STERIC ANALOGY PHARMACEUTICAL OBVIOUSNESS AT THE PTO*

DISCUSSION DRAFT FOR COMMENT  ➔ hwegner@gmail.com

Harold C. Wegner**

I. OVERVIEW

II. STERIC ANALOGY IN THE PHARMACEUTICAL LABORATORY  6

III. STERIC ANALOGY IN ACTUAL PATENT PRACTICE  11

   A. Patent Law Stalled in the Era of the Papesch Case  11
   B. Steric Analogy as a Valuable Predictive Tool  13
   C. Steric Analogy Case Law  14

IV. STERIC ANALOGY UNDER THE 2011 PATENT LAW  21

   A. Inter Partes Vehicles to Introduce Steric Chemistry to the PTO  21
   B. Post Grant Review (PGR) vs. Generic Claims  22

V. CONCLUSION  23

About the Author  24

* This is a discussion draft for comment only. Comments would be appreciated addressed to the author at his email or Post Office box address listed on the last page of this paper.

** Biographical information about the author is found on the final page of this paper. This work is pro bono without sponsorship from any other person or any organization.
I. OVERVIEW

“Steric analogy obviousness” in the integration into the determination of *prima facie* obviousness of a chemical compound of the fields of steric analogy as an integral part of the determination of prima facie obviousness of claims to chemical compounds, particularly in the pharmaceutical field. Steric analogy in the context of patent law obviousness is defined here as the integration of the modern fields of classic isosterism, non-classical isosterism and bioisosterism as adjuncts to classic “structural obviousness” as key integers in the determination of prima facie obviousness of claims to chemical compounds, particularly in the pharmaceutical field.

Beginning with late nineteenth century case law and continuing through most of the twentieth century as confirmed through *In re Hass*, 141 F.2d 122 (CCPA 1944), and *In re Henze*, 181 F.2d 196 (CCPA 1950), a claim to a new chemical compound was judged for patentability based primarily on whether that compound was “structurally obvious”, a two dimensional inquiry that focused on whether the claimed formula differed only as an adjacent homolog or position isomer or other minor structural variation where one could *predict* that the claimed compound would share common properties with the prior art.

In the wake of *In re Papesch*, 315 F.2d 381 (CCPA 1963), it became possible to gain a claim to a structurally obvious compound if one could establish through declaration evidence that the three dimensional thing claimed, the actual chemical compound, possessed an unexpected difference in actual properties. (What had, pre-*Papesch*, been referred to as “structural obviousness” now became
known as “prima facie obviousness” based on close structural relationship to the
prior art.)

The more than fifty years since *Papesch* the Patent Office has for the most
part strictly divided the examination of claims to a chemical compound based upon
a first, purely two dimensional structural analysis under the Haas Henze line of
case law, ignoring for the most part the properties of the claimed compound on the
often unstated basis that the Patent Examiner is a “paper chemist” without the
laboratory tools to consider the properties of the compound claims he or she
examines.

A true picture of the scope of prima facie obviousness surrounding a known
compound is only known by making the prima facie inquiry based upon *both* the
classic patent search for “structurally obvious” compounds, but also including in
the inquiry principles of steric analogy. Thus, for example, if the claimed
compound and the prior art have a common structure except for one substituent,
the difference as to that one substituent may well not be prima facie obvious. But,
if there is a known steric equivalence between the two groups for compounds
sharing the same utility as the prior art compound, then this steric equivalence may
mean that an otherwise structurally unobvious compound is prima facie obvious.

Concurrently with the evolution of the case law leading up to the *Papesch*
case, the theoretical and laboratory scientists of the world exemplified by the late
Alfred Burger developed a science summarized in this paper as “steric analogy”.
In essence, steric analogy in the patent world looks to the common “base”
molecule of a claimed invention versus the prior art and then analyzes the
structural substituents of the claimed and prior art compounds to determine of they
are *equivalent* in the context of the utility disclosed for the claimed compound.
Thus, whereas two groups in a particular setting may be neither a homolog, isomer nor other structurally closely related group, as a matter of steric analogy the two groups often are equivalent. Conversely, while this paper focuses upon steric analogy principles to establish obviousness the converse may also be true.¹

The starting point for this paper is an overview of the history of steric analogy in the laboratory, focusing upon the pioneer work of the late Alfred Burger and others. See § II, Steric Analogy in the Pharmaceutical Laboratory.

Steric analogy has had a long history in the patent field, while paradoxically the leadership of the Patent Office has sub silentio denied its existence. See § III, Steric Analogy in Actual Patent Practice

Steric analogy practice has been seemingly nonexistent to anyone who does not go beyond the Manual of Patent Examining Procedure which is silent on this topic. See § III, Steric Analogy in Actual Patent Practice. The patent law insofar as the Patent Office leadership is concerned is a law without steric analogy principles. See § III-A, Patent Law Stalled in the Era of the Papesch Case. But, steric analogy is a powerful predictive tool, to suggest the equivalency of various substituent groups that provide equivalent results based upon their three dimensional characteristics. See § III-B, Steric Analogy as a Valuable Predictive Tool. Steric analogy is on the one hand accepted in the administrative and judicial case law, see § III-C, Steric Analogy Case Law. At the same time, the PTO

¹ This topic is outside the scope of the present paper. But, as one example, consider the situation where a Patent Examiner rejects a claimed invention to a compound with substituent “X” where “X” is a completely different group that would not raise a case of “structural obviousness” under Haas-Henze principles. But, if the substituents at the “X” position are steric analogs with identical physical characteristics, perhaps a different result would be reached as to prima facie obviousness.
leadership as manifested through its *Manual of Patent Examining Procedure* has *sub silentio* denied the existence of steric analogy; *see* § III-D, *PTO Leadership Sub Silentio Repudiation of Steric Analogy.*

Modern steric analogy principles in many ways go beyond being a mere adjunct to structural obviousness. The famed scientist Alfred Burger compares the real world of what is termed here as steric analogy to the prior study of structures as what we would today call the difference between night and day, or, to use the words of Professor Burger, the era of selecting new chemical structures without steric principles is akin to “molecular roulette”.  

Whether the Administration takes a more positive view of steric analogy chemistry or not than the recently retired Director, the *sub silentio* suppression of steric analogy chemistry as part of the *prima facie* obviousness inquiry is over. Given the positive attitude of the Patent Trial and Appeal Board to consider steric principles as seen through the case law, it is now anticipated that third parties will more and more challenge patents using the procedural vehicles of the *Leahy Smith America Invents Act of 2011*. *See* § IV, *Steric Analogy under the 2011 Patent Law*

---

II. STERIC ANALOGY IN THE PHARMACEUTICAL LABORATORY

As explained by Professor Burger more than a generation ago: “The time of random structural variations in molecular modification (‘molecular roulette’) prevalent throughout the first three decades of the twentieth century is past. Molecular modification now always involves drug design as far as the state of the art permits.” The role of steric analogy in drug design is explained by Kobayashi in the context of bioisoteres: “As an established and powerful concept in medicinal chemistry, the application of bioisosteres will continue to play an important role in drug discovery. Isosterism can also contribute to the productive application in the design and optimization of catalysts on organic chemistry.”

Steric analogies are important beyond simply looking to find equivalent compounds. He further explains that biosteric relationships are important for a variety of ways to improve upon existing pharmaceutical products which is explained by Kobayashi:

---

3 Burger, supra, PROGRESS IN DRUG RESEARCH, § 1.2, Molecular modification at p. 290 (emphasis added).

The development and application of bioisosteres have been adopted as a fundamental tactical approach useful to address a number of aspects associated with the design and development of drug candidates. The utility of bioisosteres is extending to

- Improving potency
- Enhancing selectivity
- Altering physical properties
- Reducing or redirecting metabolism
- Eliminating or modifying toxicophores
- Acquiring novel intellectual property.

To be sure, there are inherent predictive problems in certain areas involving isosteres an bioisosteres.

Professor Burger in his discussion of isosterism provides the following introduction to the early studies that evolved into the modern day views of that subject. He traces the roots of such studies to the nineteenth century “proposal that there is a skeletal center of a molecule (a pharmacophore) equipped with substituents and that these substituents make additive quantitative contribution to the biological activity has been in the minds of medicinal chemists for a long time.”

5 Id.

6 Burger, supra, PROGRESS IN DRUG RESEARCH, § 1.2, Molecular modification, p. 315 (“Among steroidal hormones, minor alterations can produce a range of overlapping, agonistic, antagonistic or widely different biological consequences.”)

Kobayashi adds that “[t]he design and application of isosteres have inspired medicinal chemists for almost 80 years, fostering creativity toward solving a range of problems in drug design, including understanding and optimizing drugs – target interactions and specificity, improving drug permeability, reducing or redirecting metabolism, and avoiding toxicity.”

Concerning more modern advances, he states that:

“An early attempt to compare chemical and physical properties of diatomic molecules such as N$_2$ and CO was made by [J. Moir, J. Chem. Min. Soc. S.A., 98, 335 (1909), J. Moir, Chem. News, 124, 105, 118, 133, 149 (1922)]. His reasonings about ‘isomerism’ of these two gases are no longer compatible with present-day views; nevertheless, his ideas were expanded by [O. Hinsberg, J. Prakt. Chem., 93, 302 (1916); 94, 179 (1916),] who applied them to partial structures of organic compounds. He defined groups which can be exchanges for each other in aromatic ring systems without considerable change of the physical properties of the resulting compounds as ring equivalents, citing benzene, thiophene and pyridine as examples. A –CH=CH- group in benzene is replaced by a divalent sulfur, -S-, in thiophene, or its –CH= by trivalent nitrogen, -N=, in pyridine.”

---


9 Burger, supra, PROGRESS IN DRUG RESEARCH, § 1.2, Molecular modification, p. 292.
The integral relationship between bioisosterism and isosterism is explained thusly:

“To deal with the divergent possibilities in interpretation, Harris L. Friedman [Symposium on Chemical-Biological Correlation, Nat. Acad. Sci. Natl. Research Council. Publ. No. 206, Washington, D.C. 1951, p. 295,] coined the term bioisosterism for the relationship of compounds ‘which fit the broadest definition of isosteres and have the same type of biological activity.’ In other words, bioisosterism should account for structure-activity relationships (SAR) of biologically active chemicals. The purpose of the SAR studies is the elucidation of the reasons for equivalence or nonequivalence of biologically active compounds.”

Professor Burger expanded the scope of his inquiry to coin a definition for bioisosteres:

“We would like to suggest an expanded statement which takes into account biochemical views of biological activity. ‘Bioisosteres are compounds or groups [within compounds] that possess near-equal molecular shapes and volumes, approximately the same distribution of electrons, and which exhibit similar physical properties such as hydrophobicity. Bioisosteric compounds affect the same biochemically associated systems as agonists or antagonists and thereby produce biological properties that are related to each other.’”

\[\text{10} \quad \text{Burger, supra, PROGRESS IN DRUG RESEARCH, § 1.2, Molecular modification, p. 298.}\]

\[\text{11} \quad \text{Burger, supra, PROGRESS IN DRUG RESEARCH, § 1.4.1, Bioisosterism 298.}\]
To add a further degree of complexity to the studies Professor Burger notes that there are two schools of bioisosteres today. There is thus “[a] subdivision of bioisosteres [ ] now also in use.” Thus:

“The cases that satisfy the conditions set forth by Langmuir, Grimm, and Erlenmeyer are called \textit{classical bioisosteres} if biochemical or pharmacological interactions are concerned. \textit{Nonclassical bioisosterism} refers to a more widely applicable set of compounds which cause qualitatively similar agonistic or antagonistic biochemical or pharmacological responses at the molecular level. Hansch recommended for such compounds the term partial bioisosteres but “non-classical bioisosteres” is used more often.”

Professor Burger explains some of the variables that must be considered:

Interactions of substrates or drugs at biomacromolecules could be electrostatic, steric (blockade or repulsion), and hydrophobic and dispersive. Since partition coefficients are so easily determined, they can indicate what other compounds with similar numerical values one should choose in planning molecular modifications. Sometimes, agreements between partition coefficients has been calculated only after a series of molecular analogs had been prepared and tested intuitively. In any event, if two compounds exhibit the same degree of hydrophobicity, isosterism could be involved.

---


13 \textit{Id.}

14 \textit{Id.}
III. STERIC ANALOGY IN ACTUAL PATENT PRACTICE

A. Patent Law Stalled in the Era of the Papesch Case

Today, obviousness of a chemical compound involves a two-step inquiry: Is the claimed compound as a two-dimensional picture representation “structurally” or “prima facie” obvious; and, if the answer is affirmative, do the three dimensionally-based properties of the claimed compound exhibit an unexpected difference versus the prior art compound so that the claimed prima facie obvious invention as a whole is nonobvious? With tweaks along the way, this has been the law of chemical compound obviousness for the more than fifty years since In re Papesch, 315 F.2d 381 (CCPA 1963).

From the late nineteenth century through and beyond the Haas-Henze cases, In re Hass, 141 F.2d 122 (CCPA 1944), and In re Henze, 181 F.2d 196 (CCPA 1950), the law of obviousness of chemical and particularly pharmaceutical patent claims has focused upon whether a claimed compound as represented by its two dimensional structural formula is “structurally obvious” over the closest prior art compound, again focusing upon its two dimensional formula. Even if the claimed compound in its three dimensional form had unexpectedly superior or different properties than the prior art compound, the claimed compound was considered “structurally obvious” based upon its structural similarity to the prior art structural compound. Properties of the claimed compound were disregarded at this stage.
In *Papesch*, the claimed compound closest to the prior art was admittedly *structurally obvious*, but its *properties* were unexpectedly different, based upon which the court said that the claimed invention *as a whole* is unobvious, ushering in a second phase to the nonobviousness determination: If a claimed compound in its two dimensional representation through a structural formula is “structurally obvious” as such a two dimensional representation, *then* the question is whether the three dimensional compound including all its properties is unobvious? The affirmative answer to this question resulted in a two part test to determine obviousness: The first, pre-*Papesch* test of structural obviousness was restyled as a question whether the claimed invention is “prima facie obvious” based upon the structural similarity, while a new, second test asks whether such a prima facie obvious compound based upon such structural obviousness is nevertheless *unobvious* because of the unexpected difference in properties of the compound as a whole?

While there have been minor adjustments over the years since *Papesch* to the determination of both prima facie obviousness and the subsequent determination whether the invention as a whole is patentable based upon an unexpected difference in properties, the patent law of nonobviousness for chemical compounds, per se, has been relatively stable. There has been a sharp divide in a two stage inquiry: If the first inquiry, the question is whether the two dimensional structural representation of the claimed molecule is or is not “structurally” or “prima facie” obvious, while the second question asks whether in spite of structural obviousness the applicant has demonstrated through expert declaration practice that the claimed invention *as a whole* including its properties is unobvious.
B. Steric Analogy as a Valuable Predictive Tool

The era of older forms of drug discovery based on simple homology or isomerism has passed. As explained by Professor Burger a generation ago in relation as to how molecules are chosen as drug candidates, “[t]he time of random structural variations in molecular modification (‘molecular roulette’) prevalent throughout the first three decades of the twentieth century is past. Molecular modification now always involves drug design as far as the state of the art permits.” The role of steric analogy in drug design is explained by Kobayashi in the context of bioisoteres: “As an established and powerful concept in medicinal chemistry, the application of bioisosteres will continue to play an important role in drug discovery. Isosterism can also contribute to the productive application in the design and optimization of catalysts on organic chemistry.”

Long before Papesch in the patent world, the real world of three dimensional chemistry had gone beyond patent law structural obviousness to consider the compound as a whole including a study of how a variation in substituent groups on a basic molecule could provide predictable variations in properties. Thus, while paper chemistry in the patent field focused on whether a two dimensional compound should be modified to make an adjacent homolog or position isomer, often a safe bet to gain a compound of similar properties, the real world of chemical research had made a shift to the three dimensional focus on the size and other steric properties of compounds and their properties to see how “steric analogs” behave.

---

15 Id.
C. Steric Analogy Case Law

As explained by Circuit Judge Lourie, “[b]ioisosterism refers to a process that involves replacing one atom or functional group in a molecule with another of similar chemical, physical, or electronic properties in hopes that the substitution will result in similar or enhanced activity.” Bioisosteres are explained in Argentum Pharmaceuticals LLC as substituents or groups that have chemical or physical similarities and which produce broadly similar biological properties. Bioisosterism is a lead modification approach that has been shown to be useful to attenuate toxicity or to modify the activity of a lead, and it may have a significant role in the alteration of metabolism of a lead [compound].

Buteau summarizes the impact of this development: “Analogs, homologs, and bioisosteres all bear some structural similarity to prior art compounds. However, whether they are obvious depends on the degree of predictability and ultimate allocation of their properties. The structural similarity of analogs, homologs, and bioisosteres to the prior art suggests that the compounds would possess similar properties, thereby satisfying the requirements for prima facie obviousness.” She concludes that “[w]hen analogs or bioisosteres exhibit

---

unexpectedly different properties from those of the prior art compound, the analogs or bioisosteres may be unobvious precisely because their structural similarity to the prior art would imply otherwise.”

In *In re Merck* Judge Davis explained that substitution of a ring nitrogen with an unsaturated carbon atom is prima facie obvious, where the motivation to make the substitution was “‘bioisosteric replacement’ or the theory of bioisosterism—where the substitution of one atom or group of atoms for another atom or group of atoms having similar size, shape and electron density provides molecules having the same type of biological activity.”

More completely Judge Davis provides context for this statement:

“The prior art taught that amitriptyline and imipramine are both psychotropic drugs which react on the central nervous system and which were known in the art prior to the time of appellant's invention. Imipramine was known to possess antidepressive properties in humans. While amitriptyline was known to possess psychotropic properties such as sedative and narcosis-potentiating properties, the drug was not known to be an antidepressant. However, the prior art has shown that imipramine and amitriptyline are unquestionably closely related in structure. Both compounds are tricyclic dibenzo compounds and differ structurally only in that the nitrogen atom located in the central ring of imipramine is interchanged with an unsaturated carbon atom in the central ring of amitriptyline. To show obviousness, it was necessary to determine from knowledge already available in the art at the time of appellant's invention that one skilled in the medicinal chemical art would have expected amitriptyline, like imipramine, to be useful in the treatment of depression in humans. *In re Papesch*, 315 F.2d 381 (CCPA 1963).

---

20 *Id.*

“As found by the Board, the Roche Reports recognized the structural relationship between amitriptyline and imipramine and concluded that amitriptyline should be tested for its antidepressant activities. In fact, the Roche Reports expressly stated that amitriptyline was expected to resemble imipramine clinically in its depression alleviation effects.

“‘Structural similarity, alone, may be sufficient to give rise to an expectation that compounds similar in structure will have similar properties.’ In re Payne, 606 F.2d 303, 313 (CCPA 1979). However, the Board did not rest its conclusion of obviousness on structural similarity alone. Rather, the Board further recognized that in attempting to predict the biological activities of a drug, a skilled medicinal chemist would not proceed randomly, but would base his attempts on the available knowledge of prior research techniques, and literature used in his field.

“The prior art showed that one such technique was bioisosteric replacement” or the theory of bioisosterism—where the substitution of one atom or group of atoms for another atom or group of atoms having similar size, shape and electron density provides molecules having the same type of biological activity. Finding that the Friedman, Burger and Petersen references taught that bioisosterism was commonly used by medicinal chemists prior to 1959 in an effort to design and predict drug activity, the Board concluded that one of ordinary skill in the arts would have been aware of this technique at the time of appellant's invention.

“We see no clear error in the Board's determination as to the teachings of the prior art references, in combination. In view of these teachings, which show a close structural similarity and a similar use (psychotropic drugs) between amitriptyline and imipramine, one of ordinary skill in the medicinal Further, the Board found that Petersen taught as bioisosteric the interchange of the nitrogen and unsaturated carbon atoms—the precise structural difference between imipramine and amitriptyline.chemical arts, possessed of the knowledge of the investigative techniques used in the field of drug design and pharmacological predictability,
would have expected amitriptyline to resemble imipramine in the alleviation of depression in humans. Accordingly, we agree with the Board that appellant’s invention was prima facie obvious over the prior art of record.”

Judge Fredman explains biosteric replacement in several cases. In the Torrens case he explains that “[b]ioisosteric replacement forms a rational medicinal chemistry approach for the discovery of new leads or series, based on existing key ligands. The three-dimensional structures of thiazoles, triazoles, and imidazoles maintain a high similarity to that of the pyrazole.” In the the Ryde case he points out that “[i]sosteres are atoms or functional groups of similar size and molecular orientation relative to each other.” Judge Smith in the Acey case, where the Board found the claimed fluoro substituted compound obvious over the corresponding hydrogen-substituted compound, explained that “[b]ioisosterism represents one approach used by the medicinal chemist for the rational modification of lead compounds into safer and more clinically effective agents” and that “[t]he substitution of hydrogen by fluorine is one of the more commonly employed monovalent isosteric replacements.”

22 In re Merck, 800 F.2d at 1096-97 (footnotes omitted).


In the *Park* case, Judge New explained that “the sole difference between the core structure of Wehr and that of the claims is the substitution of sulfur atoms (at the locations taught by Masakatsu) for oxygen atoms taught by examples 2 and 3 of Wehr. Furthermore, the Examiner finds, and Appellants do not contest, that both references teach these core structures are useful as semiconductor elements in electronic circuits.” Judge New then notes that:

King teaches, as a matter of general principle, that: “[i]sosteres are substituents or groups which have the same size or volume.” King 207. King also teaches that: “[b]ioisosteres ... are substituents or groups that do not necessarily have the same size or volume, but have a similarity in chemical or physical properties which produce broadly similar biological properties.” *Id.* King further teaches oxygen, sulfur, and methyl and amino groups are “[c]lassical isosteres which may function as bioisosteres” when acting as ring equivalents. King 208, Table 1.

Judge New concludes that:

Although we acknowledge Appellants' contention that King is primarily directed to medicinal chemistry, we agree with the Examiner that King teaches that isosteric substitution was broadly known in the organic chemistry arts. Moreover, King teaches not only that oxygen and sulfur are ring equivalents known to be “classical isosteres,” which we interpret to mean that they are broadly well-known in the art of organic chemical substitution as having “the same size or volume,” but also that these classical isosteres “have a similarity in chemical or physical properties,” because they may function as bioisosteres. *Id.* at 207. We agree with the Examiner that a person of ordinary skill would find it obvious to substitute sulfur atoms for oxygen atoms, as taught by the core structures of Wehr, positioned in the same location as taught by Masakatsu, and have a reasonable expectation that such a substitution would also successfully function as a semiconductor.

---

26 *Id.*
27 *Park*, slip op. at 4 (emphasis added).
28 *Id.*
One problem with reliance on isosteres is determining whether there is an isosteric relationship involved in a particular setting. This was involved in the Oda case, where it was “[t]he examiner's position is that a methylene group (Y) and the sulfur atom bridging the carbonyl group and the nitrogen ring in the Oida III compounds (formulae (V-VIII)) are known structural isosteres, i.e. the methylene group (Y) is interchangeable with the sulfur atom. The examiner relies on Mead Johnson v. Premo Pharmaceutical Labs, 207 USPQ 820 (D.N.J. 1980) to support his position.”

But, the matter was not so simple. The Board reversed the Examiner:

“We do not find in the record before us that the examiner has established that sulfur and methylene in the Oida III compounds are isosteres. Drawing a conclusion from the Mead case that sulfur and methylene are isosteres because evidence in Mead led the judge to conclude that oxygen and methylene are isosteres for compounds such as nylidrin and isoxsuprine without any further evidence is pure speculation. The examiner has not presented any evidence that sulfur and methylene isosterism is known in the art for the claimed compounds and that such interchange would have been considered to be within the skill of the art. The court in the Mead case based its decision on isosterism on evidence. Here the examiner has provided no such evidence. The examiner is in error in relying on the Mead case to establish isosterism rather than presenting scientific reasoning to show that Oida III's and appellants' compounds are isosteric compounds. In re Brouwer, 77 F.3d 422, 425 (Fed. Cir. 1996). Furthermore, the examiner's reliance in this case on In re Durden, 763 F.2d 1406 (Fed. Cir. 1985) and In re Albertson, 332 F.2d 379 (CCPA 1964) to support a conclusion of obviousness is also misplaced. See In re Ochiai, 71 F.3d 1565, 1569-72 (Fed. Cir. 1995).”


30 Id.
D. PTO Leadership Sub Silentio Repudiation of Steric Analogy

We have recently witnessed the leadership tenure of a Silicon Valley engineer-lawyer coming from the heart of the scientific leadership community of the United States. Now that she has retired from her leadership position, as a post mortem on the Office during her tenure, precisely what, if anything, has she said about the various steric analogy principles that apply to modern pharmaceutical patenting? Insofar as can be ascertained from the public record, the answer is nothing.

Absolutely nothing.

The Patent Office leadership in its Manual of Patent Examining Procedure never even mentions any of the words that can be used to describe a field of Steric analogy, where one refers to “isosterism”, “isostere”, “isosteric”, “classic isosterism”, “classic isostere”, “non-classical isosterism” “non-classical isosteres”, “bioisosterism”, “bioisostere” or “bioisostere”.
IV. STERIC ANALOGY UNDER THE 2011 PATENT LAW

The Leahy Smith America Invents Act of 2011 has new procedures available for third parties to introduce patent challenges keyed to steric analogy principles.

A. Inter Partes Vehicles to Introduce Steric Chemistry to the PTO

The Leahy Smith America Invents Act of 2011 now provides an excellent opportunity for third parties to participate in the examination process through a preissuance challenge available under the Leahy Smith America Invents Act of 2011. See Wegner, FIRST TO FILE DRAFTING: A PRACTITIONER’S GUIDE, § 2:30, Pre-Grant (Preissuance) Patentability Challenges (Thomson Reuters 2017). Under this new provision of the patent law, a third party may challenge the grant of claims during ex parte prosecution of a patent application without a fee and with presentation of arguments to deny patentability.

To be sure, there are two major reasons why this new procedure will not be used for important cases. First of all, if there is a challenge to a claimed invention that can be overcome by amendment of the claims, the amended claims that issue as patent will not be subject to “intervening rights”. This is a serious drawback to challenging a patent before grant under the preissuance challenge procedure. (In contrast, a Post Grant Review or Inter Partes Review that takes place after grant subjects the amended claims to what may be effective evisceration of patent rights because new or amended claims in a PGR or IPR are subject to statutory “intervening rights.”)
Secondly, there is no *inter partes* participation for the third party challenger, beyond his original pleading.

While preissuance challenges may find only limited applicability to challenge patents valuable to a company, there are distinct advantages for a test cae. Given that this proceeding may be filed “blind” by a strawman, without fee and without participation beyond the initial pleading, this provides an excellent opportunity for a third party to help shape the law to introduce the use of steric analogy chemistry into the examination practice.

**B. Post Grant Review (PGR) vs. Generic Claims**

Where the sole objective of a third party is to destroy the viability of the generic “claim 1” a Post Grant Review, the “PGR”, represents a viable option to use steric analogy chemistry. Provided there is a “printed publication” detailing the relevant steric analogy relationship, the patent challenger may have a full blown *inter partes* proceeding to knock out “claim 1”, all the way through the Patent Office and up to the Federal Circuit. Even if an amended claim 1 is maintained in the patent, the challenger may still benefit from statutory “intervening rights” that will not block his continued commercialization of the compound.

(If “claim 15” is to a commercial species that is the object of the commercial controversy with the patentee, this procedure to knock out “claim 1” may be problematic.)
V. CONCLUSION

It is no longer a question whether the Patent Office leadership will integrate steric analogy principles into the examination system, it is only a question of when this will happen.

Thus, no matter what the new leadership of the PTO decides to do about steric analogy principles, it is inevitable that the dam will be broken through patent challenges under the Leahy Smith America Invents Act of 2011 that will reach the Patent Trial and Appeal Board. That portion of the patent community that puts its head in the sand to ignore the advent of steric chemistry principles as central to prima facie obviousness of pharmaceutical products fails to properly represent the inventive community.
About the Author

Prof. Wegner’s practice includes expert opinions; he develops strategies on complex claim drafting and prosecution matters at the Examiner level and at the Board; and he has been involved with appeals at the Federal Circuit.

Professor Wegner’s professional roots are in chemical patents, and particularly pharmaceuticals. After receiving a degree in chemistry from Northwestern University he spent four years as a Patent Examiner focused on claims to new compounds, and thereafter spent many years in private practice where his principal specialty was in pharmaceuticals.

Prof. Wegner has recently published the treatise:


The work is now also available electronically on Westlaw.

Prof. Wegner is President Emeritus of The Naples Roundtable, Inc., a 501(c)3 nonprofit corporation dedicated to “finding ways to strengthen and improve the patent system.” thenaplesroundtable.org/

business address:

Harold C. Wegner
Suite 300
1101 Pennsylvania Ave N.W.
Washington D.C. 20004
(202) 756-1084

hwegner@gmail.com