This black-letter patent law has also specifically been applied by the PTO's Board of Patent Appeals and Interferences in holding that claims in pending applications directed to specific fragments of a disclosed protein are not supported by a specification disclosing a genus encompassing those fragments. For example, in *Forssmann v. Matsuo*, the patentee sought to rely upon a parent application directed to a 126 amino acid hormone "cardiodilatin" to support a claim to a specific fragment of that protein (the fragment containing amino acids 99-126).

The parent application disclosed that (i) fragments of the peptide could be therapeutically useful; (ii) at least two cleavage methods could be used to prepare such fragments; and (iii) at least 20 such fragments (including the 99-126 fragment). The parent application also included an original claim directed to such fragments.[15]

The *Forssmann* court held that despite this extensive disclosure of the genus of potential peptide fragments, a claim to the 99-126 fragment was not supported by the specification's description of a larger peptide fragment embracing the 28 amino acid sequence of claim 28 because the specification did not provide any direction to that specific fragment nor did it "indicate any recognition by the inventor of this specific sequence."[16]

At the July 28 hearing, Defendants pointed to certain language in Amgen's specification as purportedly providing written support for a claim to 165 human EPO.[17] But the specification only speaks of generic "fragments" of EPO or "DNA sequences encoding part or all of" the EPO sequence. Such references to a genus of fragments or to DNA sequences of different lengths

[15] *Forssmann v. Matsuo*, 23 U.S.P.Q.2d 1548, 1550 (Bd. Pat. App. & Int. 1992).

[16] *Id.* at 1552. *See also Yamada v. Aggarwal*, 57 U.S.P.Q.2d 2002 (Bd. Pat. App. & Int. 2000).

[17] *See* 7/28/03 Hearing Transcript at p. 98, line 19 to 99, line 2.

cannot constitute "blazemarks" pointing to the particular 165 amino acid EPO equivalent in question here, and therefore could not support a claim specifically to such a species.

Consequently, although Amgen's specification provides written support for broader claims drawn to EPO glycoproteins and generically to fragments,[18] Amgen could not reasonably be expected to have described, or drafted a claim to, an EPO composition having only the 1-165 amino acid sequence of Figure 6, *i.e.*, the "particular equivalent" and "insubstantial substitute" in question here.[19]

Defendants argue that Amgen cannot rebut the presumption of estoppel unless it shows that it could not have drafted a claim that encompasses 165 human EPO. As Amgen has explained, the dispositive issue is not whether Amgen could have drafted ***any*** claim that would cover 165 human EPO. If that were the dispositive issue, the Federal Circuit would not have remanded the issue of rebuttal for decision by this Court. As this Court previously found and the Federal Circuit affirmed, Amgen drafted another claim that encompasses Defendants' 165 amino acid EPO product (claim 1 of the '422 patent). If the only question was whether Amgen could

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[18] *See, e.g., Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.*, 93 F.3d 1572, 1582, fn. 7 (Fed. Cir. 1996) ("[T]he district court confused a claim not supported by the specification, which is not allowable, with a broad claim, which is. Claim 1 was properly rejected because it *recited* an element not supported by Fox's disclosure, i.e., a lockout 'on the stapler.' It does not follow, however, that Fox's disclosure could not support claims sufficiently broad to read on a lockout off of the cartridge. *See, e.g., In re Vickers*, 141 F.2d 522, 525 (C.C.P.A. 1944) ('an applicant . . . is generally allowed claims, when the art permits, *which cover more than the specific embodiment shown.*"). If Fox did not consider the precise location of the lockout to be an element of his invention, he was free to draft claim 24 broadly . . . .") and *Application of Smith*, 458 F.2d 1389, 1395 (C.C.P.A. 1972) ("We see nothing inherently wrong with a particular principle of patentability which under certain circumstances operates to defeat the patentability of a narrow, but not a broader, claim, and, ordinarily, the mere fact that under such a principle a broader claim would pass muster is not a basis for adjusting the principle to render the narrower claim patentable.")

[19] *Festo*, 535 U.S. at 740-41.

have drafted a claim that encompassed 165 human EPO, the Federal Circuit would have held that Amgen had already done so in '422 claim 1 and therefore could not rebut the presumption.

Rather, the relevant inquiry is whether Amgen could have literally claimed mature human EPO having the specific 1-165 amino acid sequence of Figure 6. That is the "particular equivalent" and "insubstantial substitute" to which the Supreme Court's *Festo* standards are directed. As demonstrated above, Amgen could not have claimed that particular equivalent at the time of its amendment. Even though 165 human EPO was inherently produced in Example 10, it was not expressly recited as being Amgen's invention in the '080 patent specification. Moreover, as shown below, simply because Amgen could have sought broader claims that literally "encompassed" 165 human EPO, and did in fact do so in the '422 patent, does not foreclose equivalents to the '080 claims because the amendment was made for an unrelated purpose and did not distinguish 165 human EPO from 166 human EPO.

B. The rationale underlying Amgen's amendment was not related to the particular equivalent in question

Amgen can also rebut the presumption of estoppel by showing that the rationale underlying its amendment bears "no more than a tangential relation to the equivalent in question."[20] As explained in Amgen's motion papers and at the July 28 hearing, Amgen has rebutted the presumption under this second prong of *Festo* because the rationale underlying Amgen's amendment, which was to avoid any double-patenting between its '080 claims and the claims of its then-recently issued '933 patent, was not even tangentially related to the particular "equivalent in question" (HMR 4396, a 165 human EPO product).

Defendants cannot dispute the following facts:

[20] *Festo*, 535 U.S. at 740.

(1) There was no prior art disclosing the sequence of 165 human EPO, and thus no need for Amgen to distinguish its claims over any such equivalent;[21]

(2) Claim 1 of the '933 patent encompasses both human and non-human EPO,[22] whereas the amended '080 claims are limited to human EPO;

(3) Amgen voluntarily added the limitation "comprises the mature erythropoietin amino acid sequence of Figure 6" to each of the asserted claims of the '080 patent to distinguish those claims from claim 1 of its '933 patent;

(4) Amgen did not make the amendments in response to any rejection, objection, or observation by the patent examiner;[23]

(5) Amgen told the Patent Office that it amended its '080 claims to distinguish those claims from claim 1 of the '933 patent in "specifying that the claimed subject matter [of the new '080 claims] comprises the mature ***human*** erythropoietin sequence of Figure 6";[24]

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[21] As Amgen explained in its remarks accompanying its amendment, to the extent it needed to distinguish prior-art human urinary EPO, it did so by including limitations directed to differences in glycosylation or isolation from human urine. *See* Amgen's Motion App. Tab C (Trial Ex. 2005) (December 20, 1996 Third Preliminary Amendment) at p. 9 ("Claim 69 (like ['933] glycoprotein claim 1) recites carbohydrate differences in comparison to human urinary erythropoietin and claim 70 recites a negative limitation with respect to isolation from human urine.").

[22] *See, e.g.*, Amgen's Motion App. Tab D (Trial Ex. 2035 at col. 10:65-11:2; col. 38:17-21, Figure 5 (disclosing monkey EPO cDNA and amino acid sequences), and Figure 6 (disclosing human EPO genomic DNA and the deduced amino acid sequences)).

[23] *Amgen Inc. v. Hoechst Marion Roussel, Inc. and Transkaryotic Therapies, Inc.*, 126 F. Supp. 2d 69, 135 (D. Mass. 2001), *aff'd in part, vacated in part*, 314 F.3d 1313, 1345 (Fed. Cir. 2003). *See also* 7/31/03 Hearing Transcript at p. 77, lines 1-8.

[24] Amgen's Motion App. Tab C (Trial Ex. 2005) (December 20, 1996 Third Preliminary Amendment) at 9 (emphasis added). *See also* 7/31/03 Hearing Transcript at p. 77.

(6) In doing so, Amgen further explained to the Patent Office that glycosylation and source limitations, not the Figure 6 sequence limitation, distinguished the EPO of its amended '080 claims from human urinary EPO;[25] and

(7) Human urinary EPO has the 1-165 amino acid sequence of Figure 6.[26]

Nevertheless, Defendants argue that Amgen could not have intended its amendment to distinguish the human erythropoietin of the amended '080 claims from the human and non-human erythropoietins of '933 claim 1 because the "original" '080 claims contained the word "human."[27] But that argument is contradicted by the fact that at the time Amgen made its amendment, the pending '080 claims were ***not*** limited to human EPO.

When the application which issued as the '080 patent was filed, it contained 60 claims.[28] None of the originally claimed EPO protein products in that group of 60 was limited to "human" EPO. In a Preliminary Amendment submitted with that application, those original 60 claims were canceled, and new claims 61-67 were added.[29] Some of these new claims (claims 61-63) were directed to "an isolated human erythropoietin glycoprotein product."[30] But in a second

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[25] *See* Amgen's Motion App. Tab C (Trial Ex. 2005) (December 20, 1996 Third Preliminary Amendment) at p. 9.

[26] *See, e.g.*, Trial Ex. 53 (Recny *et al.* (1987)) at 17156 ("Structural characterization of natural human urinary EPO (uEPO) . . . reveals that the urinary hormone is also missing the COOH-terminal Arg^{166} amino acid residue, a modification that remained undetected until now.") Amgen disclosed the Recny *et al.* reference to the Patent Office during prosecution (*see* Trial Ex. 3, Tab 3 at p. 140), and it is cited in the '080 patent disclosure as a reference reviewed by the Examiner. *See* Trial Ex. 3 ('080 patent), p. 8.

[27] *See, e.g.*, Defs. Opp. Br. at 8-9.

[28] *See* Trial Ex. 3, Tab 1 at 99-107.

[29] *See* TKT/HMR App. Tab E (June 6, 1995 Preliminary Amendment).

[30] *Id.*