# Dispelling the Myth: 6 versus 12 Position Dissolution Apparatus

The dissolution test is based on 6 results. The apparatus has been typically built with a minimum of 6 positions to accommodate enough vessels to run a complete test. The number of units to test appears in the USP General Chapter <711> Dissolution, Acceptance Criteria tables for each type of dosage. This number and configuration has appeared during studies since it appeared in literature through 1950´s and 1960´s until it appeared officially in the US Pharmacopeial Forum in 1970. Often the acceptance criteria or comparison data requires several sets of 6 to obtain 12 or 18 results which have historically been tested on 6-position apparatus. Interestingly, the number of tablets to be tested in the ICH Harmonized Pharmacopeia (EP, USP, and JP) is described as an assembly in the singular throughout the harmonized dissolution chapter, for instance; place the stated volume of dissolution media in the vessel···place one dosage unit in the apparatus, etc.

In terms or regulatory requirements for dissolution testing, FDA guidance suggests that marketed dosage forms are tested for specification setting with 12 units. This number also correlates with FDA´s required number of tests on human subjects (n≥12) to determine the bioavailability of products and in vitro-in vivo relationships. Specifications (Q) are based on twelve units and expressed as the percentage of labeled required for demonstrating a therapeutic effect, but this does not imply or intend for this testing to be done at the same time or on a single dissolution apparatus with 12-positions. 6-Position dissolution apparatus utilized for testing products whether they are used for specification setting (testing a total of 12 dosage units) or routine quality and conformance testing which is based on sets of 6 units with tighter limits (Q+5%). FDA Guidance also requires testing a total of 12-units each for demonstrating bioequivalence between reference and generic products – but they do not require all 12 units to be tested simultaneously.

In summary, the number "12" is only a reference point of a minimum number of units to be tested to adequately set specifications and ensure bioequivalence between generic and reference drug products; it is not an apparatus requirement. Very often more units (18 or 24) may be tested to assure higher accuracy and precision in statistical comparison methods such as f2. Dissolution apparatus are developed and used worldwide based on 6-positions for matter of convenience and conformance. Twelve units are routinely tested on a single 6-position apparatus performing the method twice.

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**Why is it more advantageous to use two 6 or 8 place units versus one with 12 or 14 positions?**

1. Regulatory. Although it is a requirement for f2 comparison to utilize a minimum of 12 units, it is not a regulatory requirement to perform dissolution on a single 12-position system. There is no regulatory requirement to perform all numbers required for comparison at the same time.

2. Compendial requirement #1 — Samples are withdrawn only at specific times within 2% of the time they were dropped. You do not have a sample until it has been filtered to stop the dissolution process. This equates to pulling and filtering 6 samples in ± 36 seconds but this has to be done at the proper position. If a 12 position apparatus is used, 12 samples will need to be collected and filtered within ± 36 seconds; this is only 3 seconds per position.

3. Compendial requirement #2. Because of the previous requirement, dosage forms may be introduced at consecutive intervals (for instance every 30 seconds) to allow time to sample. Tablets may be staggered however; dosage forms are required to be dropped into non rotating medium. If someone starts the apparatus by introducing a tablet to the first vessel and starts the apparatus, all positions will rotate. The 12 position apparatus must have the ability to keep media from moving until each dose is introduced.

4. Flexibility. Two 6-position units allow you to start and stop two independent tests at different times. With a single unit, you must run the same method speed and test length for both batches. You have the ability to start and stop two apparatus independent of one another with 6-position systems.

5. Failure investigation. Two 6-position apparatus will require less investigation and retesting in the event of a failure. If one tablet among the 12 fails due to a mechanical issue, do both batches need retested? With two independent apparatus there is less ambiguity in the event of a failure since a single test is associated with a single apparatus.

6. Adherence to stricter Enhanced MQ guidelines. The tighter specifications required by the ASTM and FDA MQ procedures will be more difficult to meet. We suggest you receive assurances that any 12 or 14 place system will pass the new MQ physical parameters. Vessel/shaft centering is now only 1.0 mm; if one position is off by more than 1.0 mm in the upper and lower portion of the vessel the entire unit should be taken out of service until repaired, or readjusted and re-qualified.

7. Less downtime. If a single 12 or 14 place unit is removed from service for a mechanical or repair issue, you´ ve lost the productivity of two systems. If a problem occurs with one of two dissolution apparatus, you can still operate the other system.

8. Automation flexibility. Whether it is automated sampling, media replacement, or on line UV or LC measurement; there are a multitude of automation solutions available for 6 or 8 place systems. If your testing needs change, the more independent approach can accommodate pathways for automation. 8-position apparatus allow easy on-line UV integration since the spare vessels are used for blank and standard solutions during the test.

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# 消除误解：
# 6 杯位和 12 杯位溶出度仪

溶出度测试基于 6 个样品的测试结果。溶出度仪通常设计为包含至少 6 个溶出杯位置，以提供足够的溶出杯来运行完整的测试。对测试样品单位数量的要求见于美国药典 USP 通则 <711>：溶出度分析 - 针对每种剂型的验收标准表。从历史角度，这一数量和配置要求随着溶出度研究的不断深入逐渐被提出，首先见于 1950 和 1960 年代的文献中，直到 1970 年被美国药典论坛正式采纳。通常验收标准或对比数据需要多次 6 片一组的结果（历史上采用 6 杯位溶出度仪进行测试），以获得 12 或 18 个样品的测试结果。有趣的是，在 ICH 协调药典（EP、USP 和 JP）中的协调溶出度分析章节，涉及测试片剂数量的内容通篇描述为单数形式，如“将所述体积的溶媒加至一个溶出杯中……投入一个单位的制剂”等等。

对于溶出度测试的法规要求，FDA 指南建议上市药品需要经过 12 单位制剂的测试以用于标签规格。这一数量也与 FDA 针对用于确定药品生物利用度和体内 - 体外关系的人体实验所要求的测试数量（n≥12）相匹配。标签规格 (Q) 基于 12 个单位的测试并表述为标签含量的百分比范围，以表明其对应的治疗效果，但这并不意味着或暗示该测试需要在同一时间进行或在同一台溶出度仪（12 杯位）上进行。6 杯位溶出度仪可用于标签规格的设定（测试总共 12 单位制剂）或常规的质量和一致性测试，而后者是基于一系列具有更严格的限值要求（Q±5%）的 6 个单位一组的测试。FDA 还要求执行 12 个单位的测试以证明原研药和仿制药之间的生物等效性——但并未要求所有 12 个单位必须同时进行测试。

综上，数量“12”仅仅是为满足设定标签规格和确保原研药和仿制药之间的生物等效性而设置的最小测试数量参考点，它不是一个仪器规格要求。并且常常会遇到需要测试更多单位样品（18 或 24）的情况，比如在统计比较方法（如 f2）中为确保更高的准确度和精密度进行的测试。考虑到便利性和一致性，基于 6 杯位的溶出度仪在全球得到了广泛的开发和使用。12 单位的测试常规通过采用 6 杯位仪器执行两次方法来实现。

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## 为什么使用 6 或 8 杯位的仪器比使用 12 或 14 杯位的仪器更有利?

1. 法规因素。尽管进行 f2 比较需要测试至少 12 个单位的样品，但法规并未要求必须在一台 12 位系统上执行所有测试，也不要求同时进行所有这些测试。

2. 药典要求 #1 – 样品抽取耗时必须不大于样品开始测试时长的 2%。由于需要过滤步骤来终止溶出过程才能获得样品，即相当于必须能够在 ±36 秒内完成 6 个溶出杯的样品抽取和过滤 (30 min 为例)，并且要保证的准确取样位置。如果使用 12 杯位仪器，则必须在 ±36 秒内完成 12 个样品的收集和过滤，即每个位置仅 3 秒。

3. 药典要求 #2 – 由于上一条要求限制，我们也许可将制剂以连续的时间间隔相继投入溶出杯（例如每 30 秒投入一个样品），从而为取样赢得时间。但这样做的后果会导致加入制剂时溶媒已经开始搅拌，而这是不允许的。如果在投入第一个制剂后即开启溶出度仪，所有杯位都将开始搅拌，这就要求 12 杯位溶出度仪具有独立控制各溶出杯搅拌开启的功能。

4. 灵活性。两台 6 杯位溶出度仪可以在不同的时间运行两个不同的试验，而单台 12 杯位仪器则只能对两批样品采用相同方法转速和测试时长。使用 6 杯位系统，您可以独立控制两台仪器的启动或停止 .

5. 错误调查。两台 6 杯位仪器在运行出错时需要较少的调查和重新测试。而如果 12 杯位仪器的一个片剂测试样品由于机械故障导致测试失败，将导致两批样品均需重新测试。使用两台独立的仪器能大大减少这种困扰，因为一组测试仅与一台仪器相关联。

6. 遵循更严格的增强型机械认证指南。ASTM 和 FDA 机械认证规程要求的更严格的指标将更难于满足。我们建议您进一步确认 12 或 14 杯位系统是否能够满足这些新的要求。溶出杯 / 轴杆的轴心误差要求仅为 1mm，如果某一个杯位的上部或下部溶出杯区域超过这一限值，整个系统都需要停止工作，直到维修完成，或经过重新调整并重新认证。

7. 更短的停机时间。如果一台 12 或 14 杯位系统由于机械或维修原因停止工作，您将损失两台系统的分析能力。而如果是独立的两台仪器中的一台出现问题，您至少还能使用另一台进行分析。

8. 自动化灵活性。无论是自动化取样，溶媒置换，或在线紫外或液相色谱测量，都有大量的针对 6 或 8 杯位系统的自动化解决方案可供选择。如果测试需求发生变化，更独立的方法才能够适应自动化升级路径。8 杯位溶出度仪可实现简单的在线紫外溶出测定，因为多出的两个溶出杯可在测试中用于空白和标准溶液。