

## Understanding Nominal Particle Size Differences in 4 $\mu\text{m}$ vs 5 $\mu\text{m}$ C18 Columns - HPLC Primer

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### Overview

The particle size listed on an HPLC column—such as 4  $\mu\text{m}$  or 5  $\mu\text{m}$ —represents an average or most common value within a broader size distribution. Silica particles are not perfectly uniform; instead, they follow a Gaussian distribution resulting from the manufacturing process. Because of this natural variation, the performance difference between a 4  $\mu\text{m}$  and 5  $\mu\text{m}$  particle column is minimal and often unnoticeable in routine chromatography.

Particle sizes (e.g., 1.8  $\mu\text{m}$ , 2.2  $\mu\text{m}$ , 3  $\mu\text{m}$ , 5  $\mu\text{m}$ , 10  $\mu\text{m}$ ) are best understood as categories, each representing a range of particle diameters used for packing the column. These sizes are measured before chemical bonding and surface modification.

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#### ◆ Particle Size Explanation (What the Numbers Really Mean)

- Not exact measurements: A “4  $\mu\text{m}$ ” particle is not measured as exactly 4.000  $\mu\text{m}$ .
- Gaussian distribution: Particles are produced in batches containing a spread of sizes.
- Name based on mode: Columns are named for the most common particle diameter, not the mean or median.
- Packing benefit: Allowing a distribution improves packing efficiency, surface coverage, and column stability.

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#### ◆ How Particle Size Affects Performance

Depending on the method, particle size influences:

##### 1. Efficiency (Plates)

Smaller particles → Higher efficiency

Larger particles → Lower efficiency (but often acceptable)

##### 2. Back Pressure

Smaller particles → Higher pressure

Larger particles → Lower pressure (useful for preparative or older systems)

##### 3. Peak Shape

Particle size distribution and packing uniformity often matter **more** than the nominal value.

##### 4. Selectivity

Selectivity is **not** a function of particle size.

It is governed by:

- Stationary phase chemistry
  - Bonding density
  - Ligand type
  - Mobile phase composition
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#### ◆ USP L1 Requirements (C18 Classification)

For a C18 column to qualify as USP L1, it must meet the USP specification:

- Octadecylsilane bonded to porous or non-porous silica, or a ceramic support
  - Particle size from 1.5 to 10  $\mu\text{m}$
  - May be superficially porous or fully porous
  - May also be a monolithic rod
  - *(USP criteria ensure consistency across manufacturers.)*
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A particle size designation such as “4  $\mu\text{m}$ ” or “5  $\mu\text{m}$ ” refers to the approximate diameter of the silica used in the stationary phase. In practice, silica particles are produced with a distribution of sizes, not a uniform value. When plotted, this distribution forms a Gaussian curve, and the column is labeled according to the most common particle size in that distribution.

As a result, a column labeled 4  $\mu\text{m}$  behaves very similarly to one labeled 5  $\mu\text{m}$ , and the difference is typically nominal. This principle applies to most silica-based bonded phases, including C18, and extends broadly to common particle sizes such as 1.8  $\mu\text{m}$ , 2.2  $\mu\text{m}$ , 3  $\mu\text{m}$ , 5  $\mu\text{m}$ , and 10  $\mu\text{m}$ . For a C18 column to be considered a USP L1 column, it must meet the USP requirements for octadecylsilane-bonded silica or ceramic particles ranging from 1.5 to 10  $\mu\text{m}$  in diameter, including superficially porous materials or monolithic rods.

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#### ◆ Why This Is Important

1. Prevents over-interpreting particle size labels—the real difference may be negligible.
  2. Helps analysts choose columns based on performance, not nominal microns.
  3. Ensures correct expectations when switching between 4  $\mu\text{m}$  and 5  $\mu\text{m}$  columns.
  4. Clarifies why manufacturer data may vary slightly within a labeled size.
  5. Supports compliant method development when selecting USP L1 columns.
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*NOTE: Octadecyl silane chemically bonded to porous or non-porous silica or ceramic micro-particles or superficially porous particles, 1.5 to 10  $\mu\text{m}$  in diameter, or a monolithic rod.*

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