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The Crystal-Ball Problem: Early-Stage University Filings and Written Description

By Kim Vines[49]

Introduction

The written description requirement of 35 U.S.C. § 112(a) poses an enduring challenge for universities and academic research institutions. Universities file patent applications at the earliest stages of scientific discovery—when mechanistic understanding is preliminary, optimization has not begun, and the commercially relevant molecular species remain unknown. Patent law, however, requires applicants to provide structural specificity at filing, years before downstream developers, whether established biopharmaceutical companies or university-affiliated startups, identify the actual embodiments that will eventually matter.

Although companies also file early, they typically have the financial resources to file new PCT applications as incremental improvements emerge, capturing additional structural details and narrowing the invention as development progresses. Universities, by contrast, often lack the budget to pursue serial follow-on filings, making that initial early-stage disclosure carry a disproportionate burden under § 112(a).

The Federal Circuit's decision in *Seagen v. Daiichi Sankyo* underscores this structural mismatch. There, Seagen's early-stage filing attempted to claim a broad conceptual genus of peptide linkers; a decade later, Daiichi developed a specific tetrapeptide sequence that proved clinically valuable. Unable to show possession of that narrower species in its original application, Seagen lost priority—and ultimately its claim.

This Article argues that while universities cannot eliminate the inherent timing asymmetry of early-stage research, they can significantly improve written-description outcomes through institutional reform. Technology transfer offices (TTOs) can adopt practices that better capture the tacit scientific knowledge inventors already have but often fail to articulate—knowledge that frequently constitutes the very "blaze marks" § 112(a) demands. Modern AI tools can further assist TTOs in eliciting that information in a systematic, economically feasible way.

I. *Seagen v. Daiichi* and the Demands of Written Description

A. Enhertu and ADC Innovation

The dispute in *Seagen* involved Enhertu, a next-generation HER2-targeted antibody–drug conjugate (ADC). Enhertu includes several technical innovations: a potent DXd topoisomerase I inhibitor payload, a high drug-to-antibody ratio of approximately eight, and a specifically engineered tetrapeptide linker—Gly–Gly–Phe–Gly—designed for intracellular protease cleavage. The precision of its conjugation chemistry and its pronounced bystander effect distinguish it from earlier ADC platforms.

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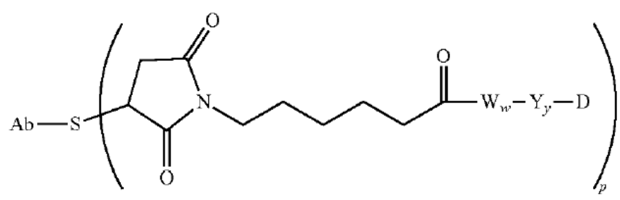
Crucially, the Enhertu linker sequence emerged from Daiichi's work and was publicly disclosed in 2015—more than a decade after Seagen's 2004 priority application.

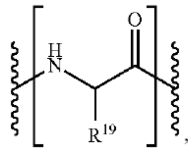
B. The Priority Problem

Seagen sought claims in a 2019 continuation (resulting in U.S. Patent No. 10,808,039 ("the '039 patent")) to encompass the Enhertu linker that claimed priority to a 2004 application.

Claim 1 of the '039 patent was directed to an antibody-drug conjugate having the formula:



each —W_w— unit is a tetrapeptide; wherein each —W— unit is independently an Amino Acid unit having the formula denoted below in the square bracket:



wherein R^{19} is hydrogen or benzyl,

wherein Y is a spacer unit; y is 0, 1 or 2; D is a drug moiety, and; p ranges from 1 to about 20, wherein the S is a sulfur atom on a cysteine residue of the antibody, and wherein the drug moiety is intracellularly cleaved in a patient from the antibody of the antibody-drug conjugate or an intracellular metabolite of the antibody-drug conjugate.

Daiichi's Enhertu uses trastuzumab (as the HER2-targeting antibody), a topoisomerase I inhibitor payload (DXd), a y value of 0, and a W_w region consisting of the tetrapeptide Gly-Gly-Phe-Gly.

Since Enhertu's 2015 disclosure would be prior art absent a valid 2004 priority date, the Federal Circuit scrutinized whether Seagen's 2004 application adequately described the specific tetrapeptide subgenus later claimed.

The 2004 application did identify peptide linkers of various lengths—including tetrapeptides—as potential embodiments within the broad W_w formulation. However, the only tetrapeptide sequences exemplified or hinted at in the filing consisted of combinations of neutral residues that did not include the glycine/phenylalanine motif that later proved crucial. Nothing in the 2004 specification suggested glycine-rich sequences, phenylalanine motifs, or any structural principle directing a skilled artisan toward the Enhertu-type tetrapeptide.

Because the priority application lacked blaze marks pointing to the claimed subgenus, Seagen was denied the 2004 priority date; Enhertu then became prior art, rendering the claim invalid as a matter of law and reversing a jury award to Seagen for more than $41 million.

C. The Structural Mismatch

The problem was not the absence of tetrapeptides from the 2004 disclosure, but the absence of directional structural information that would have signaled which tetrapeptide subclasses mattered. The case exemplifies a broader phenomenon: early-stage academic filings must satisfy a doctrine that demands structural specificity typically generated only after years of medicinal chemistry—not at the point of initial discovery.

II. The Combinatorial Explosion Problem

A theoretical solution would be to disclose every possible peptide sequence within a genus—and modern AI systems could, in principle, generate such exhaustive lists. Yet even tetrapeptides alone encompass 20^4 (160,000) combinations (and that figure counts only the twenty canonical amino acids). Enumerating this vast combinatorial space would be scientifically meaningless, economically prohibitive, and doctrinally insufficient. Written description jurisprudence does not reward brute-force disclosure; it demands blaze marks that direct a skilled artisan toward the specific subgenera the inventors actually possessed. An AI-generated wall of sequences, no matter how comprehensive, cannot substitute for the structurally meaningful guidance that § 112(a) requires.

III. The Institutional Dimension: What University TTOs Must Do

A. Correcting the Most Harmful Misconception

Inventors often mistakenly believe they may disclose only compounds they have synthesized or tested. This misconception excludes the very information § 112(a) treats as evidence of possession: predicted structures, planned variants, mechanistic explanations, and design constraints. These "in-between" embodiments frequently become critical blaze marks years later.

B. Systematically Capturing the "In-Between" Structural Space

Academic specifications routinely describe a broad genus and a handful of examples, omitting the intermediate structural territory. Yet courts increasingly look to that "in-between" zone to determine possession.

1. Example: Peptide Linkers (as in Seagen)

TTOs should elicit:

- preferred linker lengths (*e.g.*, 3–6 residues),
- amino acid preferences or exclusions,
- residue-specific functional roles (*e.g.*, glycine for flexibility),
- protease-recognition logic (*e.g.*, aromatic residues),
- non-preferred charged motifs,
- planned linker sequences yet to be synthesized.

2. Example: Broad-Structure Small-Molecule Chemistry

TTOs should elicit:

- preferred core scaffolds,
- substituent pattern rationales (*para* vs. *meta*),
- steric/electronic constraints,
- SAR hypotheses,
- preferred chain lengths or heteroatoms,
- disfavored motifs,

- planned analogs or next-generation variants.

These insights often exist in the inventor's mind but remain unstated unless intentionally elicited.

C. Budget Constraints and the Limits of Attorney-Driven Elicitation

Although patent attorneys are trained to probe for missing technical details, universities cannot depend on counsel to reconstruct the full scope of an invention's conceptual architecture. Attorney involvement typically occurs under tight deadlines, and universities—especially public institutions and smaller research organizations—operate with limited patent budgets that restrict the depth and frequency of attorney interviews. As a result, attorney-driven elicitation often captures only a fraction of the design logic, mechanistic reasoning, and predicted subgenera that inventors understood contemporaneously.

The more effective—and economically sustainable—approach is for inventors and research groups to document their reasoning at the moment of invention and communicate it to the TTO before drafting begins, ensuring the disclosure reflects their full scientific understanding rather than a compressed reconstruction.

D. Post-Draft Review Sessions as a Mechanism for Eliciting Intermediate Structural Insight

Even when patent counsel prepares the initial draft application, the disclosure almost always improves if the TTO and the inventors reconvene to review that draft together. A first-pass specification gives inventors a concrete text to react to, making omissions far more visible than during abstract questioning. When presented with draft claim sets, subgenera, or structural definitions, inventors frequently identify missing preferred linkers, disfavored residues, scaffold constraints, or mechanistic explanations they had assumed were too obvious to state. This second-stage review—conducted either before the provisional is filed or, if a provisional has already been submitted, before the non-provisional application is prepared—often surfaces the "in-between" structural knowledge that written-description doctrine treats as evidence of possession. It is also highly cost-effective: a focused session centered on an actual draft typically elicits more § 112(a)-critical detail than a lengthy open-ended interview at the outset.

The value of these post-draft discussions is underscored by cases like *Duke v. Sandoz*, where the university ultimately held a patent family that failed to disclose the specific commercial embodiment at issue—the active ingredient later marketed as Latisse. Over the course of multiple continuation applications, the specification never evolved to capture the structure of the product that eventually drove the dispute. At some point between the original provisional filing and the nth continuation, a careful post-draft review could have revealed that the commercially significant embodiment fell outside the written description, allowing the specification to be updated before any public disclosure. A structured post-draft review process is precisely the type of institutional safeguard that can prevent such omissions.

E. Requiring Structural Rationales

Even brief explanations of *why* certain motifs, ranges, or residues are preferred serve as powerful blaze marks. Courts treat mechanistic reasoning as evidence of possession and tend to discount disclosures that merely enumerate possibilities without direction.

F. AI as a Support Tool (Not a Substitute for Inventor Insight)

AI can explore structural neighborhoods, generate variants, surface patterns, identify gaps, and standardize intake interviews. But AI cannot, by itself, generate legally sufficient blaze marks. Written description requires evidence of the inventors' actual possession, and AI-generated suggestions remain inferential, not evidentiary. While emerging generative models may someday propose plausible narrowing rationales or subgenera, their contributions are ultimately conjectural. Direct conversations with inventors remain the most reliable method for uncovering mechanistic understanding, feasibility constraints, and design intent—insight that § 112(a) uniquely privileges. AI can scaffold the elicitation process, but only inventors can supply the blaze marks that withstand judicial scrutiny.

IV. How AI Can Help TTOs Elicit Inventor Knowledge

Although AI cannot satisfy the written description requirement on its own, it can substantially improve the *elicitation* of inventor knowledge—the stage where most § 112(a) failures originate. Modern generative tools can analyze draft disclosures, slide decks, or laboratory materials and produce targeted, domain-specific questions that prompt inventors to articulate preferences, constraints, mechanistic rationales, and plausible subgenera they would not otherwise verbalize.

AI can also identify doctrinally relevant gaps, such as unexplained ranges or overly broad Markush groups, and can generate hypothetical structural variants that help inventors clarify which designs are preferred, disfavored, or mechanistically implausible. By mining lab notebooks, emails, and presentations, AI can surface implicit reasoning that inventors assumed was obvious or did not think to include, and it can produce structured interview guides to ensure consistent, technically adequate elicitation across TTO staff with varying scientific backgrounds.

Yet AI's role remains supportive rather than substantive. While future models may propose narrowing rationales or subgenera that resemble blaze marks, such inferences cannot replace the legally meaningful evidence of possession that comes from the inventors' own descriptions of their understanding at the time of filing. AI can help uncover blaze marks, but only inventors can supply the ones that withstand judicial scrutiny; and in all cases, universities must ensure that confidential research information is never entered into unsanctioned public AI tools, but handled only within secure, institutionally approved environments that preserve confidentiality and privilege.

Conclusion

Seagen v. Daiichi highlights the structural mismatch between early-stage academic research and the Federal Circuit's increasingly demanding written description jurisprudence. Universities cannot anticipate which specific embodiments downstream developers—or their own startups—will ultimately adopt. But they can capture far more of the design logic, mechanistic insight, and "in-between" structural knowledge that inventors already possess.

By dispelling misconceptions, eliciting intermediate structural understanding, recognizing budget constraints, conducting post-draft review sessions, and using AI to surface tacit knowledge, university TTOs can materially strengthen their § 112(a) position. Applications with richer intermediate disclosure not only fare better under written-description scrutiny but also present more credible and commercially attractive patent assets.

These reforms cannot eliminate § 112(a)'s crystal-ball problem, but they can substantially improve the durability and value of university patents in an era of increasingly exacting written-description doctrine.

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