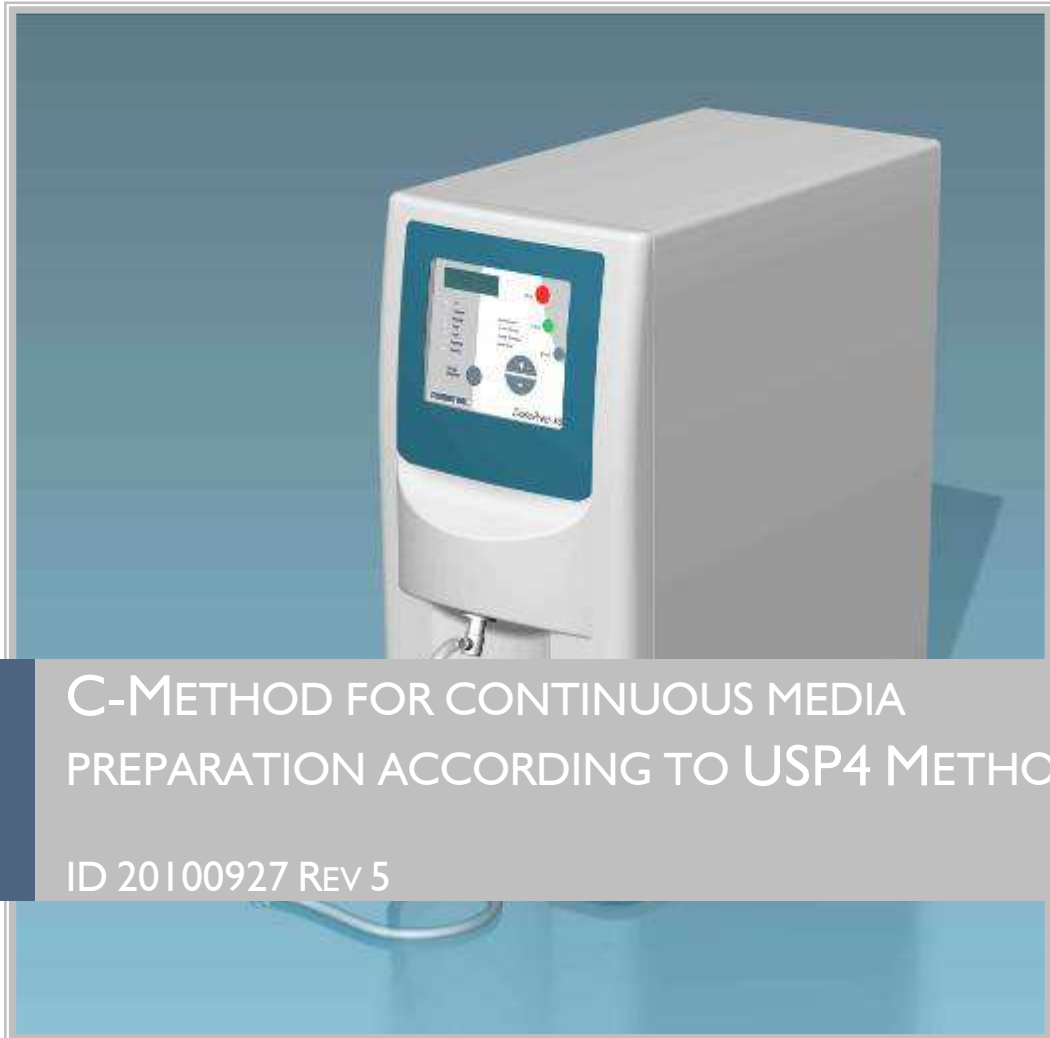
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E N D of DissoPrep VE Water Connection



C-METHOD FOR CONTINUOUS MEDIA PREPARATION ACCORDING TO USP4 METHOD

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I Instrumentation

DissoPrep X8 can be used in combination with the DMDC1 for dissolution essay according to the USP4 method (continuous mode). DissoPrep X8 prepares the media in batches, e.g. 8 liters per preparation cycle, and transfers the ready to use media to the tank DMDC1. The tank has an outlet that can be connected to a 7-channel pump through a manifold. The pump sucks the media from the tank (via the manifold) and delivers it to the individual flow-through cells (see Illustration 3).

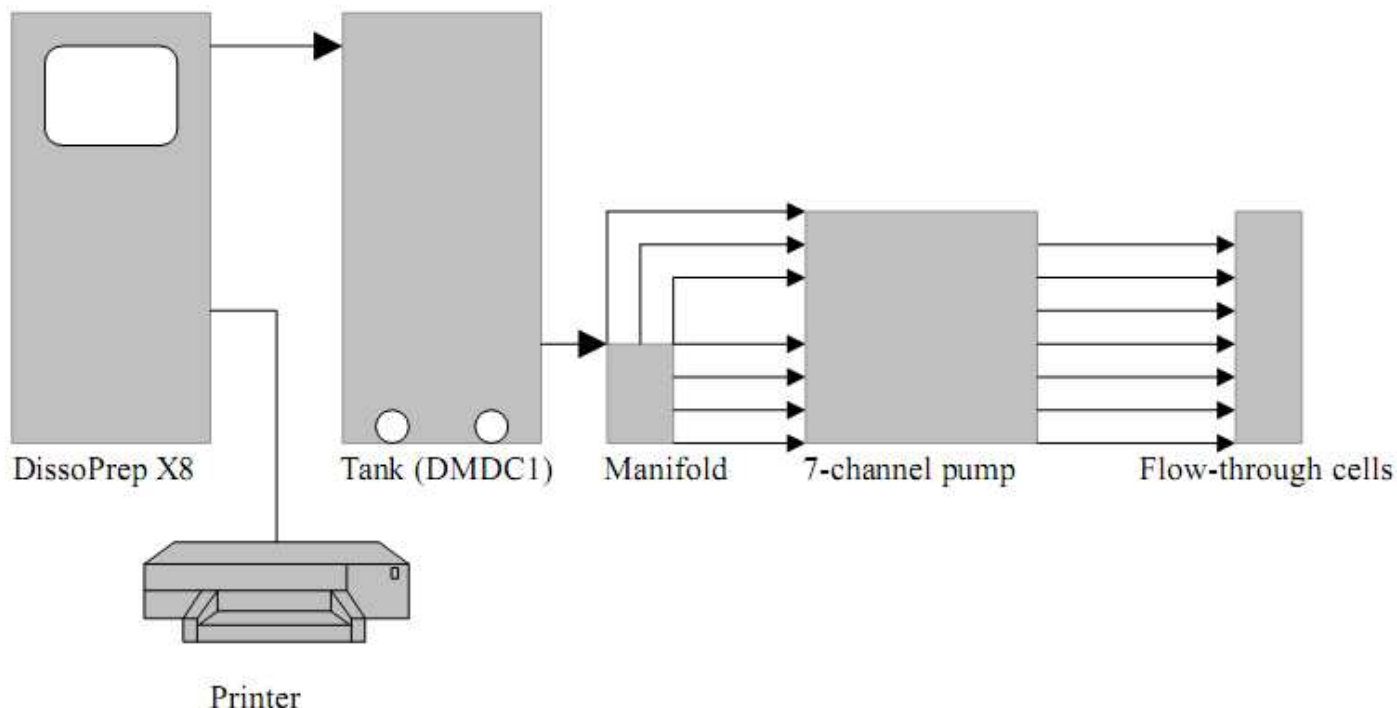


Illustration 3: Setup of DissoPrep and DMDC1 for continuous operations according to the USP4 method

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2 Operation

In order to switch DissoPrep X8 to continuous operation, following steps need to be performed.

- (1) DissoPrep X8 should be in the **Setup Mode**
- (2) Pressing +/- button leads to the list of available methods. Using + or – sign allows to choose the needed method. For continuous operations choose **Method C**.

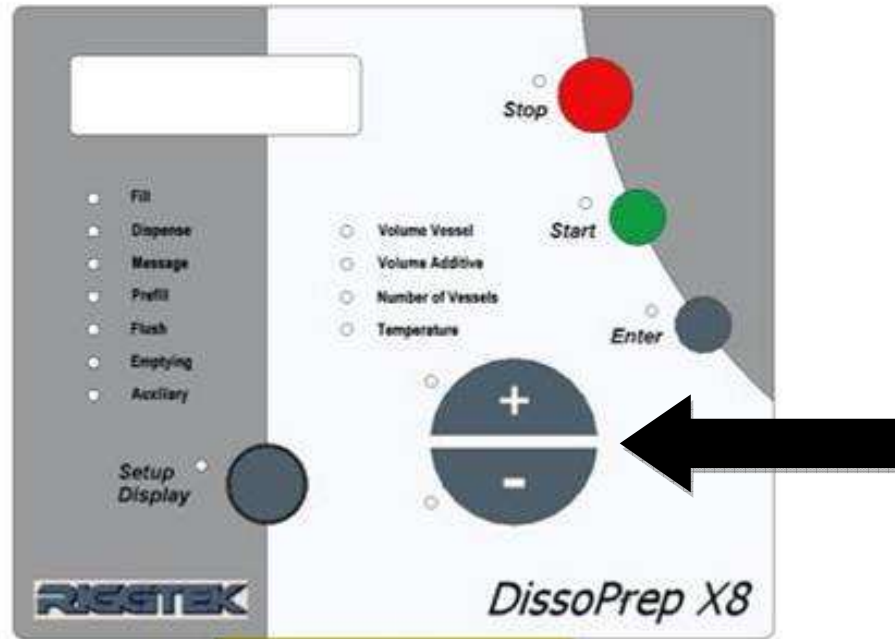


Illustration 4: DissoPrep X8 Panel

- (3) Pressing the **Setup** button allows to enter the number of vessels, volume of the additive, number of vessels, and temperature (preset to 37 °C for USP4 method)
- (4) Set volume vessel to 8000 (8 liters).
- (5) Set number of vessels to 0 (from 0 to 99).
Choosing 0 vessels means that DissoPrep prepares 8 liters of media in each cycle continuously. The process can only be stopped manually by pressing the Stop button. If for example only 80 liters of media are needed, the number of vessels should be 10 and the vessel volume 8000. In this case, DissoPrep performs 10 cycles where 8 liters are prepared and transferred to the tank in each cycle. Once the 80 liters have been prepared, DissoPrep stops automatically.

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Connection between DissoPrep X8 (9-pin "Remote Control") and tank DMDCI using a Zero-Modem Cable.

The tank DMDCI is connected to the DissoPrep X8 via a null-modem cable (scheme 2). The connection is established depending on the volume needed. There are two options, the lower level (30 liters) and the upper level (60 liters).

If during the media preparation and delivery to the tank the chosen level is reached, DissoPrep X8 stops and proceeds only if the media level is below the level mark. This ensures that no overflow occurs, especially during unattended operation.

Whenever DissoPrep X8 performs a cycle, a printout is generated automatically (see protocol below).

MEDIA DISPENSE PROTOCOL
No: 2

DissoPrep X8 RIGGTEK GmbH Germany

Serial Number : R30030356
Firmware Version: 7.108

General Data:
Nominal filter capacity [l]: 5000
Remaining filter capacity [l]: 4948
Volume throughput up to now : 52

Method C:

Result of the dosages [g]:

	MEDIUM	ADDTV	RATIO	DEV%
Fill Nominal:	8000	0.0	0.000	
Fill Actual :	8019	0.0	0.000	+0.0

	MEDIUM	DEV%	ADDTV	DEV%
Vessel No. *:	8000	-0.0	0.0	+0.0

Temperature (average): 38.1 C

MAX.VACUUM at 89 mbar absolute pressure *

Date, Time:
.....

Name:
.....

Signature:
.....

* The information of the maximal vacuum is made after the serial number 2408XXXX

E N D of C-Method



DISSOPREP X8 FAQ 's

ID 20100927 REV 5

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The FAQ's should give you a short summarize of the most often asked questions concerning the DissoPrep X8. This list not complete. If you have further questions, we are available by phone or email service@riggtek.de.

I Questions concerning the investment of the DissoPrep X8:

I.1 What is the main advantage of the DissoPrep X8 in comparison with its competitors? (*precision of the gravimetric principle*)

The main advantage of the DissoPrep X8 is, that it uses as unique feature the gravimetric principle for mixing and dispensing the media. That means, the DPX8 weighs the used media and the additive for mixing, and it weighs the dispensed media. So the DPX8 fulfills the USP requirements concerning volume precision for all kinds of media.

Measuring the weight for mixing and dispensing a media is the only correct way, because different media have different volumes at different temperatures and pressures. Only the weight of a liquid is not changing when warming it or changing the pressure! According the USP, the wished volume is to dispense at standard condition - this is 25°C – and then afterwards the liquid has to be heated up. So in accordance with the USP e.g. 900ml dispensed at 37°C into a vessel weigh 897,4g, which is the mass of 900ml at 25°C!

So it would be wrong to measure warm media in a volumetric flask or device calibrated at 20°C. And it would be also wrong to use the specific weight (density) for gravimetric volume measuring of the media at e.g. 37°C. With this gravimetric principle a calibration of the DPX8 for each media and each temperature is NOT necessary!

Further information concerning the correct media preparation (incl. degassing) you will find in the RIGGTEK article "The correct Media Preparation" on our webpage www.riggtek.de → products → DissoPrep X8 → Information.

I.2 What are the further advantages of the DissoPrep X8?

- precise and repeatable mixing of the media: Mixing Accuracy < 0,5% of ratio 1:3 to 1:100, typically 0,2%, monitored
- precise and fast dispensing of the media directly into the vessels: Dosing Accuracy < 1% at 500-8.000g, typically 2g; 8L of dissolution media is ready in **less than 15 minutes** (12 minutes with prepared media without mixing), Dispensing Rate 2L/min, total Throughput: 24-32L/h
- timesaving warming of the media: Preheating 20 – 45°C
- degassing of the media with high efficiency and low costs : measured after dispensing into the vessels typ. 3 - 5ppm O₂ , degassing with vacuum
- documentation of the media preparation: All internal dosage processes are accurately controlled and monitored by a Precision Load Cell. The individual dosage processes are documented and can be printed on an external printer or administrated with PC (Option: RC Software). After each DISPENSE cycle the DissoPrep X8 provides a "DISPENSE Protocol" reporting the weights, the mixing ratio, the vacuum and the temperature. Also a "CALIBRATION Protocol" is provided.
- USP, EP, FDA, GLP/GMP comformity: DissoPrep X8 fulfills all requirements of the media preparation according to the demanded rules of the USP and EP, as well as according to the recommendations of the FDA and of the GLP/GMP

- **Reproducibility of the results:** Reproducibility of the test results is independently of the operators (a result of the automation of the media preparation).
- **Safety in the Laboratory:** By automating the process - particularly the acid preparation and media dispensing - the risk to laboratory personnel is minimized
- **easy handling:** The user-interface of the DissoPrep X8 is quite simple with only a few buttons. The Remote Control Nozzle simplify the dispensing into the vessels.
- **space saving:** The dimensions of the DissoPrep X8 are W 30cm x H 66cm x D 59cm quite compact to fit in every lab.
- **Simplification of administrative documentation:** With the optional available Remote Control Software all methods can be administrated and all protocols which are generated with the DissoPrep X8 can be transferred in a PC network "21CFR Part 11 compliant".

Further information you will find in the „DPX8 Additional Information Sheet“, all chapters are separately available on our webpage www.riggtek.de → products → DissoPrep X8 → Information.

1.3 How fast is the amortization of the DPX8 investment?

The saving of time is considerable. DissoPrep X8 prepares up to 8L of dissolution media automated in less than 15 minutes (12 minutes with prepared media). The fast and precise dosage by a tube into the individual vessels (~25 seconds for 900ml) saves time-consuming handling steps. The preheated media saves up to 45 minutes for media heating with a conventional water bath dissolution tester.

If you calculate with:

- 180€ full costs of a manual test (135€ labor costs for at least 1,5h manual work + 15€ consumables to prepare the media + 30€ raw material for the media),
- 30€ costs of a test with the DissoPrep X8 (30€ raw material for the media) and
- an investment of 14.544,05€ for a DPX8,

the ROI will already be reached after 90 tests!

Further information you will find in the „DPX8 Additional Information Sheet“, chapter “Profitability Analysis of DPX8” available on our webpage www.riggtek.de → products → DissoPrep X8 → Information.

2 Questions concerning the specifications of the DissoPrep X8:

2.1 What is the meaning of a gravimetric dosing principle?

A gravimetric dosing principle means dosing "by weight" or "by mass". For further information see question 1.1

2.2 Why is the volume of the tank only 8L? Is a larger tank available?

The volume of 8L is sufficient to fill all vessels of one dissolution bath. It is not being the correct way to prepare media on stock, because the resaturation of gases happens very quickly. So the degassing would be useless, if the media is prepared on stock and not just "fresh" before use.

Currently, a 15L tank is planned for the year 2012. This tank is foreseen for those customers, who want to prepare always two dissolution baths at the same time with "fresh" media.

2.3 Why is the brutto - volume of the tank 11L? What does this mean?

For prefilling the unit (tubings and death volume of the tank) an additional volume is required as well as for mixing media in the right concentration. This is why the tank has an actual volume of 11L, but only 8L are for net use.

2.4 Of which material is the tank?

The tank is made of PP (Polypropylen).

2.5 How large is the prefill-volume? How much DI-water is required for prefilling the unit?

The prefill – volume is 1L. This volume is needed to prefill (filling tubings etc.) the unit incl. the Flush-volume at the beginning of the dispensing.

2.6 How does the DissoPrep X8 degass the media?

The DissoPrep X8 is degassing while exposing the media to vacuum, typically < 100mbar pressure absolute. The vacuum is monitored and documented on the protocol.

2.7 What is the degassing efficiency of the DissoPrep X8?

The degassing efficiency depends generally on

- the size of the vacuum
- the time the media is exposed to the vacuum
- the temperature of the media

- the stirring of the media

For a normal routine the interaction of heating, stirring and degassing (vacuum exposure) generates an effective de-aeration of the medium e.g. for water with typically 3 - 5ppm residual oxygen (measured after filling into the vessel).

Further information you will find in the „DPX8 Additional Information Sheet“, chapter “Dissolution Media Degassing Efficiency Investigation with DissoPrep X8”, available on our webpage www.riggtek.de → products → DissoPrep X8 → Information.

2.8 How is the DissoPrep X8 ensuring the homogenously mixing of the media?

The DissoPrep X8 is mixing the media with a magnetic stirrer continuously in the tank. The magnetic stirrer is functionally monitored to ensure a continuously mixing of the media.

2.9 How much media can the DissoPrep X8 prepare in one hour?

The throughput of DissoPrep X8 is 24 – 32 L/h, depending on the selected temperature, additional degassing time, mixing of additive and numbers of dispensed vessels. Throughput is in the meaning of preparing the media (sucking in the raw material, degassing, mixing, warming) and dispensing into the vessels. This is equal to 400-533 mL/min.

If the media is prepared and ready for dispensing, the dispensing rate is 2L/min. So typically a vessel with 900ml is filled in 25 sec.

2.10 Are there any restrictions for the DissoPrep X8 concerning the laboratory environment?

The DissoPrep X8 is prepared to work in a laboratory environment of 18 – 30°C and maximum 85% humidity.

3 Questions concerning the use of the DissoPrep X8:

3.1 Is it possible to use the DissoPrep X8 mobile, so that I can place it where I need it? Do I have to consider anything when moving the DissoPrep X8 from place to place?

The DissoPrep X8 can be used mobile (RIGGTEK offers a suitable cart – called LabCart – to place the DissoPrep X8 and all reservoirs etc. safely on it). But there are to consider some restrictions.

During PREFILL, FILL and DISPENSE, the DissoPrep X8 has to be placed on a stable base without any vibrations. And it is not allowed to move during these states. Otherwise the internal load-cell will be influenced and the mixing and dispensing results will be wrong.

Due to the power supply, it is not possible to move and disconnect the DissoPrep X8 from the mains power supply after state FILL. So it is not possible to prepare a media and then move the DissoPrep X8 towards individual baths. After disconnecting from the mains power during FILL or DISPENSE and switching it on again, the DissoPrep X8 will force you to EMPTYING the system.

To avoid this, there is an UPS (Uninterruptible Power Supply) available. Please ask us, if it is available for your mains power supply / voltage.

3.2 Do I have to enter the wished volume or the weight / mass per vessel?

The DissoPrep X8 uses a gravimetric principle (why? see question 1.1 or below), so you have to enter the wished weight / mass per vessel.

RIGGTEK is sometimes speaking from "volume per vessel", because most customers want to have a specific volume at first - e.g. 900ml – at a wished temperature – e.g. 37°C. According the USP, the wished volume is to dispense at standard condition - this is 25°C – and then afterwards the liquid has to be heated up. So the weight of this liquid at 37°C has to be the same weight as at 25°C. So for the wished "volume per vessel" has to be entered the weight at 25°C – RIGGTEK is speaking from entering the volume per vessel in weight equivalents per vessel. How to make the needed Volume to Mass Conversion – see question no.3.3

3.3 Why do I have to enter the mass instead of the volume?

Measuring the weight for mixing and dispensing a media is the only correct way, because different media have different volumes at different temperatures and pressures. Only the weight/mass of a liquid is not changing when warming it or changing the pressure! According the USP, the wished volume is to dispense at standard condition - this is 25°C – and then afterwards the liquid has to be heated up. So in accordance with the USP e.g. 900ml dispensed at 37°C into a vessel weigh 897,4g, which is the mass of 900ml at 25°C.

So you have to enter always the weight of your wished media volume at standard condition (according USP 25°C) – RIGGTEK is speaking to enter the weight equivalents of your wished "volume per vessel". Therefore you have to calculate what is the weight of your wished media volume at standard condition – RIGGTEK calls this "Volume to Mass Conversion".

3.4 How do I have to do the Volume to Mass Conversion?

Most accurate and precise proportioning is performed when the "quantity of the mass" of a "stated volume" is weighed under "normalized conditions". The density of the "normalized conditions" is inherently included.

If this is not possible you have to calculate the mass of the "normalized volume" with its known density at "normalized conditions".

Example I:

You wish to dispense 900ml water per vessel.

According the standard conditions of the USP with 25°C and 1bar the density of water is 997,1g / L. Consequently 1000ml H₂O weigh 997,1g and 900ml H₂O = 0,9L * 997,1g / L =897,4g.

You have to enter 897 g for the parameter „Volume Vessel“ for the wished 900ml..

Example II:

You want to mix 1000ml media of 0,1 N HCL diluted from 1 N HCL.

1 N HCL has a density of 1,02 kg/L.

Density of water is 0,997 kg/L (USP related at 25°C).

Dilution ratio is 1:10, because of dilution from 1 N HCL.

Calculate with the dilution ratio your volumetric mixture (900 mL water + 100 mL additive = 1000 mL media) and calculate the weight of the media for one vessel with the density:

$$0,9L * 0,997kg/L + 0,1L * 1,02kg/L = 897,4 g + 102 g = 999 g.$$

Enter "Volume Vessel = 999".

Enter "Volume Additive = 102".

Further examples and information you will find in the „DPX8 Additional Information Sheet“, chapter "Volume to Mass Conversion", available on our webpage www.riggtek.de → products → DissoPrep X8 → Information.

3.5 How do I have to enter the wished additive?

The parameter "Volume Additive" determines the portion, e.g. acid, in gram for one vessel (setting in 0,1g digits) and has to be within the specification from 1:3 to 1:100 dilution ratio and is not allowed to exceed 1000g per vessels. So the required volumes have to be entered in weight equivalents per vessel.

3.6 What is the meaning of the dilution ratio 1:3 to 1:100?

The parameter "Volume Additive" has to be within the specification from 1:3 to 1:100 dilution ratio and is not allowed to exceed 1000g per vessels.

Example:

- If you want to have 1000g media for each vessel, the maximum dilution ratio of 1:3 means a maximum of 333g of additive
Enter "Volume Vessel = 1000" and "Volume Additive = 333,3".
- If you want to have 1000g media for each vessel, the minimum dilution ratio of 1:100 means a minimum of 10g of additive.
Enter "Volume Vessel = 1000" and "Volume Additive = 10,0".

3.7 Do I have to calibrate the DissoPrep X8 for each different media and temperature?

No, this is not necessary, because the DissoPrep X8 uses a calibrated pondering cell to weigh any arbitrary mass (volume) / the gravimetric principle (see question 1.1)!

Compared to all other competitive instruments, the DissoPrep X8 prepares and dispenses the media according the weight and not according the volume. The weight is specific for each media and is not changing for different temperatures (see also question 1.1).

3.8 Why should I heat the media for degassing only to the temperature of my dissolution test – e.g. 37°C - and not to 41°C as the USP is recommending?

RIGGTEK has made some tests with water, which are proving, that the degassing efficiency at 45,5°C is only 0,5ppm (total 3,09ppm) better than at 36,7°C (total 3,59ppm). You have to consider, that in case of water with a temperature

of 20°C and an ambient air pressure of 1 bar, there are 9,08ppm oxygen and further air components dissolved, in case of 37°C it's 6,72ppm oxygen, the increase of degassing efficiency when overheating the media is not reasonable better.

But when cooling down the media from e.g. 41°C to the dissolution test temperature of e.g. 37°C the resaturation of gases to the "normal" value of 6,72 ppm will be much more than this 0,5ppm difference. So RIGGTEK does not recommend to increase the temperature due to a theoretic better degassing efficiency.

Further information and the test results on the degassing efficiency you will find in the „DPX8 Additional Information Sheet“, chapter “Dissolution Media Degassing Efficiency Investigation with DissoPrep X8”, available on our webpage www.riggtek.de → products → DissoPrep X8 → Information.

3.9 Is it possible to degas and heat a ready mixed hydrochloric acid-solution?

Yes, it is possible. Instead of DI-water you can connect the ready mixed acid-solution to the water-inlet-channel. But the maximum allowed acid concentration at the water-inlet and the outlet-channel is 0,5% hydrochloric-acid.

3.10 Is it possible to use SLS (surfactant), buffer (basic reagent), acid and organic / alcoholic media?

It is possible to use SLS (surfactant). There are no general problems known, although it is foaming.

Buffer and acid is possible. For Acid the maximum acid concentration at the additive input line is 36% hydrochloric acid, but for the medium-/ water-input-line and the output-line the maximum hydrochloric acid concentration is 0,5%.

Organic / alcoholic media is NOT usable (NOT allowed)! The sucked in organic / alcoholic media flows through a heater – there you have the risk of an explosion. All internal parts are not usable (inert) for alcohol.

3.11 Does PREFILL also need additive from the additive-line? How much additive is needed?

No, the PREFILL itself is just to prefill the tank to the Minimum Switch with DI-water (from the water-inlet-line), the additive will be only sucked in during the FILL state. The total sucked in additive is also in relation to the prefill-volume.

Because the tubings of the DissoPrep X8 has to be prefilled, you need more additive as the additive which would be needed for the wished concentration. For safety, 150% of the normal amount should be provided at the additive-line.

3.12 How to verify, that the proportion of water and additive is correct, if the dispensed liquid is always a mixture of them?

In the implemented Performance Qualification Test, RIGGTEK trust the before calibrated pondering cell, that it is measuring the added "additive" correctly and so we trust that the DPX8 has produced the right mixing ratio.

In case you will prove the realistic mixing amounts, you have to measure the weight of the INTAKEN water and additive. Therefore

- make a full run (PREFILL, FILL, DISPENSE) with your wished additive and water to fill all tubings
- measure the weight of the reservoirs of water and additive
- note the weights of both tanks. Be careful - do not shake the inlet-tubings when taking them out of the tank for measuring the reservoirs, otherwise the result will be wrong
- make a second full run
- measure the weight of the reservoirs again
- calculate the differences of the water-reservoir before and after and also of the additive-reservoir before and after
- with the differences of the water and additive you can calculate your mixing ratio.

It is not recommended to check the correct mixing ratio with ph-value or UV-marker.

3.13 Is it possible to use prepared media concentrates?

Yes, it is possible. But one bottle, which is normally ready for a certain volume of media, is not sufficient for exactly one media preparation. Because the tubings of the DissoPrep X8 has to be prefilled, so you need more media concentrate. How to use the concentrates:

- Fill a few bottles of the concentrate in a larger bottle (because the prefilling needs a uncertain volume - depending of length of the sucking-tube and the Flush Volume before dispensing) and connect it to the additive-inlet-tube of the DissoPrep X8,
- you have to know / measure / calculate the weight of your concentrate at ambient temperature (USP 25 °C), for entering it as "Volume Additive" at the DissoPrep X8
- you have to know / measure / calculate the weight of the ready mixed media at this temperature, for entering it as "Volume Vessel" at the DissoPrep X8
- enter in both weights "Volume Additive" and "Volume Vessel" at the DissoPrep X8
- DPX8 is mixing, warming, degassing and dispensing the wished media

Example:

using the product "DMC020-06, HCl 0.01N, dilute to 6L, 1 btl.", in the meaning, that one bottle with 230,8ml concentrated Hydrochloric Acid is ready to dilute to 6L media as a 0.01N HCl.

- Take e.g. 2 bottles of this in a larger bottle
- If the concentrate has e.g. a specific weight of (supposed !!!) 1.0g/L at 25°C then the content of 38,46 ml of the concentrate in 1 Liter weighs $230,8\text{mL} / 6\text{L} = 38,46\text{g}$

- weight of ready mixed media of wished 1 Liter per Vessel is
 - 1 Liter – 38,46ml = 961,54 ml water
 - $961,54\text{ml} * 0,997 \text{ kg/l} = 958,7\text{g}$ of water
 - plus your 38,46g of your concentrate
 - is for 1 Liter of your ready mixed media $958,7\text{g (water)} + 38,46\text{g (additive)} = 997,16\text{g}$
- Data entry in DPX8 is 38,5 g for “Volume Additive” and 997g for “Volume Vessel” to achieve 1L per vessel of your 0,01N HCL media.
- DPX8 is mixing, warming , degassing and dispensing the wished media

So it's of course possible to use the concentrates, but not emptying one bottle exactly for one mixing / preparation.

3.14 How often do I have to clean the DissoPrep X8? How to clean it?

A regular cleaning of DissoPrep X8 should be done to prevent a possible contamination with bacteria. The cleaning intervals depend on the following individual factors:

- the type of media (especially in the use of foaming media the cleaning interval should be shorter)
- the frequency of use of the DissoPrep X8
- the total volume of media that is prepared with the DissoPrep X8

The DissoPrep X8 can be cleaned with very effective 0,2% Sodium-Hypo-Chlorid or more compatible 5% Hydrogen-Peroxid. For the filter cartridge at the inlet tubing, the cleaning medium is as safe as for the transparent PVC tubings, which could get milky. DI water for rinsing the DissoPrep X8 is recommended.

The cleaning can be done in two complete runs (PREFILL, FILL, DISPENSE, EMPTYING).

- In the first run with the washing media as input medium.
- In the second run with DI water as input medium for rinsing.

Or the cleaning is done with the AUTOWASH function

RIGGTEK recommends generally a monthly cleaning with 5 l of 5% hydrogen peroxide as washing media for

- a full run (PREFILL, FILL, DISPENSE, EMPTYING) at 37 ° C or
- the AUTOWASH function with two wash cycles and 2500ml flushing volume

Afterwards RIGGTEK recommends for rinsing 5l DI water in another full run at 37 ° C or to make a further run of the AUTOWASH function with two wash cycles and 2500ml flushing volume.

If the input and outlet hoses are not clean after the cleaning, we also recommended changing all tubing's (see also question 3.19)

In case that there is a Water Interface (optional) in use, it is to clean regularly, so that the float valve is free moveable and so keeping it fully functional. All sediments incl. limescale / calcium carbonate are to be removed. Please consider the following hint for the Water Interface. The Water Interface is not part of the Installation and maintenance of the RIGGTEK GmbH. The Installation and cleaning / maintenance has to be organized / done by the customer himself. A not fully functional Water Interface can cause overflowing water!

3.15 How much time does the AUTOWASH-function take?

It depends on the setted volume and the amount of cycles at the AUTOWASH-function. E.g. one cycle with 1500ml takes approximately 7min.

3.16 Is the AUTOWASH-function able to clean the DissoPrep X8 completely? Even when SLS was used?

The user has to specify and verify for himself how often, with which cycle-volume and with which amount of cycles they have to use the AUTOWASH-function for the used media. There are too many different media and user habits, so that RIGGTEK can not recommend or even garantuee an AUTOWASH setting for all different media.

But with the AUTOWASH-function, the DissoPrep X8 is able to clean all the internal components. It is not necessary to open the tank etc. for cleaning.

To verify the setted AUTOWASH-function, the user has to make a full run with DI-water after AUTOWASH and analyze the possible remaining contents of the previous used media. E.g. the user should use a normal method 6 Vessels, 900g DI- Water, 0g Additive, 37°C. After the DPX8 is ready for dispensing the user should fill up a beaker with media and take a sample of the media for analyzing it with HPLC or UV. So they can find out if there are some rests of additives in the dispensed water after AUTOWASH.

3.17 If I want to prepare different medium in the same day, do I always need to do an AUTOWASH between preparing different media?

If you don't switch to different additive, but only change the concentration of the additive, you don't have to use the AutoWash.

If you change the additive, you should do an AUTOWASH. How to verify, that the internal wetted materials are clean, see question 3.13

3.18 After AUTOWASH the unit starts from PREFILL – is this normal?

This is normal - if you perform an AUTOWASH, the unit is totally empty and starts with PREFILL (so there is even no Prefill- / reserve-volume in the tank). That is the best starting position every morning - a total empty and clean unit.

If you will switch off the unit after FILL, the tank is full and the DissoPrep X8 will force you to EMPTYING (the tank) before starting a new method.

3.19 When or how often do I have to change the inlet-filter, tubings and the outlet-frit?

The regular / periodical exchange of the filter (filter capsule) prevents the DissoPrep X8 that harmful particles can enter, and with the regular exchange of the tubings bacterial growth is avoided.

The regular / periodical exchange of the frit (outlet) secures the precision of the dosing and that gases are re-aerated in the media while dosing into the vessels. Recommendation:

- complete inlet tubing incl. filter (= filter capsule) – **exchange every 12 months** – artitel-no. DPX-INLETMED-C
- filter – **exchange every 6 months or 5.000 liter** – artitel-no. SAR-559132P5-OO
- additive inlet tubing – **exchange every 12 months** – artitel-no. DPX-INLETACID-C
- outlet tubing (also for Remote Control Nozzle) – **exchange every 12 months** – artitel-no. DPX-INLETACID-C
- outlet frit – **exchange every 6 months or 5.000 liter** – artitel-no. DPX-OUT-FRIT

3.20 Does the unit alarm when the remaining filter life time is elapsed?

Yes, the DPX8 suggests a filter change in the display, if the predefined filter volume capacity ("Remaining Filter Capacity") is expired. You have to reset the remaining filter capacity in the AUXILLARY-Mode after the filter-change. The "Remaining Filter Capacity" is always shown on the printer protocols, so that it is possible to order a new filter in advance.

3.21 Why is there only one method modifiable at the DissoPrep X8?

According the GLP (Good Laboratory Practice) only registered / legitimated users are allowed to adapt methods. So according GLP the user should have to register at the DissoPrep X8 with a User-Login to modify any method. This is the reason why the DissoPrep X8 allows only to adapt the Method 0 at the unit itself. For modifying any other method, the RC-software (installation on a connected computer) with an User-Login is required. So only the use of the Methods higher than Method 0 - which are only to adapt by the RC-software - is really according GLP.

If there are users who use many methods very regularly and alternately, they should use the Remote Control Software, where they can adjust and store up to 50 methods in a very easy and clear way. RIGGTEK or the distributor can also store for him the wished methods. Of course, such methods can not be modified.

3.22 How do I connect my computer with the RC-Software to the DissoPrep X8?

You will need a "Zero-Modem-Cable" (available everywhere or at RIGGTEK) to connect the DissoPrep X8 with the computer (COM-Port).

3.23 The RC-Software is "RFC 21 Part II compliant" – what does this mean?

"RFC 21 Part II compliant" means, that data from the DPX8 (such as protocols) can't be manipulated from the user before printed out. Also any user login or any handling step is documented in a log-file.

3.24 Is it possible to connect more than one DissoPrep X8 to one computer with the RC-Software installed?

Unfortunately it is not possible with the actual RC-Software to control more than one DissoPrep X8 from one computer (with the RC-Software installed). It is NOT possible to install the RC-Software several times to control multiple DissoPrep X8 connected to different COM-Ports.

3.25 The temperature of the first batch is sometimes lower than setted?

At the first batch, the internal tank must be temperature conditioned. Therefore we recommend (see Operation Manual chapter 6..5.2 Prefill, page 19) to waste the first batch. Additionally, if you mix media with acid, all internal parts have to be conditioned to the new media, so that the first batch is also to be wasted.

The inlet water should be at least 15°C, and the minimum volume should be 5000 mL to reach temperature specification of +/- 1,5°C at setted temperature of 32°C - 37°C for more than 5000ml.

3.26 The setted temperature is not reached?

The temperature accuracy is 1,5°C at setted temperature of 32°C - 37°C for more than 5000ml. If there is prepared less than 5000ml in total, it is possible, that the temperature is not reached, as well if the temperature should be higher than 37°C.

If you are using a 100V or 115V power supply, please make sure that RIGGTEK or your distributor has done the correct instrument presettings ("TINI file is for 100V or 115V).

3.27 When calibrating the DissoPrep X8, the documented weight on the protocol is higher than the setted weight, but it is right according an external balance. Why is this?

The calibration run uses a virgin dispense control and compares only an arbitrary amount. Therefore the calibration compares only the internal load-cell measure against the external reference measure. Any deviation to the setted volume is not relevant for the calibration. Finally the dispensing accuracy will then be proofed in the performance run..

3.28 Is it possible to connect the media-inlet directly to the faucet?

No, it is not possible to connect the inlet tube directly to the faucet! The pressure is too high and the principle of the DPX8 of sucking in the media is not working then anymore. Besides the valves would be destroyed. As option RIGGTEK offers the "Water-Interface" (article-no. DPX-WI2), which you connect between the faucet and the DPX8.

The Water-Interface is like a tank which is filled up automatically. Because the installation has to do with the building equipment (maybe a pressure reducer is necessary), the installation has to be done by the building service of the customer and there is no guarantee from RIGGTEK's side for the long-time function (because it depends on the water-pressure of the faucet). We also strongly recommend to install a shut-off valve, which is too use, when no person is in the room.

3.29 Is there any possibility to avoid an AUTOWASH when changing the media to save time. So is there any possibility to flush the system without doing a PREFILL?

No, you can't flush the system without "flushing out" = emptying all the existing media. The PREFILL is necessary then.

3.30 Is it possible to use water for the PREFILL and prepared media afterwards for the FILL?

No, it is not possible to use water for the PREFILL and the prepared media for the FILL. The water as PREFILL-media would be mixed with the prepared media and would change the concentration and density of the prepared media.

3.31 Is it possible to use detergent as SLS, SDS and do the bubbles influence the accuracy of the dispensing?

Yes, some customers use it, there are no problems known. So no, the bubbles should not influence the accuracy of the dispensed media.

3.32 When entering e.g. 43,8 g for the additive, the display shows 44 during the preparation. Does the unit take 43,8g or 44 g for each vessel?

The unit takes 43,8, the displayed value is only rounded up because of the limited place on the display.

3.33 Is the maximum volume of 8L limiting the possible volume entry (weight equivalents) per vessel? E.g. is it possible to enter 1003g per vessels for 8 vessels, which is a total volume of 8024g?

For firmware versions > 7.113 you can enter "Volume Vessel" (weight equivalents) that are in sum for all vessels (Total Volume) <= 9.000g. If it is higher, you will get an error message "TotalVol tooHigh" and the LED "Message" will light when starting the method and you have to press the button STOP for returning to adapt the method. Then you have to reduce the volume per vessel or the number of vessels, so that the total volume is <= 9.000g. At firmware versions <= 7.113 it is NOT allowed to enter volumes per vessel (weight equivalents) that are in sum for all vessels (Total Volume) >8.000g, because there is a security limitation. But be careful, there is no warning message or a limitation for the volume entry! You can start the method, but then only the volume for one vessel will be prepared. So after the first dispensed vessel, air will be dispensed and the DissoPrep X8 will not stop to dispense air. You have to shut down the unit.