

CD14 Vessel to Vessel Temperature Stability over Extended Time Periods

Ashvin Patel, PhD.

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Introduction

The Teledyne LABS 14-vessel CD14 Comparative Dissolution Tester runs two methods simultaneously or independently, making it an ideal apparatus to evaluate bioequivalence for abbreviated new drug applications (ANDA) for generic drugs. The 14 stirring positions allow for 6+1 or 12+2 configurations for improved workload efficiency in R&D, formulation development, quality control, and for stability test labs. With digital temperature probes at 12 positions, the CD14 can test two different formulations with separate settings for every parameter under the same environment. The CD14 is controlled by a fast, powerful computer built into the color touchscreen display mounted to the drive head. The adjustable tilt angle accommodates operators of different heights, while the Linux-based operating system with its own SQL database responds instantly to user input. The highly durable resistive touch screen works with or without the protective

gloves generally used by chemists in a laboratory setting. The CD14 has an easy-to-use interface that includes context-sensitive help. It logs events, errors, test reports, test history, service, and any changes made by users. The new methods or test parameters can be programmed quickly.

The CD14 Tester is very useful for performing a comparative dissolution test for oral solid products like tablets, capsules, etc. These products exist in a variety of release characteristics such as immediate-release, sustained-release, delayed-release, extended-release, etc. A comparative dissolution test in various dissolution medium must be performed during product development, ANDA submission, and after approval for Scale-Up and Post-Approval Changes (SUPAC). The Federal Drug Administration (UD-FDA) has published multiple guidance documents regarding the dissolution test and its requirements, including much product-specific guidance.

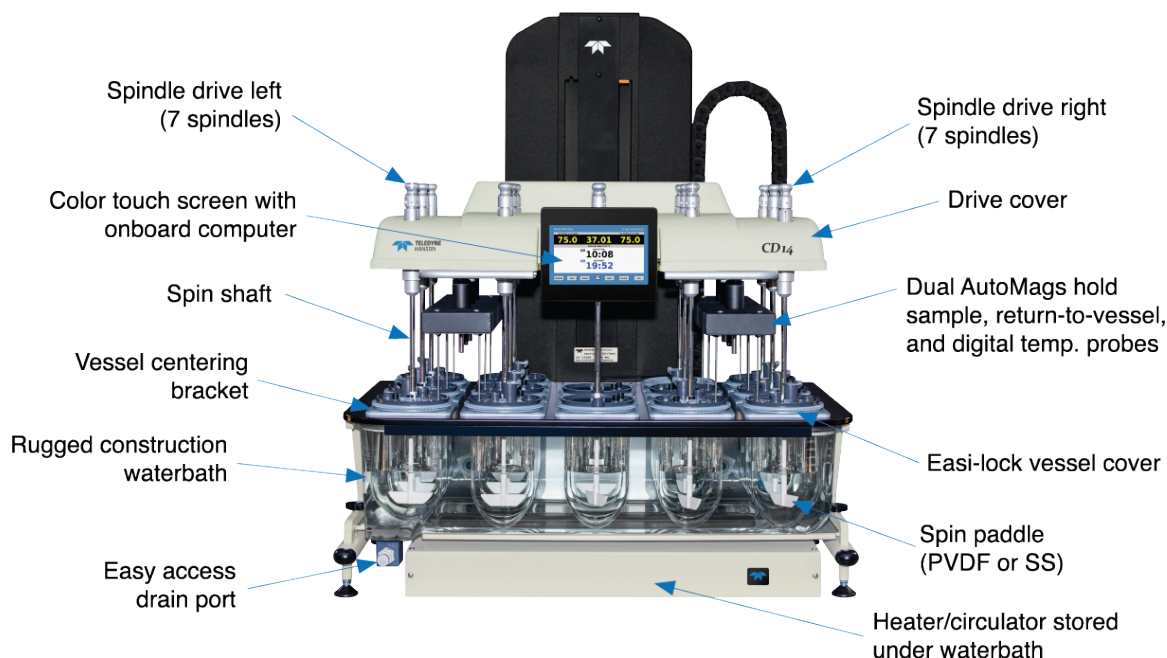


Figure 1. The CD14 Apparatus.

Procedure

For almost all extended-release products, a longer dissolution test is required. Typically, this test lasts up to 24 hours; in certain cases, it could be extended for days. In either situation, multiple sample withdrawal and replacement of withdrawn volume using a fresh dissolution medium at the same temperature is warranted.

To evaluate the temperature variations between the vessels for a longer period, a dissolution test using a CD14 apparatus with autosampler was performed. The instrument was equipped with an AutoMag magazine with a digital temperature probe, as well as with an external temperature probe to automatically measure the bath temperature. The test was started with following parameters:

Dissolution Medium	Purified Water
Volume	900 mL
Stirring Speed	50 RPM
Apparatus	Paddles (II)
Sampling Time point (hrs)	4,8,12,24,30,36,48, and 72
Rinse Volume	5 mL
Collect Volume	5 mL
Replace volume	5 mL

During this test, the temperature was measured automatically with digital temperature probes for the water bath and for vessels 1 through 12. The stirring speed was also measured and recorded at the start of the test, during the test, and at the end of the test. The results of the temperature were saved by the on-board computer in a data file and printed using a network printer. A snapshot of statistics from that printed report is shown in Table 1, providing the average, minimum, and maximum temperatures and the stirring speeds.

For vessels 13 and 14, the temperature was measured using a calibrated digital thermometer at random time points throughout the 72-hour period. Those temperature readings are reported in Table 2.

Conclusion

Based on the study results obtained above, it can be concluded that the Teledyne LABS CD14 dissolution tester is capable of maintaining a very consistent temperature for a very long period with minimum variations amongst the vessels and between the readings. We are very confident that the same temperature stability will also be maintained during long-acting implant dissolution testing, if required. The CD14 is a very robust instrument for any type of dissolution test: it has the best quality possible and delivers worry-free data integrity for 21 CFR Part 11 compliance.

Duration of test: 72:00:56

Group	Min speed (rpm)	Max speed (rpm)	Avg speed (rpm)
A	49.8	50.0	49.9
B	49.8	50.1	49.9
	Min (°C)	Max (°C)	Avg (°C)
Bath	37.15	37.26	37.20
Vessel	Min (°C)	Max (°C)	Avg (°C)
1	36.96	37.08	37.03
2	36.93	37.06	37.01
3	36.92	37.06	37.01
4	36.89	37.05	36.99
5	36.91	37.04	37.00
6	36.86	37.05	37.00
7	36.97	37.10	37.05
8	36.84	36.99	36.95
9	36.83	37.02	36.97
10	36.91	37.06	37.01
11	36.95	37.06	37.01
12	36.93	37.06	37.01

Table 1. 72 hour dissolution test temperatures and stirring speeds.

Time (Hrs)	Vessel #13 Temp.°C	Vessel # 14 Temp.°C
Prior to Start test	37.05	36.99
After 4 hours	37.02	37.01
After 24 hours	37.06	37.04
After 48 hours	37.08	37.04
After 64 hours	37.10	37.10
After 72 hours	37.09	37.09

Table 2. Temperatures for vessels 13 and 14

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<https://www.teledynelabs.com/en-us>

Or send an email to hansontechsupport@teledyne.com or
ashvin.patel@teledyne.com