EXHIBIT D

ROCHE'S STATEMENT OF LEGAL STANDARDS AND BURDENS OF PROOF[1]

1. Whether any of the asserted claims of Amgen's patents[2] are invalid as anticipated under 35 U.S.C. § 102(a), (b), and/or (e) by any prior art reference or use.

2. Whether any of the asserted claims of Amgen's patents are invalid under 35 U.S.C. § 102(g) due to prior invention by another.

3. Whether any of the asserted claims of Amgen's patents are invalid under 35 U.S.C. § 103 because the claimed subject matter would have been obvious to one of ordinary skill in the art at the time of invention.

4. Whether any secondary considerations of non-obviousness are sufficient to overcome a conclusion of obviousness under 35 U.S.C. § 103 with respect to any of the asserted claims of Amgen's patents.

5. Whether any of the asserted claims of Amgen's patents are invalid under 35 U.S.C. § 102(f) in combination with 35 U.S.C. § 103 because Dr. Lin derived enough of the subject matter of the claimed invention to render it obvious.

6. Whether any of the asserted claims of Amgen's patents are invalid for failure to comply with the written description requirement of 35 U.S.C. § 112, ¶1.

7. Whether any of the asserted claims of Amgen's patents are invalid for lack of enablement under 35 U.S.C. § 112, ¶1.

8. Whether any of the asserted claims of Amgen's patents are invalid for indefiniteness under 35 U.S.C. § 112, ¶2.

9. Whether any of the asserted claims of Amgen's patents are invalid for same invention type double patenting. 35 U.S.C. § 101.

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[1] To the extent any of the issues of law in the case are impacted or affected by the Court's claim construction, Roche respectfully reserves its objections to these constructions, which may be provided as a glossary to the jury during the trial, and further reserves the right to raise arguments at the time that this Court entertains proposed jury instructions and, if necessary, on appeal. Roche's objections are to the extent the Court's construction did not adopt and apply Roche's positions and a statement regarding Roche's objections is included separately as Section VI.B.3 to this Joint Pretrial Memorandum.

[2] As used herein, the "asserted claims" of Amgen's patents includes all the claims that are the subject of Roche's pleaded counterclaims of invalidity, including claims 4 and 5 of the '698 patent.

By agreement of the parties, this preliminary statement of issues of law may be modified, supplemented and/or amended, up to and including the time of final submission to the Court or thereafter should additional relevant evidence arise.

10. Whether any of the asserted claims of Amgen's patents are invalid for obviousness type double patenting. *In re Longi*, 759 F.2d 887 (Fed. Cir. 1985).

11. Whether any of the asserted claims of Amgen's patents are protected from obviousness-type double patenting under 35 U.S.C. § 121.

12. Whether a one-way test or two-way test applies for determining obviousness type double patenting of any of the claims of Amgen's asserted patents in view of any other commonly owned Amgen patent claims. *In re Berg*, 140 F.3d 1428, 1435-37 (Fed. Cir. 1998).

13. Whether any of the claims of Amgen's asserted patents are invalid and/or expired pursuant to 35 U.S.C. § 103(b).

14. Whether MIRCERA™, if sold or offered for sale in the United States, literally infringes any of the asserted claims of Amgen's '422, '933, '868, '698 and/or '349 patent(s). 35 U.S.C. §271(a); *Cybor Corp. v. FAS Tech., Inc.*, 138 F.3d 1448, 1454 (Fed. Cir. 1998) (en banc).

15. Whether MIRCERA™ if sold or offered for sale in the United States, infringes any of the asserted claims of Amgen's '422, '933, '868, '698 and/or '349 patent(s) under the doctrine of equivalents. 35 U.S.C. §271(a); *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 24-25 (1997).

16. Whether Amgen is precluded by the doctrine of prosecution history estoppel from asserting infringement of any of the asserted claims of the '422, '933, '868, '698 and/or '349 patent(s) under the doctrine of equivalents. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 733-35 (2002).

17. Whether CERA does not infringe the asserted claims of the '868, '698 and/or '349 patent(s) because it is materially changed by subsequent processes. 35 U.S.C. §271(g)(1); *See Eli Lilly & Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1572 (Fed. Cir. 1996).

18. Whether MIRCERA™ does not infringe the asserted claims of the '868, '698 and/or '349 patent(s) because it is materially changed by subsequent processes. 35 U.S.C. §271(g)(1); *See Eli Lilly & Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1572 (Fed. Cir. 1996).

19. Whether the reverse doctrine of equivalents applies to MIRCERA™ with respect to the asserted claims of the '422, '933, '868, '698 and/or '349 patent(s). *Texas Instruments, Inc. v. U.S. Int'l Trade Comm.*, 846 F.2d 1369, 1371-72 (Fed. Cir. 1988).

By agreement of the parties, this preliminary statement of issues of law may be modified, supplemented and/or amended, up to and including the time of final submission to the Court or thereafter should additional relevant evidence arise.

20. Whether Roche's current activities in the United States with respect to MIRCERA™ are exempt from infringement. 35 U.S.C. §271(e)(1).

21. Whether Roche will make any use of MIRCERA™, if approved by the FDA, that will directly infringe the asserted method claims of the '933 patent.

22. Whether Roche actively induces infringement of the asserted method claims of the '933 patent. 35 U.S.C. § 271(b).

23. Whether anyone at Amgen or acting on Amgen's behalf owing a duty of candor to the United States Patent Office, misrepresented, buried or omitted material information with an intent to deceive the examiner, with respect to the prosecution of any of the patents-in-suit or any related patents. 37 CFR 1.56; *eSpeed Inc. v. BrokerTec USA LLC*, 480 F.3d 1129 (Fed. Cir. 2007).

24. Whether as a result of inequitable conduct the patents-in-suit are unenforceable. *Kingsdown Med. Consultants, Lt. v. Hollister Inc.*, 863 F.2d 867, 877 (Fed. Cir. 1988).

25. Whether as a result of inequitable conduct the patents-in-suit are unenforceable under the doctrine of infectious unenforceability. *Agfa Corp. v. Creo Prods. Inc.*, 451 F.3d 1366, 1379 (Fed. Cir. 2006); *Fox Indus., Inc. v. Structural Preservation Sys., Inc.*, 922 F.2d 801, 803 (Fed. Cir. 1990).

Roche reserves the right to supplement this filing to address Amgen's antitrust violations and Amgen's lack of entitlement to an injunction prior to the trial of those issues.

I. Invalidity for Prior Art

A. Source Limitations

26. "A claimed product shown to be present in the prior art cannot be rendered patentable solely by the addition of source or process limitations." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 n.20 (Fed. Cir. 2003).

27. "[A] patentee who does not distinguish his product from what is old except by reference, express or constructive, to the process by which he produced it, cannot secure a monopoly on the product by whatever means produced." *General Elec. Co. v. Wabash Appliance Corp.*, 304 U.S. 364, 373 (1938).

28. A source limitation must confer a distinctive character and use as compared to a product occurring in nature. *See Diamond v. Chakrabarty*, 447 U.S. 303, 309-10 (1980).

B. Critical Date for Prior Art

29. A patentee "would bear a burden of production to present evidence of its asserted actual reduction to practice prior to the filing date of its patent application" to establish an invention date earlier than asserted prior art. *Loral Fairchild Corp. v. Matsushita Elec.*, 266 F.3d 1358, 1361 (Fed. Cir. 2001)

C. Invalidity under 35 U.S.C. § 102

30. "A claim is anticipated under 35 U.S.C. § 102 'if each and every limitation is found either expressly or inherently in a single prior art reference.'" *IPXL Holdings, LLC. v. Amazon.com, Inc.*, 430 F.3d 1377, 1381 (Fed. Cir. 2005), (*quoting Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1373 (Fed. Cir. 2001)).

31. "[A] patent may be found to be anticipated on the basis of a reference that had properly been before the patent examiner in the United States Patent and Trademark Office ('PTO') at the time of issuance." *IPXL Holdings, LLC. v. Amazon.com, Inc.*, 430 F.3d 1377, 1381 (Fed. Cir. 2005).

32. The presumption of validity of a patent is weakened when considering prior art that was not before the examiner because "the rationale underlying the presumption -- that the PTO, in its expertise, has approved the claim" is diminished. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1745 (2007).

33. "'[N]otwithstanding abandonment of the prior use-which may preclude a challenge under section 102(g)-prior knowledge or use by others may invalidate a patent under section 102(a) if the prior knowledge or use was accessible to the public.'" *Eolas Tech. Inc. v. Microsoft Corp.*, 399 F.3d 1325, 1334 (Fed Cir. 2005), (*quoting Woodland Trust v. Flowertree Nursery*, 148 F.3d 1368, 1370 (Fed. Cir. 1998)).

34. "[T]hird party prior use accessible to the public is a section 102(b) bar." *Eolas Tech. Inc. v. Microsoft Corp.*, 399 F.3d 1325, 1334 (Fed Cir. 2005).

35. "Regardless of how broadly or narrowly one construes a product-by-process claim, it is clear that such claims are always to a product, not a process. It has long been established that one cannot avoid anticipation by an earlier product disclosure by claiming the same product more narrowly, that is, by claiming the product as produced by a particular process." *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1317 (Fed. Cir. 2006).

36. "'[I]f a patentee's invention has been made by another, prior inventor who has not abandoned, suppressed, or concealed the invention, § 102(g) will invalidate that patent.'" *Dow Chem. Co. v. Astro-Valcour, Inc.*, 267 F.3d 1334, 1339 (Fed. Cir. 2001), (*quoting Apotex USA, Inc. v. Merck & Co.*, 254 F.3d 1031, 1035 (Fed. Cir. 2001)).

37. A determination that a patent is invalid for prior invention under 35 U.S.C. § 102(g) requires a showing of either prior reduction to practice or prior conception coupled with reasonable diligence in reducing the invention to practice. *See Mycogen Plant Sci. v. Monsanto Co.*, 243 F.3d 1316, 1332 (Fed. Cir. 2001).

38. Conception is the "formation, in the mind of the inventor of a definite and permanent idea of the complete and operative invention, as it is thereafter to be applied in practice..." *Coleman v. Dines*, 754 F.2d 353, 359 (Fed. Cir. 1985).

39. "An invention is reduced to practice when the patentee has an embodiment that meets every limitation and operates for its intended purpose. An invention works for its intended purpose when there is a demonstration of the workability or utility of the claimed invention." *Honeywell Intern. Inc. v. Universal Avionics Systems Corp.*, 488 F.3d 982, 997 (Fed. Cir. 2007) (internal citations omitted).

40. "[T]he challenger of the validity of a patent must establish prior invention by clear and convincing evidence. If the challenger does so, the burden of production shifts to the patentee to produce evidence sufficient to create a genuine issue of material fact as to whether the prior inventor abandoned, suppressed, or concealed the invention. If the patentee carries this burden of production, the challenger may rebut the evidence of abandonment, suppression, or concealment, with clear and convincing evidence to the contrary." *Dow Chem. Co. v. Astro-Valcour, Inc.*, 267 F.3d 1334, 1339 (Fed. Cir. 2001) (*quoting Apotex USA, Inc. v. Merck & Co.*, 254 F.3d 1031, 1037-38 (Fed. Cir. 2001)).

41. Prior holdings and findings preclude Amgen from arguing that the EPO products claimed in the patents-in-suit differ structurally from naturally-occurring EPO. For issue preclusion to apply, the following requirements must be met: (1) both proceedings involved the same issue of law or fact; (2) the parties actually litigated the issue in the prior proceeding; (3) the first court actually resolved the issue in a final and binding judgment; and (4) its resolution of that issue of law or fact was essential to its judgment. *See Global Naps, Inc. v. Mass. Dept. of Telecomm. and Energy*, 427 F.3d 34, 44 (1st Cir. 2005).

42. Collateral estoppel or issue preclusion may apply to claims of a patent not litigated in the prior determination. "It is the issues litigated, not the specific claims around which the issues were framed, that is determinative." *See Westwood Chemical, Inc. v. U. S.*, 525 F.2d 1367, 1372, 207 Ct.Cl. 791 (1975), *see also South Corp. v. United States*, 690 F. 2d 1368 (Fed. Cir. 1982) (adopting the decisions of predecessor courts including the United States Court of Claims and the United States Court of Customs and Patent Appeals, as binding precedent).

43. "In determining the applicability of the estoppel, the first consideration is 'whether the issue of invalidity common to each action is substantially identical.'"

Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1136 (Fed. Cir. 1985) (citing *Carter-Wallace, Inc. v. United States*, 496 F.2d 535, 538, 204 Ct.Cl. 341, 182 USPQ 172, 175 (1974)).

D. Obviousness under 35 U.S.C. § 103

44. Pursuant to 35 U.S.C. § 103 "[a] claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the pertinent art." *In re Kahn*, 441 F.3d 977, 985 (Fed. Cir. 2006).

45. "[O]bviousness depends on (1) the scope and content of the prior art; (2) the differences between the claimed invention and the prior art; (3) the level of ordinary skill in the art; and (4) any relevant secondary considerations, including commercial success, long felt but unsolved needs, and failure of others. *Dystar Textilfarben GmbH &Co Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1360 (Fed. Cir. 2006) (*citing Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)).

46. Where all the limitations of a claim are found in a number of prior art references, the fact-finder must consider "whether a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and whether there would have been a reasonable expectation of success in doing so." *See Dystar Textilfarben GmbH &Co Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1360 (Fed. Cir. 2006) (*citing Brown & Williamson Tobacco Corp. v. Philip Morris, Inc.*, 229 F.3d 1120, 1124 (Fed. Cir. 2000)).

47. "[T]here is no requirement that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art" *Dystar Textilfarben GmbH &Co Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1361 (Fed. Cir. 2006) (*quoting Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1472 (Fed. Cir. 1997).

48. Motivation to combine prior art references for purposes of § 103 "need not be found in the references sought to be combined, but may be found in any number of sources, including common knowledge, the prior art as a whole, or the nature of the problem itself." *See Dystar Textilfarben GmbH &Co Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1361 (Fed. Cir. 2006) (*citing In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999)).

49. "[O]bviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007); (*citing In re Corkill*, 771 F.2d 1496, 1500 (Fed. Cir. 1985); *Brown & Williamson*

Tobacco Corp. v. Philip Morris Inc., 229 F.3d 1120, 1125 (Fed. Cir. 2000); *Merck & Co., Inc. v. Biocraft Labs., Inc.*, 874 F.2d 804, 809 (Fed. Cir. 1989); *In re Merck & Co., Inc.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986).

50. Many techniques that require extensive time, money, and effort to carry out may nevertheless be arguably routine to one of ordinary skill in the art and do not equate to a conclusion that an expectation of success was unlikely. *See Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1367-68 (Fed. Cir. 2007); *Velander v. Garner*, 348 F.3d 1359, 1368 (Fed. Cir. 2003).

51. "Obviousness does not require absolute predictability of success. Indeed, for many inventions that seem quite obvious, there is no absolute predictability of success until the invention is reduced to practice. There is always at least a possibility of unexpected results, that would then provide an objective basis for showing that the invention, although apparently obvious, was in law nonobvious. For obviousness under § 103, all that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903-904 (Fed. Cir. 1988) (internal citations omitted) (citing *In re Longi*, 759 F.2d 887, 897 (Fed. Cir. 1985); *In re Clinton*, 527 F.2d 1226, 1228 (CCPA 1976)); *see also In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986).

52. There is flexibility in the obviousness inquiry "because a motivation may be found implicitly in the prior art." *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286, 1291 (Fed. Cir. 2006).

53. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1739 (2007); *see also Leapfrog Enterprises, Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1161 (Fed. Cir. 2007).

54. "[W]hen a patent 'simply arranges old elements with each performing the same function it had been known to perform' and yields no more than one would expect from such an arrangement, the combination is obvious" *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. Ag Pro, Inc.*, 425 U.S. 273, 282 (1976)).

55. "When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007).

56. In a determination of whether a claimed invention is obvious it is proper to consider "interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background

knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740-41 (2007).

57. "A person of ordinary skill is also a person of ordinary creativity, not an automaton." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1742 (2007).

58. The consideration of whether a teaching, suggestion or motivation to combine prior art elements existed should not be rigidly applied. "The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents. The diversity of inventive pursuits and of modern technology counsels against limiting the analysis in this way. In many fields it may be that there is little discussion of obvious techniques or combinations, and it often may be the case that market demand, rather than scientific literature, will drive design trends." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007).

59. "In determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls. What matters is the objective reach of the claim. If the claim extends to what is obvious, it is invalid under § 103. One of the ways in which a patent's subject matter can be proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741-42 (2007).

60. It is erroneous to "look only to the problem the patentee was trying to solve. ...[T]he problem motivating the patentee may be only one of many addressed by the patent's subject matter. The question is not whether the combination was obvious to the patentee but whether the combination was obvious to a person with ordinary skill in the art. Under the correct analysis, any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1742 (2007).

61. It is erroneous to assume " a person of ordinary skill attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1742 (2007).

62. "Common sense teaches ... that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able

to fit the teachings of multiple patents together like pieces of a puzzle." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1742 (2007).

63. A patent claim may be proved obvious under §103 by showing that a particular combination of elements was obvious to try. For example, "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1742 (2007).

64. "Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, [for] patents combining previously known elements, deprive prior inventions of their value or utility." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007).

65. "[T]he results of ordinary innovation are not the subject of exclusive rights under the patent laws." *KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1746 (2007).

66. "Scientific confirmation of what was already believed to be true may be a valuable contribution, but it does not give rise to a patentable invention. Good science and useful contributions do not necessarily result in patentability." *PharmaStem Therapeutics, Inc. v. Viacell, Inc.*, 2007 WL 1964863, *19 (Fed. Cir. 2007) (internal citations omitted) (*citing KSR Intern. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1732 (2007); *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1367-69 (Fed.Cir.2007); *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed.Cir.1986)).

67. Evidence of obviousness of a patent may be found in that patent's characterization of the prior art. "Admissions in the specification regarding the prior art are binding on the patentee for purposes of a later inquiry into obviousness." *PharmaStem Therapeutics, Inc. v. Viacell, Inc.*, 2007 WL 1964863, *17 (Fed. Cir. 2007); (citing *Constant v. Advanced Micro Devices, Inc.*, 848 F.2d 1560, 1570 (Fed. Cir. 1988); *Sjolund v. Musland*, 847 F.2d 1573, 1577-79 (Fed. Cir. 1988); *In re Fout*, 675 F.2d 297, 300 (CCPA 1982); *In re Nomiya*, 509 F.2d 566, 571 (CCPA 1975)).

68. In the context of method of treatment claims, "providing proof sufficient to justify conducting in vivo procedures on humans, while useful, is not a test of patentability" under § 103. *PharmaStem Therapeutics, Inc. v. Viacell, Inc.*, 2007 WL 1964863, *20 (Fed. Cir. 2007).

69. In the context of secondary considerations of non-obviousness, praise by others for the inventors' work must be directly tied to an actual inventive contribution

rather than confirmation of what the state of knowledge in the art was already indicating. "The former is a basis for patentability; the latter is not." *PharmaStem Therapeutics, Inc. v. Viacell, Inc*., 2007 WL 1964863, *20 (Fed. Cir. 2007).

70. Simultaneous or near simultaneous invention by others of the patented subject matter is a secondary consideration favoring obviousness. *See Ecolochem, Inc. v. Southern California Edison Co.*, 227 F.3d 1361, 1379 (Fed. Cir. 2000); *Monarch Knitting Machinery Corp. v. Sulzer Morat GMBH*, 139 F.3d 877, 883-84 (Fed. Cir. 1998); *Ortho-McNeil Pharm., Inc. v. Mylan Labs, Inc.*, 348 F. Supp. 2d 713, 757-58 (N.D. W. Va. 2004); *Northern Telecom, Inc. v. Datapoint Corp.*, 1988 WL 156280, *60 (N.D. Tex. 1988); *Minnesota Mining and Manuf. Co. v. Research Med., Inc.*, 679 F. Supp. 1037, 1056 (D. Utah 1987) ("Just as evidence of nonobviousness may be inferred from the failure of others to find a solution to a problem, evidence of obviousness can be inferred from the success of others."); *Reed Tool Co. v. Dresser Indus., Inc.*, 499 F. Supp. 935, 945 (S.D. Tex. 1980); *Clarke v. K-Mart*, 481 F. Supp. 470, 473 (W.D. Pa. 1979); *Schimizzi v. Chrysler Corp.*, 462 F. Supp. 630, 639 (S.D.N.Y. 1978); *Reeves Bros., Inc. v. U.S. Laminating Corp.*, 282 F. Supp. 118, 140 (E.D.N.Y. 1968).

71. "Objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983).

72. In order to overcome a conclusion of obviousness, a patentee must demonstrate a "nexus between merits of invention and evidence of secondary considerations." *Pfaff v. Wells Electronics, Inc.*, 124 F.3d 1429, 1439 (Fed. Cir. 1997).

73. The presumption of validity of a patent is weakened when considering prior art that was not before the examiner because "the rationale underlying the presumption -- that the PTO, in its expertise, has approved the claim" is diminished. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1745 (2007).

74. "A single, obvious species within a claimed genus renders the claimed genus unpatentable under § 103." Thus an obvious method of obtaining a single nucleic acid sequence may be all that is required to show that a particular genus of nucleic acids is unpatentable under § 103. *Ex Parte Kubin*, Appeal 2007-0819, Slip Op. at 7 (B.P.A.I. 2007).

75. "[T]he Supreme Court recently cast doubt on the viability of *Deuel* [*In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995)] to the extent the Federal Circuit rejected an 'obvious to try' test. Under *KSR*, it's now apparent 'obvious to try' may be an appropriate test in more situations than ... previously contemplated." *Ex Parte Kubin*, Appeal 2007-0819, Slip Op. at 8 (B.P.A.I. 2007).

76. Where the problem facing those in the art is to isolate a particular DNA sequence and there are a limited number of methodologies available to do so, the skilled artisan would have reason to try these methodologies with the reasonable expectation that at least one would be successful, and a method to isolate that DNA sequence is thus not patentable under § 103. *See Ex Parte Kubin*, Appeal 2007-0819, Slip Op. at 9 (B.P.A.I. 2007).

77. In light of the Supreme Court's *KSR* decision the "teaching, suggestion, or motivation" test could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a) but the rigid application of the teaching, suggestion or motivation test has been repudiated. USPTO, May 3, 2007 Memorandum from Deputy Commissioner for Patent Operations Margaret A. Focarino to Technology Center Directors.

78. "[S]ubject matter derived from another not only is itself unpatentable to the party who derived it under § 102(f), but, when combined with other prior art, may make a resulting obvious invention unpatentable to that party under a combination of § § 102(f) and 103." *Oddzon Products, Inc. v. Just Toys, Inc.*, 122 F.3d 1396, 1403-04 (Fed. Cir. 1997).

79. "To invalidate a patent for derivation of invention, [under 102(f)] a party must demonstrate that the named inventor in the patent acquired knowledge of the claimed invention from another, or at least so much of the claimed invention as would have made it obvious to one of ordinary skill in the art." *New England Braiding Co., Inc. v. A.W. Chesterton Co.*, 970 F.2d 878, 883 (Fed. Cir. 1992).

80. "[T]o show derivation under §102(f), 'the party asserting invalidity must prove both prior conception of the invention by another and communication of that conception to the patentee.' . . . Yet, there is no corresponding requirement . . . that the requisite 'communication' for purposes of invalidity by derivation under §102(f) take place in any particular form or that it occur directly between the prior inventor and the patentee." *Synthon IP, Inc. v. Pfizer Inc.*, 2007 WL 1075194, *3 (E.D. Va. 2007) (internal citations omitted).

81. 102(f) "mandates that a patent accurately list the correct inventors of a claimed invention[.] . . . Accordingly, if nonjoinder of an actual inventor is proved by clear and convincing evidence, . . . a patent is rendered invalid." *Pannu v. Iolab Corp.*, 155 F.3d 1344, 1349 (Fed. Cir. 1998) (internal citations omitted).

82. "Promising to pay royalties on patents [pursuant to a license agreement] that have not been held invalid does not amount to a promise not to seek a holding of their invalidity." *MedImmune Inc. v. Genentech, Inc.*, 127 S. Ct. 764, 776 (2007).

83. A licensee is not required "to break or terminate its . . . license agreement before seeking a declaratory judgment in federal court that the underlying patent is

invalid, unenforceable, or not infringed." *MedImmune Inc. v. Genentech, Inc.*, 127 S. Ct. 764, 777 (2007).

II. Invalidity under 35 U.S.C. § 112

A. Written Description

84. Section 112 of the patent law provides that "[t]he specification shall contain a written description of the invention . . ." 35 U.S.C. § 112, ¶1.

85. "The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not; the applicant for a patent is therefore required to 'recount his invention in such detail that his future claims can be determined to be encompassed within his original creation.'" *Amgen, Inc. v. Hoechst Marion Roussel,* 314 F.3d 1313, 1330 (Fed. Cir. 2003), (quoting *Vas-Cath Inc. v. Mahurkar,* 935 F.2d 1555, 1561 (Fed. Cir. 1991) (citation omitted)).

86. "[I]t is in the patent specification where the written description requirement must be met." *Univ. of Rochester v. G.D. Searle & Co.,* 358 F.3d 916, 927 (Fed. Cir. 2004).

87. "Application of the written description requirement . . . is not subsumed by the 'possession' inquiry. A showing of 'possession' is ancillary to the ***statutory*** mandate that '[t]he specification shall contain a written description of the invention,' and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 969 (Fed. Cir. 2002) (emphasis in original)

88. Compliance with the written description requirement is determined as of the filing date of the application upon which the patentees relies. *TurboCare Div. of Demag Delaval Turbomachinery Corp. v. GE,* 264 F.3d 1111, 1118 (Fed. Cir. 2001).

89. Although a patent specification may render the claimed invention obvious, that disclosure "is not sufficient to satisfy the written description requirement of that invention." *Regents of Univ. of Cal. v. Eli Lilly & Co,* 119 F.3d 1559, 1567 (Fed. Cir. 1997) (*citing Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572 (Fed. Cir. 1997)).

90. The description of a single species within a claimed genus may not be sufficient to support patentability under § 112, ¶1. *Regents of Univ. of Cal. v. Eli Lilly & Co,* 119 F.3d 1559, 1567 (Fed. Cir. 1997).

91. Just because a patentee has isolated and physically possessed a protein does not amount to knowledge of that protein's amino acid sequence or possession of any of its other descriptive properties. *See In re Wallach*, 378 F.3d 1330, 1334-35 (Fed. Cir. 2004).

92. For purposes of written description claims to polypeptides encoded by particular DNA sequences are limited to the known polypeptide products of that DNA at the time of filing. Polypeptides unknown at the time of filing constitute new matter unsupported by the specification. *See Schering Corp. v. Amgen Inc.*, 222 F.3d 1347, 1354 (Fed. Cir. 2000).

B. Lack of Enablement

93. The test for enablement is whether one reasonably skilled in the art could make or use the invention based on the written disclosures of the patent coupled with information known in the art, without undue experimentation. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999).

94. "In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970).

95. The Federal Circuit has found that claims lacked enablement when the patent's specification taught only how to approximate the claimed result. Donald S. Chisum, (2007) Chisum on Patents, Vol. 3, § 7.03(4)(b); *see Nat'l Recovery Techs., Inc. v. Magnetic Separations Sys., Inc.*, 166 F.3d 1190, 1196-98 (Fed. Cir. 1999) (holding that although the patent specification disclosed a method for detecting signals this method was insufficient to select signals as claimed).

96. For purposes of enablement, whether the experimentation required to make and use a claimed invention is undue depends on considerations including "'(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.'" *Warner-Lambert Co. v. Teva Pharmaceuticals USA, Inc.* 418 F.3d 1326, 1337 (Fed. Cir. 2005) (*quoting In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)).

C. Indefiniteness

97. "The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112, ¶2.

98. Failure to particularly point out and distinctly claim an invention renders the claim invalid. *Default Proof Credit Card Sys., Inc. v. Home Depot U.S.A., Inc.*, 412 F.3d 1291, 1298 (Fed. Cir. 2005).

99. "The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested [persons] . . . can determine whether or not they infringe." *Default Proof Credit Card Sys., Inc. v. Home Depot U.S.A., Inc.*, 412 F.3d 1291, 1302-03 (Fed. Cir. 2005) (*quoting All Dental Prodx, LLC. v. Advantage Dental Products, Inc.*, 309 F.3d 774, 779-80 (Fed. Cir. 2002).

100. "In determining whether [a] claim is sufficiently definite, [a court] must analyze whether 'one skilled in the art would understand the bounds of the claim when read in light of the specification.'" *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1348 (Fed. Cir. 2002) (quoting *Personalized Media Commc'ns, LLC v. ITC*, 161 F.3d 696, 705 (Fed. Cir. 1998)).

101. Indefiniteness often arises when the claim language is "not sufficiently precise to permit a potential competitor to determine whether or not he is infringing." *Morton Int'l. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470 (Fed. Cir. 1993); *Semmler v. American Honda Motor Co., Inc.*, 990 F. Supp. 967, 975 (S.D. Ohio 1997); *Halliburton Energy Servs., Inc. v. M-I, LLC*, 456 F. Supp. 2d 811, 817 (E.D. Tex. 2006).

III. Invalidity for Double Patenting

102. "The public should ... be able to act on the assumption that upon the *expiration* of the patent it will be free to use not only the invention claimed in the patent but also modifications or variants which would have been *obvious* to those of ordinary skill in the art at the time the invention was made, taking into account the skill of the art and prior art other than the invention claimed in the issued patent." *In re Longi*, 759 F.2d 887, 892-893 (Fed. Cir. 1985) (emphasis in original) (quoting *In re Zickendraht*, 319 F.2d 225, 232, 50 C.C.P.A. 1529, 1536, 138 USPQ 23, 27 (1963) (Rich, J., concurring)).

103. The judicially created doctrine of obviousness-type double patenting prevents extension of patent rights beyond their terms by barring claims that are different, but not patentably distinct, from claims in an earlier-issued, commonly owned patent. *In re Longi*, 759 F.2d 887, 892 (Fed. Cir. 1985).

104. A two step analysis is employed. First, the court construes the claims in the earlier- and later-issued patents and compares them for any differences; second,

the court decides whether there are any differences that rise to the level of a patentable distinction; if the later claim is not patentably distinct from the earlier claim, then it is invalid. *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001).

105. A claim is not patentably distinct from an earlier claim if it is merely an obvious variation of the earlier claim from the point of view of one of ordinary skill in the art. *Application of Vogel*, 422 F.2d 438, 441-42 (CCPA 1970).

106. Courts equate the second part of the obviousness-type double patenting analysis to that performed under 35 U.S.C. § 103 obviousness. *In re Longi*, 759 F.2d 887, 892 n.4 (Fed. Cir. 1985); MPEP § 804 (5th ed. Rev. 8, May 1998); MPEP § 804 (8th ed. Rev. 5, Aug. 2006)..

107. That claims in a later-issued patent are in a different class from the earlier issued claims does not provide a patentable distinction under obviousness-type double patenting. Thus claims directed to methods of using a composition can be obvious in light of claims directed to the composition (*see, e.g., Geneva Pharm., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1385-86 (Fed. Cir. 2003); *In re Lonardo*, 119 F.3d 960, 964-65 (Fed. Cir. 1997)); claims directed to a product can be obvious in light of claims directed to producing the product (*see, e.g., In re Freeman*, 166 F.2d 178, 180 (CCPA 1948)) and claims directed to a composition can be obvious in light of claims directed to a method of using the composition (*see, e.g., Research Corp. Techs., Inc. v. Gensia Labs., Inc.*, 10 Fed. Appx. 856, 863-64 (Fed. Cir. 2001)).

108. "[D]isputes 'about the characterization of the relation between the two claims' in a double patenting context [such as species/genus relationship or element/combination relationship] are irrelevant. ...'[T]he critical inquiry remains whether the claims .... define an obvious variation of the invention claimed in the [prior patent].'" *In re Metoprolol Succinate Patent Litigation*, 2007 WL 2080390, *5 (Fed. Cir. 2006) (*citing In re Emert*, 124 F.3d 1458, 1461-62 (Fed. Cir. 1997).

109. A claim to a pharmaceutical composition comprising an active compound and other components may render invalid by obviousness double patenting a later issued commonly owned claim to the active compound itself when it is obvious to omit the other components. *In re Metoprolol Succinate Patent Litigation*, 2007 WL 2080390, *7 (Fed. Cir. 2006).

110. The two-way test for double patenting is limited to circumstances "when the applicants filed first for a basic invention and later for an improvement, but, though no fault of the applicants, the PTO decided the applications in reverse order of filing..." *In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998).

111. The two-way test applies only where the patent holder could not have avoided separate filings, and, even then, only where the PTO was solely responsible for the fact that the later-filed claims issued first. *In re Berg,* 140 F.3d 1428, 1435, 1437 (Fed. Cir. 1998).

112. Claims in a divisional application may be immune from an obviousness-type double patenting rejection when the claims were elected in a restriction requirement. 35 U.S.C. § 121.

113. In order to obtain the protection of Section 121, consonance must exist between the earlier restriction requirement and the claims later prosecuted, *i.e.*, the applicant's actions must be consistent with the initial restriction requirement dividing groups of claims into distinct categories. *Gerber Garment Tech., Inc. v. Lectra Sys., Inc.*, 916 F.2d 683, 688 (Fed. Cir. 1990); *Bristol-Myers Squibb Co. v. Pharmachemie B.V.*, 361 F.3d 1343, 1348 (Fed. Cir. 2004); *Geneva Pharms., Inc. v. Glaxosmithkline PLC*, 349 F.3d 1373, 1381 (Fed. Cir. 2003).

114. "Consonance requires that the line of demarcation between 'independent and distinct inventions' that prompted the restriction requirement be maintained ... Where that line is crossed the prohibition of the third sentence of Section 121 does not apply." *Gerber Garment Tech., Inc. v. Lectra Sys., Inc.*, 916 F.2d 683, 688 (Fed. Cir. 1990).

115. It is the patentee's burden to show the protections of 35 U.S.C. § 121 apply by establishing a "clear demarcation between restricted subject matter to allow determination that claims in continuing applications are consonant and therefore deserving of § 121 's protections." *Geneva Pharms., Inc. v. Glaxosmithkline PLC*, 349 F.3d 1373, 1381 (Fed. Cir. 2003) ("GSK does not meet its burden to show that the record provides a clear demarcation of the allegedly restricted subject matter").

IV. 35 U.S.C. § 103(b)

116. "Notwithstanding [35 U.S.C. § 103] subsection (a), and upon timely election by the applicant for patent to proceed under this subsection, a biotechnological process using or resulting in a composition of matter that is novel under section 102 and nonobvious under subsection (a) of this section shall be considered nonobvious if--

(A) claims to the process and the composition of matter are contained in either the same application for patent or in separate applications having the same effective filing date; and

(B) the composition of matter, and the process at the time it was invented, were owned by the same person or subject to an obligation of assignment to the same person.

(2) A patent issued on a process under paragraph (1)--

(A) shall also contain the claims to the composition of matter used in or made by that process, or

(B) shall, if such composition of matter is claimed in another patent, be set to expire on the same date as such other patent, notwithstanding section 154.

(3) For purposes of paragraph (1), the term "biotechnological process" means--

(A) a process of genetically altering or otherwise inducing a single- or multi-celled organism to--

(i) express an exogenous nucleotide sequence,

(ii) inhibit, eliminate, augment, or alter expression of an endogenous nucleotide sequence, or

(iii) express a specific physiological characteristic not naturally associated with said organism;

(B) cell fusion procedures yielding a cell line that expresses a specific protein, such as a monoclonal antibody; and

(C) a method of using a product produced by a process defined by subparagraph (A) or (B), or a combination of subparagraphs (A) and (B)." 35 U.S.C. § 103(b)

117. "If there are two different patents issued for the composition of matter and for the biotechnological process claims relating to the composition of matter, the process patent must expire on the same date as the patent on the composition of matter, notwithstanding the statutory patent term set pursuant to 35 U.S.C. section 154." H. Rep. No. 104-178, at 9 (1995), *as reported in* 1995 U.S.C.C.A.N. 395, 403.

118. "[D]ependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. Notwithstanding the preceding sentence, if a claim to a composition of matter is held invalid and that claim was the basis of a determination of nonobviousness under section 103(b)(1), the process shall no longer be considered nonobvious solely on the basis of section 103(b)(1)." 35 U.S.C. § 282.

V. Non-infringement

119. Amgen bears the burden of proving infringement. *Ultra-Tex Surfaces, Inc. v. Hill Bros. Chemical Co.*, 204 F.3d 1360, 1364 (Fed. Cir. 2000).

120. Whether Roche's activities in the United States with respect to MIRCERA™ are reasonably related to the development and submission of information to the FDA. 35 U.S.C. §271(e)(1); *Integra Lifesciences I, Ltd. v. Merck KGaA*, 2007 WL 2142878, *3-5 (Fed. Cir. 2007); *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 195-96 (2005).

121. The §271(e)(1) safe harbor "necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process." *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 202 (2005).

122. The §271(e)(1) safe harbor does not categorically exclude "(1) experimentation on drugs that are not ultimately the subject of an FDA submission or (2) use of patented compounds in experiments that are not ultimately submitted to the FDA. ...[I]f it was reasonable to believe that the compound under study may work in the intended use and that the experiments will produce the types of information that are relevant to [a new drug application], then the FDA Exemption applies to studies that are appropriate for submission." *Integra Lifesciences I, Ltd. v. Merck KGaA*, 2007 WL 2142878, *5 (Fed. Cir. 2007).

123. "To establish liability under section 271(b), a patent holder must prove that once the defendants knew of the patent, they 'actively and knowingly aid[ed] and abett[ed] another's direct infringement.'" *DSU Medical Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1305 (Fed. Cir. 2006) (en banc) (quoting *Water Technologies Corp. v. Calco, Ltd.*, 850 F.2d 660, 668 (Fed.Cir.1988).

124. The patentee bears the burden of showing that an alleged infringer's actions "induced infringing acts and that he knew or should have known his actions would induce actual infringements." *DSU Medical Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1304 (Fed. Cir. 2006); *Manville Sales Corp. v. Paramount Systems, Inc.*, 917 F.2d 544, 553 (Fed. Cir. 1990).

125. "[T]he intent requirement for inducement requires more than just intent to cause the acts that produce direct infringement. Beyond that threshold knowledge, the inducer must have an affirmative intent to cause direct infringement. ... inducement requires 'that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement.'" *DSU Medical Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006) (internal citations omitted) (*quoting MEMC Elec. Materials, Inc. v. Mitsubishi Materials Silicon Corp.*, 420 F.3d 1369, 1378 (Fed. Cir. 2005); *Minn. Mining & Mfg. Co. v. Chemque, Inc.*, 303 F.3d 1294, 1304-05 (Fed. Cir. 2002)).

126. "Accordingly, inducement requires evidence of culpable conduct, directed to encouraging another's infringement, not merely that the inducer had knowledge of the direct infringer's activities." *DSU Medical Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006); *Metro-Goldwyn-Mayer Studios, Inc. v. Grokster, Ltd.*, 545 U.S. 913, 937 (2005); *Manville Sales Corp. v. Paramount Systems, Inc.*, 917 F.2d 544, 553 (Fed. Cir. 1990).

127. A finding that an alleged infringer did not believe they infringed, based on evidence such as opinion of counsel, may negate the intent finding necessary for inducement of infringement. *See*, *DSU Medical Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1307 (Fed. Cir. 2006).

A. Literal Non-Infringement

128. Whether CERA or MIRCERA™ embodies each and every element of the asserted product claims of the '422 and/or '933 patent. *Terlep v. Brinkmann Corp.*, 418 F.3d 1379, 1384 (Fed. Cir. 2005); *Mass. Inst. of Tech. v. Lockheed Martin Global Telecomms., Inc.*, 251 F. Supp. 2d 1006, 1010 (D. Mass. 2003).

129. Whether the administration of MIRCERA™ to patients in the United States would practice each and every element of the asserted method claims of the '933 patent. *Terlep v. Brinkmann Corp.*, 418 F.3d 1379, 1384 (Fed. Cir. 2005); *Mass. Inst. of Tech. v. Lockheed Martin Global Telecomms., Inc.*, 251 F. Supp. 2d 1006, 1010 (D. Mass. 2003)

130. Whether the process by which CERA or MIRCERA™ is manufactured embodies each and every element of the asserted process claims of the '868, '698 and/or '349 patent(s). *Terlep v. Brinkmann Corp.*, 418 F.3d 1379, 1384 (Fed. Cir. 2005); *Mass. Inst. of Tech. v. Lockheed Martin Global Telecomms., Inc.*, 251 F. Supp. 2d 1006, 1010 (D. Mass. 2003)

131. It is error, for purposes of the infringement analysis, to compare CERA or MIRCERA™ or their methods of manufacture with Amgen's commercial embodiment or other version of the products or processes of the asserted claims; the only proper comparison is with the claims of the patents. *See Zenith Labs., Inc. v. Bristol-Myers Squibb Co.*, 19 F.3d 1418, 1423 (Fed. Cir. 1994).

132. A claim to a chemical composition does not cover reaction products of ingredients not recited in the claim. *See Exxon Chem. Patents, Inc. v. Lubrizol Corp.*, 64 F.3d 1553, 1557-58 (Fed. Cir. 1995).

133. A chemical substitution is a change that results in a new compound. *See Eli Lilly & Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1573 (Fed. Cir. 1996).

134. A claim to a chemical composition that does not refer to possible substitutions for a particular chemical group does not cover a chemical composition possessing a substitution in that chemical group. *See Dow Agrosciences LLC v. Crompton Corp.*, 381 F. Supp. 2d 826, 833 (S.D. Ind. 2005), *aff'd*, 182 Fed. Appx. 978 (Fed. Cir. 2006).

135. In order to infringe a product by process claim, the accused product must possess the same material structural and functional characteristics as the claimed product by process. *See Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565, 1580 (Fed. Cir. 1991).

136. "[P]rocess terms in product-by-process claims serve as limitations in determining infringement." *See Atlantic Thermoplastics Co., Inc. v. Faytex Corp.*, 970 F.2d 834, 846-47 (Fed. Cir. 1992).

137. Prior holdings and findings preclude Amgen from arguing that the EPO products claimed in the patents-in-suit differ structurally from naturally-occurring EPO. For issue preclusion to apply, the following requirements must be met: (1) both proceedings involved the same issue of law or fact; (2) the parties actually litigated the issue in the prior proceeding; (3) the first court actually resolved the issue in a final and binding judgment; and (4) its resolution of that issue of law or fact was essential to its judgment. *See Global Naps, Inc. v. Mass. Dept. of Telecomm. and Energy*, 427 F.3d 34, 44 (1st Cir. 2005).

138. Collateral estoppel or issue preclusion may apply to claims of a patent not litigated in the prior determination. "It is the issues litigated, not the specific claims around which the issues were framed, that is determinative." *See Westwood Chemical, Inc. v. U. S.*, 525 F.2d 1367, 1372, 207 Ct.Cl. 791 (1975), *see also South Corp. v. United States*, 690 F. 2d 1368 (Fed. Cir. 1982) (adopting the decisions of predecessor courts including the United States Court of Claims and the United States Court of Customs and Patent Appeals, as binding precedent).

139. "A Markush group is a listing of specified alternatives of a group typically expressed in the form: 'a member selected from the group consisting of A, B, and C.'" However, claim language in the format 'A, B, C, or D' is equally acceptable for Markush claiming. *Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 334 F.3d 1274, 1280 (Fed. Cir. 2003)

140. A Markush group is a claim that is "closed, i.e., it must be characterized with the transition phrase 'consisting of' rather than 'comprising' or 'including.'" "Thus 'members of the Markush group are used <u>singly</u>.'" *Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 334 F.3d 1274, 1280-1281 (Fed. Cir. 2003) (internal citations omitted).

141. "If a patentee desires mixtures or combinations of the members of the Markush group, the patentee would need to add qualifying language while drafting the claim ... such as: 'and mixtures thereof' and 'at least one member of the group.' ... '[W]ithout expressly indicating the selection of multiple members of a Markush grouping, a patentee does not claim anything other than the plain reading of the closed claim language. *Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 334 F.3d 1274, 1281 (Fed. Cir. 2003) (internal citations omitted).

B. Material Change Under 35 U.S.C. § 271(g)

142. Amgen bears the burden of proof on the issue of material change under 35 U.S.C. § 271(g). *Genentech, Inc. v. Boehringer Mannheim GmbH*, 47 F. Supp. 2d 91, 108 (D. Mass. 1999).

143. "[§ 271(g)] permits the importation of an item that is derived from a product made by a patented process as long as that product is 'materially changed' in the course of its conversion into the imported item." *Eli Lilly & Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1572 (Fed. Cir. 1996)

144. To determine whether an imported product is "materially changed," one must look to the substantiality of the change between the product of the patented process and the imported product. *See Eli Lilly & Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1573 (Fed. Cir. 1996); *Genentech, Inc. v. Boehringer Mannheim GmbH*, 47 F. Supp. 2d 91, 107 (D. Mass 1999); *Eli Lilly & Co. v. American Cyanamid Co.*, 896 F. Supp. 851, 856 (S.D.Ind. 1995).

145. "In the chemical context, a 'material' change in a compound is most naturally viewed as a significant change in the compound's structure and properties." *Eli Lilly & Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1573 (Fed. Cir. 1996)

146. A finding that subsequent processes confer an additional, distinct, and valuable property to the product of a patented process supports a finding of material change. *See Eli Lilly & Co. v. American Cyanamid Co*., 66 F. Supp. 2d 924, 932 (S.D. Ind. 1999)

147. A finding that subsequent processes confer superior properties relating to the basic utility of the product of the patented process, *e.g.* increased potency, supports a finding of material change. *See Eli Lilly & Co. v. American Cyanamid Co*., 66 F. Supp. 2d 924, 932 (S.D. Ind. 1999)

148. A finding that subsequent processes confer significant structural differences to the product of the patented processes such as the removal and/or addition of certain chemical groups of a compound supports a finding of material change. *See Eli Lilly & Co. v. American Cyanamid Co*., 66 F. Supp. 2d 924, 932 (S.D. Ind. 1999)

149. A finding that subsequent processes applied to the product of a patented process are complex and involve multiple steps supports a finding of material change. *See Eli Lilly & Co. v. American Cyanamid Co.*, 66 F. Supp. 2d 924, 932 (S.D. Ind. 1999)

150. That the individual steps of the subsequent processes administered to the product of a patented process involve relatively routine chemical reactions does not preclude a finding of material change. *See Eli Lilly & Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1572-73 (Fed. Cir. 1996).

C. Doctrine of Equivalents

151. A patentee may invoke the doctrine of equivalents "to proceed against the producer of a [product] 'if it performs substantially the same function in substantially the same way to obtain the same result'" as the claimed invention. *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 608 (1950).

152. For purposes of the doctrine of equivalents, equivalency must be proven on a limitation-by-limitation basis. *Texas Instruments Inc. v. Cypress Semiconductor Corp.*, 90 F.3d 1558, 1566 (Fed. Cir. 1996); *Pennwalt Corp. v. Durand-Wayland, Inc.*, 833 F.2d 931, 935 (Fed. Cir. 1987) (*en banc*), *cert. denied*, 485 U.S. 961 (1988); *Athletic Alternatives, Inc. v. Prince Mfg., Inc.*, 73 F.3d 1573, 1582 (Fed. Cir. 1996).

153. Equivalency must be proven with "particularized testimony and linking argument." *Texas Instruments Inc. v. Cypress Semiconductor Corp.*, 90 F.3d 1558, 1566 (Fed. Cir. 1996); *Lear Siegler, Inc. v. Sealy Mattress Co.*, 873 F.2d 1422, 1426 (Fed. Cir. 1989); *Malta v. Schulmerich Carillons, Inc.*, 952 F.2d 1320, 1324 (Fed.Cir.1991), *cert. denied*, 504 U.S. 974 (1992).

154. "Generalized testimony as to the overall similarity between the claims and the accused infringer's product or process will not suffice" under the doctrine of equivalents. *Texas Instruments Inc. v. Cypress Semiconductor Corp.*, 90 F.3d 1558, 1567 (Fed. Cir. 1996).

155. "The evidence and argument on the doctrine of equivalents cannot merely be subsumed in plaintiff's case of literal infringement." *Lear Siegler, Inc. v. Sealy Mattress Co.*, 873 F.2d 1422, 1425 (Fed. Cir. 1989).

156. For purposes of the doctrine of equivalents, the definition of the "function" of a claimed product cannot be read too broadly to encompass equivalents which impermissibly read on the prior art. *See Genentech, Inc. v. Wellcome Found. Ltd.*, 29 F.3d 1555, 1567-68 (Fed. Cir. 1994).

157. For purposes of the doctrine of equivalents with respect to claims to biological products, reduced binding affinity and increased half-life is evidence that the accused product does not perform substantially the same function in substantially the same way with substantially the same result as the claimed invention. *See Genentech, Inc. v. Wellcome Found. Ltd.*, 29 F.3d 1555 (Fed. Cir. 1994).

158. Application of the doctrine of equivalents may be foreclosed by prosecution history estoppel where the applicant surrenders subject matter embracing the asserted equivalent during the prosecution of the patent, either by a narrowing amendment or argument. *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 30 (1997); *DeMarini Sports, Inc. v. Worth, Inc.*, 239 F.3d 1314, 1332 (Fed. Cir. 2001).

159. "A patentee who narrows a claim as a condition for obtaining a patent disavows his claim to the broader subject matter, whether the amendment was made to avoid the prior art or to comply with Section 112." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 737 (2002).

160. When the prosecution history reveals no reason for the narrowing amendment, a presumption arises that the patentee had a substantial reason relating to patentability. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1366-67 (Fed. Cir. 2003); *Warner Jenkinson Co. v. Hilton Davis Chemical Co.*, 520 U.S. 17, 33 (1997).

161. "Just as ... the patentee bears the burden of proving that an amendment was not made for a reason that would give rise to estoppel, ... the patentee should bear the burden of showing that the amendment does not surrender the particular equivalent in question." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 525 U.S. 722, 740-41 (2002) (internal citations omitted) (*citing Warner Jenkinson Co. v. Hilton Davis Chemical Co.*, 520 U.S. 17 (1997)).

162. When a patentee is found to have surrendered subject matter through a narrowing amendment related to patentability, a presumption of prosecution history estoppel applies which can only be rebutted by the patentee in one of the following "narrow ways": "(i) showing that an equivalent was unforeseeable; (ii) demonstrating that the purpose for an amendment was merely tangential to the alleged equivalent; or (iii) establishing 'some other reason' that the patentee could not have reasonably been expected to have described the alleged equivalent." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1310-11 (Fed. Cir. 2006); (*citing Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 525 U.S. 722, 740-41 (2002)).

163. "[A]n equivalent is foreseeable when the equivalent is known in the pertinent prior art at the time of amendment." For example, where "'the patentee admittedly knew about the ... equivalent at the time of the ... amendment' and

informed the examiner of the equivalent during prosecution" the equivalent was foreseeable. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 2007 WL 1932269, * 7 (Fed. Cir. 2007) (*quoting Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1313 (Fed. Cir. 2006)).

164. The "tangential relation criterion for overcoming the *Festo* presumption is very narrow..." *Cross Medical Prods., Inc. v. Medtronic Sofamor Danek Inc.*, 480 F.3d 1335, 1342 (Fed. Cir. 2007).

165. "'[A]n amendment made to avoid prior art that contains the equivalent in question is not tangential.' ...It does not follow, however, that equivalents not within the prior art must be tangential to the amendment." *Chimie v. PPG Industries, Inc.*, 402 F.3d 1371, 1383 (Fed. Cir. 2005) (*quoting Festo*, 344 F.3d at 1369).

166. "[T]he third way to rebut the *Festo* presumption, the 'some other reason' route, is a narrow one. ... 'the third criterion may be satisfied when there was some reason, such as the shortcomings of language, why the patentee was prevented from describing the alleged equivalent when it narrowed the claim.'" *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1313 (Fed. Cir. 2006); (*quoting Festo*, 344 F.3d at 1370).

D. Reverse Doctrine of Equivalents

167. Even if Amgen's claims are found to be literally infringed, Roche may still avoid infringement under the "reverse" doctrine of equivalents. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F. Supp. 2d 202, 283-303 (D. Mass. 2004).

168. The reverse doctrine of equivalents is a fairness doctrine that may be applied when a product or process is so fundamentally different from the patented invention that a judgment of infringement would constitute an unwarranted extension of the claims beyond a fair scope of the invention. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F. Supp. 2d 202, 283 (D. Mass. 2004).

169. A product or process is fundamentally different if it performs the same or a similar function in a substantially different way. This determination is made by considering the originally intended scope of the patent and the "spirit and intent" of the claims, keeping in mind the particular context of the patent, the prior art, and the particular circumstances of the case. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F. Supp. 2d 202, 284-86 (D. Mass. 2004).

170. A new product or process that uses a new technology that makes a real difference in how the process works or what is produced would not infringe under the reverse doctrine of equivalents. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F. Supp. 2d 202, 301 (D. Mass. 2004).

171. Changes to a drug's biologic or therapeutic effects can be considered a real difference for purposes of the reverse doctrine of equivalents. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc*., 339 F. Supp. 2d 202, 295 (D. Mass. 2004).

172. A prima facie case of reverse doctrine of equivalents exists where the alleged infringer has patent on the accused product or process. *Jewish Hosp. of St. Louis v. IDEXX Labs.*, 973 F. Supp. 24, 28 (D. Me. 1997).

173. "The reverse doctrine of equivalents protects the accused infringer when 'a product precisely described in a patent claim is in *fact* so *far* changed in principle that it performs in a *substantially different way* and is not therefore an appropriation.'" *Union Carbide Corp. v. Tarancon Corp.,* 682 F. Supp. 535, 541 (N.D. Ga. 1988).

174. "The doctrine of equivalents may also be applied in reverse, so that 'where a device is so far changed in principle from a patented article that it performs the same or a similar function in a substantially different manner, but nevertheless falls within the literal words of the patent,' no infringement will be found." *Precision Metal Fabricators, Inc. v. Jetstream Sys. Co., Div. of Oerlikon Motch Corp.*, 693 F. Supp. 814, 819 (N.D. Cal. 1988), quoting *Graver Mfg. Co v. Linde Co.*, 339 U.S. 605, 608-09 (1949).

175. "It is fundamental that the language of patent claims cannot be stretched to include products and processes essentially unlike those described by the patent." *Brenner v. Recognition Equip. Inc.*, 593 F. Supp. 1275, 1278 (S.D.N.Y. 1984).

VI. Unenforceability for Inequitable Conduct

176. Inequitable conduct occurs when a patent applicant breaches his or her "duty of candor and good faith" to the PTO. 37 C.F.R. § 1.56(a); *Bruno Indep. Living Aids, Inc. v. Acorn Mobility Servs., Ltd.*, 394 F.3d 1348, 1351 (Fed. Cir. 2005).

177. The duty of good faith and candor "is broader than the duty to disclose material information." Manual of Patent Examining Procedure ("MPEP") § 2001.04 (5th ed. Rev. 14, Nov. 1992); MPEP § 2001.04 (8th ed. Rev. 5, Aug. 2006); *Rohm & Haas Co. v. Crystal Chem. Co.*, 722 F.2d 1556, 1571 (Fed. Cir. 1983) ("Surely, a very important policy consideration is to discourage all manner of dishonest conduct in dealing with the PTO.").

178. Duty of good faith and candor "is not done by one who knowingly takes advantage of an error by the PTO." *KangaROOS U.S.A., Inc. v. Caldor, Inc*., 778 F.2d 1571, 1576 (Fed. Cir. 1985).

179. Mere submission of information is not a defense against inequitable conduct where an applicant buries material information or presents the information in a

manner so that the examiner would be likely to ignore it and permit the application to issue as a patent. *See eSpeed Inc. v. BrokerTec USA LLC*, 417 F. Supp. 2d 580, 598 (D. Del. 2006) *aff'd*, 480 F.3d 1129 (Fed. Cir. 2007) (inequitable conduct where information was buried in declarations and exhibits of over two thousand pages and "not pointed out to the examiner"); *Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1184 (Fed. Cir. 1995)("'[B]urying' a particularly material reference in a prior art statement containing a multiplicity of other references can be probative of bad faith."); *Golden Valley Microwave Foods Inc. v. Weaver Popcorn Co., Inc.*, 837 F. Supp. 1444 (N.D. Ind. 1992) *aff'd*, 11 F.3d 1072 (Fed.Cir. 1993) ("it is likewise a violation of the duty of candor and fair dealing with the Patent Office for an applicant or its attorney to disclose a pertinent prior art patent reference to the examiner in such a way as to 'bury' it ... so that the examiner would be likely to ignore the entire list and permit the application to issue."); MPEP § 2002.03 (5th ed. Rev. 3, May 1986) ("non-identification of an especially relevant passage buried in an otherwise less or non-relevant text could result in a holding of 'violation of duty of disclosure'"); *see also* MPEP § 2001.04 (8th ed. Rev. 5, Aug. 2006).

180. An applicant must disclose material information directly to the examiner to discharge the duty of good faith and candor and the duty of disclosure. See 37 CFR 1.4(b) ("Since each file must be complete in itself, a separate copy of every paper to be filed in a patent application, patent file, or other proceeding must be furnished for each file to which the paper pertains, even though the contents of the papers filed in two or more files may be identical."); 37 CFR 1.4(c) ("Since different matters may be considered by different branches or sections of the United States Patent and Trademark Office, each distinct subject, inquiry or order must be contained in a separate paper to avoid confusion and delay in answering papers dealing with different subjects.").

181. Before 1992 relevant information could be submitted by a either an information disclosure statement or through other communications with the examiner; however, information "incorporated into other communications to be considered by the examiner... shall be accompanied by explanations of relevance" and "a statement explaining why the information was not earlier submitted." MPEP §609(4) (5th ed. Rev. 8, May 1988); *see also* MPEP § 609 (8th ed. Rev. 5, Aug. 2006).

182. By 1992, "in order to have information considered by the Office during the pendency of a patent application, an information disclosure statement in compliance with 37 CFR 1.98 as to content must be filed in accordance with the procedural requirements of CFR 1.97." E.g. MPEP §609 (5th ed. Rev.14, Nov. 1992); MPEP §609 (8th ed. Rev. 5, Aug. 2001) ("In order to have information considered by the Office during the pendency of a patent application, an information disclosure statement must be (1) in compliance with the content

requirements of 37 CFR 1.98 and (2) filed in accordance with the procedural requirements of 37 CFR 1.97.").

183. To discharge the applicant's duty of disclosure, 37 CFR 1.98 mandates that a listing of a publication, in order to be considered by the examiner, "must be identified by publisher, author (if any), title, relevant pages of the publication, date and place of publication" in a separate paper. *See IDEC Pharms. v. Corixa Corp.*, 2003 WL 24147449, *11 (S.D. Cal. 2003)(unpublished); 37 C.F.R. § 1.98(b); MPEP §609 (5th ed. Rev. 14, Nov. 1992) ("A separate list is required ..."); MPEP §609 (8th ed. Rev. 5, Aug. 2006).

184. The Federal Circuit has made clear that materiality is correctly judged under the broader "reasonable examiner" standard as well as 37 CFR 1.56 previously applied by this Court. *Digital Control, Inc. v. Charles Machine Works*, 437 F.3d 1309, 1316 (Fed. Cir. 2006).

185. Under the broader reasonable examiner standard, information is material where there is a likelihood that a reasonable examiner would consider it important in deciding whether to allow the application to issue as a patent. *Li Second Family Ltd. Partnership v. Toshiba Corp*., 231 F.3d 1373, 1379 (Fed. Cir. 2000).

186. Thus, information is material even if disclosure would not have rendered the invention unpatentable. *Digital Control Inc. v. Charles Machine Works*, 437 F.3d 1309, 1318 (Fed. Cir. 2006); *Agfa Corp. v. Creo Products Inc.*, 451 F.3d 1366, 1373 (Fed. Cir. 2006) ("under the reasonable examiner standard, material prior art need not necessarily present a prima facie case of unpatentability.").

187. A reference that "explicitly and clearly" discloses limitations also found in submitted prior art is not cumulative. *See McKesson Info. Solutions, Inc. v. Bridge Med., Inc*., 487 F.3d 897, 909 (Fed. Cir. 2007).

188. With respect to rejections in co-pending applications "a showing of substantial similarity is *sufficient* to prove materiality. It does not follow, however, that a showing of substantial similarity is *necessary* to prove materiality." *McKesson Info. Solutions, Inc. v. Bridge Med., Inc.*, 487 F.3d 897, 919 (Fed. Cir. 2007).

189. "An examiner's reliance on a prior art reference in a related prosecution supports a finding of materiality" and "[a]n adverse decision by another examiner, therefore, meets the materiality, standard." *McKesson Info. Solutions, Inc. v. Bridge Med., Inc.*, 2006 WL 1652518, *10, *16 (E.D.Cal. 2006) aff'd, 487 F.3d 897 (Fed. Cir. 2007).

190. "Although examiners are not bound to follow other examiners interpretations, knowledge of a potentially different interpretation is clearly information that an

examiner could consider important when examining an application." *McKesson Info. Solutions, Inc. v. Bridge Med., Inc.*, 487 F.3d 897, 919 (Fed. Cir. 2007)

191. Arguments made by an attorney that are knowingly false breaches the duty of candor afforded the Patent Office. *See Li Second Family Ltd. Partnership v. Toshiba Corp*., 231 F.3d 1373, 1379 (Fed. Cir. 2000) (patentee's repeated arguments to Examiner that claims were entitled to benefit of earlier filing dates constituted "affirmative misrepresentation"); *A.B. Dick Co. v. Burroughs Corp*., 617 F. Supp. 1382, 1393 (N.D. Ill. 1985) (counsel's argument regarding relevance was "affirmatively misleading representation" cutting in favor of a finding of inequitable conduct); *Semiconductor Energy Lab., Co. v. Samsung Elecs. Co.*, 24 F. Supp.2d 537, 542 (E.D. Va. 1998) ("where, as here, material misrepresentations are made in a position advocated to the PTO with intent to mislead, inequitable conduct does exist"), *aff'd* 204 F.3d 1368 (Fed. Cir. 2000).

192. Concealing a best mode is particularly egregious misconduct because an examiner necessarily relies on disclosure from the applicant. *Consol. Aluminum Corp. v. Foseco Int'l, Ltd.*, 910 F.2d 804, 809 (Fed. Cir. 1990) (finding inequitable conduct due to intentional concealment of the best mode); MPEP §2004 (5th ed. Rev. 3, May 1986), MPEP §2004 (8th ed. Rev. 5, Aug. 2006).

193. "There is no requirement that intent to deceive be proven by direct evidence; in fact, it is rarely proven by such evidence." *eSpeed, Inc. v. BrokerTec USA, L.L.C.*, 480 F.3d 1129, 1138 (Fed. Cir. 2007).

194. Intent to deceive may be "inferred from the facts and circumstances surrounding the applicant's overall conduct." *eSpeed Inc. v. BrokerTec USA LLC*, 480 F.3d 1129, 1138 (Fed. Cir. 2007).

195. The finder of fact must consider all factors supporting intent, and a general denial will not negate a finding of intent. *Critikon, Inc. v. Becton Dickinson Vascular Access, Inc.*, 120 F.3d 1253, 1257 (Fed. Cir. 1997) (a "mere denial of intent (which would defeat every effort to establish inequitable conduct) will not suffice").

196. By submitting a Petition to Make Special, an applicant induces the examiner's reliance on representations regarding the prior art. *General Electro Music Corp. v. Samick Music Corp*., 19 F.3d 1405, 1407 (Fed. Cir. 1994).

197. The materiality of a reference may lead to an inference of intent (*Bruno Indep. Living Aids, Inc. v. Acorn Mobility Servs., Ltd*., 394 F.3d 1348 (Fed. Cir. 2005) ("in the absence of a credible explanation, intent to deceive is generally inferred from the facts and circumstances surrounding a knowing failure to disclose material information."); *Cargill, Inc. v. Canbra Foods, Ltd*., 476 F.3d 1359,1367 (Fed. Cir. 2007) ("We have never held that materiality is irrelevant to the question

of intent") especially where the applicant knew, or should have known, of the materiality. *Brasseler, U.S.A. I., L.P. v. Stryker Sales Corp.*, 267 F.3d 1370, 1376 (Fed. Cir. 2001).

198. An inference of intent to deceive is supported by evidence that applicant could not have made patentability argument had information been disclosed. *LaBounty Mfg., Inc. v. United States ITC*, 958 F.2d 1066, 1076 (Fed. Cir. 1992); *Agfa Corp. v. Creo Prods. Inc.*, 451 F.3d 1366, 1379 (Fed. Cir. 2006); *GFI, Inc. v. Franklin Corp.*, 265 F.3d 1268, 1275 (Fed. Cir. 2001).

199. An inference of intent is supported by evidence that the patentee submitted material information to other entities, such as FDA. *See Bruno Indep. Living Aids, Inc. v. Acorn Mobility Servs., Ltd.*, 394 F.3d 1348, 1354 (Fed. Cir. 2005); *Merck & Co., Inc. v. Danbury Pharmacal, Inc.*, 873 F.2d 1418, 1422 (Fed. Cir. 1989).

200. Burying material information also supports intent to deceive. *Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1184 (Fed. Cir. 1995)("'[B]urying' a particularly material reference in a prior art statement containing a multiplicity of other references can be probative of bad faith."); *eSpeed, Inc. v. BrokerTec USA, L.L.C.*, 417 F. Supp. 2d 580, 598 (D. Del. 2006) (the "blizzard of paper is therefore more consistent with an intent to hide than to disclose").

201. With respect to failure to disclose rejections in co-pending applications, intent may be inferred even though the same examiner ultimately issued the patents-in-suit. *McKesson Info. Solutions, Inc. v. Bridge Med., Inc.*, 2006 WL 1652518, *16-*22 (E.D.Cal. 2006); *see also Rohm and Haas Co. v. Crystal Chem. Co.*, 722 F.2d 1556, 1572-73 (Fed. Cir. 1983) (despite interview during prosecution patentee's belief that examiner appreciated information "is irrelevant").

202. "[A] patentee facing a high level of materiality and clear proof that it knew or should have known of that materiality, can expect to find it difficult to establish 'subjective good faith' sufficient to prevent the drawing of an inference of intent to mislead." *Critikon, Inc. v. Becton Dickinson Vascular Access, Inc.*, 120 F.3d 1253, 1257 (Fed. Cir. 1997); *see also, e.g., Cargil,l Inc. v. Canbra Foods, Ltd.*, 476 F.3d 1359, 1366 (Fed. Cir. 2007); *Ferring B.V. v. Barr Laboratories, Inc.*, 437 F.3d 1181, 1191 (Fed. Cir. 2006); *McKesson Info. Solutions, Inc. v. Bridge Med., Inc.*, 487 F.3d 897, 918-19 (Fed. Cir. 2007).

203. "An applicant should know information is material when the examiner repeatedly raises an issue to which the information relates." *Cargill, Inc. v. Canbra Foods, Ltd.*, 476 F.3d 1359, 1366 (Fed. Cir. 2007).

204. That material information does not meet each limitation of a claim does not negate an intent to deceive. *Agfa Corp. v. Creo Prods. Inc.*, 451 F.3d 1366, 1379

(Fed. Cir. 2006) (rejecting no intent based on alleged subjective understanding of claim limitation); *LaBounty Mfg. v. U.S. Int'l Trade Comm.*, 958 F.2d 1066, 1076 (Fed. Cir. 1992) ("Close cases should be resolved by disclosure, not unilaterally by the applicant").

205. Shielding counsel or other individuals with the duty of good faith and candor from learning of the material prior is indicative of intent to deceive. *Novo Nordisk Pharms., Inc. v. Bio-Technology Gen. Corp.*, 424 F.3d 1347, 1361-62 (Fed. Cir. 2005) (rejecting "circular logic" that failure of counsel to disclose facts was excused "because the inventors failed to fully inform them"); *Synthon IP, Inc. v. Pfizer Inc.*, 472 F.Supp.2d 760, 779-80 (E.D. Va. 2007)("Astra cannot benefit from its failure to disclose material information to its United States patent counsel and then hide behind its argument that he acted in good faith and candor."). A patent applicant cannot " cultivate ignorance, or disregard numerous warnings that material information or prior art may exist, merely to avoid actual knowledge of that information or prior art." *FMC Corp. v. Hennessy Industries, Inc.*, 836 F.2d 521, 526 n. 6 (Fed. Cir. 1987).

206. An applicant does not cure his earlier inequitable conduct where the examiner is left "to formulate his own conclusions." *Rohm & Haas Co. v. Crystal Chem. Co.*, 722 F.2d 1556, 1572 (Fed. Cir. 1983).

207. A patent may be rendered unenforceable due to inequitable conduct committed in a related application under the doctrine of "infectious unenforceability." *See Agfa Corp. v. Creo Prods. Inc.*, 451 F.3d 1366, 1379 (Fed. Cir. 2006); *Fox Indus., Inc. v. Structural Preservation Sys., Inc.*, 922 F.2d 801, 803 (Fed. Cir. 1990) (later continuation patents also unenforceable because "tainted" by misconduct).

A complete explanation of Roche's positions on issues of law relevant to invalidity, unenforceability and non-infringement was set forth in its interrogatory responses and expert reports served in this action.